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Developments in the epidemiology of drug-related mortality in the United Kingdom over the last 30 years: continuity, change, consistency, and challenge

A dissertation submitted to the University of Hertfordshire in partial fulfilment of the requirements for the degree of Doctor of Philosophy

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ABSTRACT

This thesis has its roots in and has organically grown out of the author's previous professional civil service roles and academic and related activities associated with drug indicators since 1987. However, the focus of the present work is on providing a description and critical evaluation of developments in the epidemiology of drug-related mortality in the United Kingdom (UK) over the past three decades or so, and how an understanding of that knowledge has been disseminated and impacted policy and practice.

First recognised as a major issue by the Advisory Council on the Misuse of Drugs in its seminal 2000 report, a lot of effort and resources have gone into tackling drug-related mortality. Despite this, the number of deaths rose steeply across the UK up until very recently; however, until the effects of the Covid-19 pandemic on death registrations are known and understood, the apparent levelling off may be an artefact of reporting. The increased numbers of deaths occurred against a background of improvements in case identification, investigation, and reporting - with associated public health and law enforcement initiatives.

As far as the author can establish, there has been no overview or in-depth study of drug-related deaths (DRDs) in the UK and associated issues. Furthermore, there has been no detailed description of the processes underlying how such events have been identified, investigated, recorded, analysed and the information about them disseminated. Moreover, no study of a comprehensive nature has been conducted into what has been occurring, what insights are now available that were non-existent three decades ago, and what uses have been made of that knowledge. The aim of the programme of research reported here was to rectify the lack of knowledge in these areas and to start to fill the deficits and provide a framework for future research.

Relevant chapters contain details of the materials and methods used rather being presented in a discrete methodology chapter. These choices are based on the author's knowledge, experiences, expertise with regard to sources, and the availability of methods. These factors have been influenced by what the author regards as appropriate, feasible and relevant. Given the breadth of the data being investigated, generated, analysed and evaluated, a range of methodologies have been utilised. These draw on a range of disciplines, including: criminology, epidemiology, netnography, pathology, pharmacoepidemiology, pharmacovigilance, sociology, surveillance,

toxicology, and toxicovigilance. The range of methods used include both quantitative and qualitative ones, i.e., a 'mixed methods' approach. Given the specific methods employed, ethics approval was deemed unnecessary by the relevant University of Hertfordshire Ethics Committee with Delegated Authority.

The main text of the thesis comprises five distinct parts with individual chapters looking at specific aspects, as outlined below. Each chapter includes information on the materials and methods used, as well as relevant references for ease of use.

Part 1 provides details of the structure, with Chapter 1 outlining the context of the study in terms of the varied reasons for drug use, the extent and impact of such use, especially the ultimate outcome - death. The research problem and rationale are then presented (as briefly stated above). This is followed by: an explanation of key terms; delimitation of the study's scope, aims and objectives; philosophical and paradigmatic perspectives (epistemology, ontology, axiology, etc.). A brief discussion about materials and methods is presented.

Part 2 focuses on the processes from identification and investigation of DRDs through to dissemination of statistics and other information on these events. Chapter 2 explains the wide variety of terms which are used to describe deaths associated with use of drugs, both direct and indirect. International approaches to defining deaths associated with drug use are outlined and are illustrated using descriptions of different DRD categories. Definitions and classifications of such deaths in the UK context are presented; their uses are summarised. Using a literature review approach, Chapter 3 describes the range of sources relating to information about DRDs and other drug indicators in the UK, together with methods of data generation, curation, and analyses in general terms. Appendix A provides information on the National Programme on Substance Abuse Deaths (NPSAD).

A narrative description is provided, using a literature approach, in Chapter 4 of changes in key areas associated with the investigation and recording of deaths: scene of incident preservation and recording by the police; identification of potential cases on behalf of a Coroner/Medical Examiner or Procurator Fiscal; toxicological investigation; autopsy/postmortem examination; understanding mechanisms of death; recording of substances on Medical Certificates of Cause of Death; International Classification of Diseases (ICD) coding; and counting cases. Central to such processes is toxicology in drug screening, identification, recording, and reporting of deaths. Without accurate and complete information on toxicology being passed to the UK's General Mortality Registers (GMRs), our understanding of the number and nature of drug-related deaths will remain partial and incomplete. Opportunities to address the current identified deficits are examined.

Employing personal knowledge, information from key informants and relevant literature, Chapter 5 presents a chronological narrative description of developments in what has been reported and

published in concerning DRDs, both at the sub-national, national (UK) and international levels. Data collection, analyses, sharing, and dissemination are linked together by the theme of collaboration. The number and range of agencies involved in these activities have increased across the UK. Some exercises were 'one-off' endeavours, whereas others (e.g., Special Mortality Registers (SMRs) such as NPSAD) have evolved and established themselves as 'go-to' places to obtain timely, accurate and detailed information. These resources and their major outputs are described here, together with emerging improvements and recent challenges (e.g., Covid-19).

Part 3 comprises two chapters which present empirically-based detailed epidemiological descriptions, analyses and evaluations of DRDs in the UK. Using a range of in-depth secondary analyses of UK GMR data, Chapter 6 explores the evolution of UK DRDs at a macro level, both at sub-national and UK levels. The key elements investigated include: demographic and other characteristics of those dying of drug-related poisoning; spatial, temporal and geographical characteristics of deaths; changes over time; (toxicological) nature of the drugs involved in deaths; and characteristics of deaths associated with drug poisoning. Where possible, comparisons are made between the constituent parts of the UK; similarities as well as differences are noted and explored.

Data published by the UK GMRs are limited in their ability to provide an in-depth low- or micro- level understanding of all the factors at work in DRDs and the interplay between them. To do this, it is necessary to drill down into the more comprehensive and detailed information available to the SMRs (such as NPSAD and the Scottish Drug-Related Deaths Database). Such an approach facilitates researchers in identifying those groups 'at risk' of a DRD, especially through focusing on key aspects: demographic; social; economic, health (physical and mental); and substances. A series of analyses are presented which demonstrate what sorts of insight can be gained. These analyses are a combination of *ad hoc* literature reviews on specific factors, secondary analyses of existing published GMR data, and reference to relevant studies, using NPSAD and other resources, undertaken by the author and colleagues in the past and for the purposes of this programme of research. These 15 selected studies cover a range of substances and scenarios with which the author was directly involved. His on-going data collection activities and planned outputs are also outlined. Chapter 7 illustrates how low- or micro- level information can give granularity to some of the phenomena described in GMR publications as well as an understanding of other factors to which such sources do not have access. Higher- or macro- level factors influencing DRDs at national (and international) level are considered in Part 4. Such external factors provide the backdrop against which local scenarios are enacted.

Part 4 looks at the statistical inter-relationship(s) between DRDs, using data from the UK GMRs, and other relevant key 'drug indicators' at a population level for the 1990 to 2022 period. The nine main drug indicators cover the following facets: death numbers; price; purity, drug offenders/offences; prevalence of use; availability; treatment for dependence; hospital admissions; and accesses to poison information. For each of these, the specific measures and data sources (including limitations such as availability) are described. The drug classes and specific index substances are listed (see below). A description of the Excel database designed by the author to hold the data is described. This is followed by an explanation of the statistical approach used to for investigate the relationships between indicators, i.e., the Pearson correlation coefficient with two-tailed tests, as employed by the author's previous studies. The correlation coefficient matrices can be found in Appendix F.

Chapter 9 looks at the commonest drug groups implicated in UK DRDs: opiates/opioids (heroin/morphine and methadone) and hypnotics/sedatives (barbiturates and benzodiazepines – especially diazepam and temazepam). The results are accompanied by short commentaries and comparisons with other studies (where they exist) that used the same approach; this applies to the other groups examined. Heroin and morphine are often taken together with benzodiazepines. Indeed, the latter are often a key feature of opiate/opioid related fatalities, but are also part of a polysubstance phenomenon including stimulants. Some clear narratives are provided most of the substances examined in this chapter. However, information for barbiturates is less clear; but this drug class is no longer of concern compared to the past.

Chapter 10 focuses on the main UK stimulants: cocaine, 'crack', amphetamines, 'ecstasy' (MDMA), and mephedrone/synthetic cathinones. The effects of individual stimulants overlap to some extent but there are differences between them and their mode/route of administration. These specific stimulants are often taken together with opiates/opioids and benzodiazepines. Stimulants are part of the polysubstance nature of UK drug-related deaths. Some clear narratives are provided for some of these substances i.e., cocaine/crack and amphetamine, whilst the others warrant further investigation. The paucity of data points across time and a limited range of indicators restricted what investigations could be conducted concerning mephedrone/synthetic cathinones.

The remaining drug classes and index substances are the subject of Chapter 11: cannabinoids (cannabis); anaesthetics/dissociatives (ketamine); Central Nervous System (CNS) depressants (GHB/GBL), and Novel Psychoactive Substances (NPS). Unlike the previous drug classes/index substances, there are no clear-cut narratives to present - even for cannabis. The other drug groups and index drugs considered in this chapter warrant more exploration. Paucity of adequate data points across time and a limited range of indicators restricted what could be said about NPS, and a lack of published figures for England and Wales separately prevented clearer narratives for GHB/GBL and ketamine being presented.

Chapter 12 comprises a brief discussion and summary of the main findings of detailed in Chapters 9 to 11. The statistical relationships between DRDs and eight other drug indicators have been explored using the Pearson correlation coefficient across 15 drug classes/index substances. Clear narratives have been provided for some of these substances (e.g., heroin/morphine, methadone, diazepam, temazepam, cocaine/crack, amphetamine) whilst others merit further investigation (e.g., ecstasy, mephedrone, cannabis, ketamine, GHB/GBL, NPS). The limitations of data availability, accuracy, etc. restricted what analyses could be conducted; see also Chapter 14. The strengths of this type of approach have been demonstrated through these investigations. DRD data can be used together with other drug indicators to provide a more comprehensive and holistic understanding of what higher level or macro factors may play a part in causing or contributing to such deaths, in comparison to local scenarios considered in Chapter 7. The material presented in Part 4 could provide the basis for a monograph or series of individual papers on the main drug groups covered here which would assist in informing policy development, legislation, professional practice, service and treatment provision, etc.

Part 5 comprises two chapters which pull together the various themes that have been described in the earlier parts. Chapter 13 concentrates on the practical uses of DRD data, especially in terms of decision-making in different contexts. It is argued that information from empirical research described in and conducted for this thesis can be used to feed into public health scenarios, inform policy advice and formulation, inform drug control and regulation, develop education, and provide evidence-based professional guidance and practice. This is demonstrated by reference to real-life examples taken from activities in which the author and colleagues have been engaged during the course of his doctoral research programme. Further details are given in Appendices C, D, E and G.

The final chapter (Chapter 14) briefly summarised the findings of the previous ones, draws together the activities described in them, illustrating how the themes examined are complementary and coalescent. It takes a look back at what has happened over the last three decades and what positive developments have occurred or been put in train. Patterns of drug-related deaths in and across the UK over the past three decades are reviewed. An update on the position regarding UK DRDs registered in 2022 is presented. An attempt has been made to see what the future may hold, including: evolving drug scenarios, future information needs; improving the range of information collected and how DRD patterns can be better understood; and ‘horizon scanning’. The conclusions revisit the themes that run through this thesis: continuity, change, consistency, and challenge.

The issues discussed in this thesis, especially those covered in the final chapter, have a resonance with the author's proposed future activities (see Chapters 7 and 13). He aims to take forward and complete the activities undertaken with his recent and present ACMD activities, inform the knowledge-base for the various stakeholders identified earlier in this chapter, and provide a solid basis for dealing with future compounds, contexts, changes, and challenges in a multidisciplinary approach. Drug-related deaths will continue, but better identification of risks and harms will hopefully mitigate such final consequences of substance use.

Overall word count for main text, excluding table contents, references, etc. = 113,890
(Word limit extension granted for up to 120,000 words.)

PREFACE

I have been aware of prescription and illicit drugs for most of my life. I can recall my father, a Senior Charge Nurse, telling my mother in the early 1960s about the barbiturates, especially phenobarbitone, he administered on the night shift to geriatric patients to help them sleep. I can recall that I had ephedrine prescriptions for my asthma. In my late teens I was aware of cannabis and amphetamines ('purple hearts') being used and sold in local pubs and discotheques on the Isle of Wight. I recall my father being offered a cannabis 'reefer' when he took myself aged 16 and one of my younger sisters and her French 'pen-friend' to the Isle of Wight Festival in August 1970! I still have a copy of the student handbook given to me when I was a student at Portsmouth Polytechnic; it had a section devoted to the dangers of the then current recreational drugs - quite far-sighted.

I have been working in research and statistics using drug data, particularly epidemiological data, for over 37 years. For the last three decades or so I have been working as a psychoactive substances' epidemiologist focusing on drugs and, to a lesser extent, volatile substances, alcohol, caffeine and nicotine. Through this work, I have become a nationally and internationally recognised expert on drug-related mortality and drug statistics more widely. The late Professor Griffith Edwards once described me at a 1999 meeting of the Drug-Related Deaths Working Group of the Advisory Council on the Misuse of Drugs as "Mr Drug Stats"; a sobriquet of which I am proud.

Through the various roles I have had over the years, I have gained considerable experience of and insights into these fields. These posts range from the Home Office (Executive Officer, Research Officer, Senior Research Officer), St George's Hospital Medical School (see below), and the University of Hertfordshire (UH), to external roles with the United Kingdom (UK) Focal Point on Drugs, the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), temporary advisor to the World Health Organization and United Nations Office on Drugs & Crime (UNODC), and on various committees and working groups of the UK Advisory Council on the Misuse of Drugs (ACMD) and other advisory bodies.

These experiences mean that I have developed a unique knowledge of UK drugs epidemiological indicators and their generation and uses, including limitations, etc. Some of this information has been disseminated as official government statistical bulletins (i.e., Home Office Statistical

Bulletins and Research Findings 1994 - 2003), as contributions to the UK Focal Point annual reports to the EMCDDA (1994 - 2018), and Home Office reports on behalf of the UK government to the United Nations (1994 - early 2010s).

In addition, I have contributed to EMCDDA and ACMD working groups developing and refining drug-related death definitions and to work by the UK's Office for National Statistics on defining alcohol-related deaths.

My first connection with official drugs data was in 1987 when I was responsible for converting historic datasets (drug treatment, addict fatalities, offences, seizures) from a Home Office in-house format (SDTAB – Statistics Department Tabulations) to a format (TAU) being developed by the Office for National Statistics' (ONS') predecessor agency (the Office for Population Censuses and Surveys), and assisting statisticians in developing computer programs to generate the Home Office statistics on these data, which at the time were the only routine epidemiological data available in the UK on drugs. Later in my Home Office career, I took over responsibility for these statistics (1994-2003), overseeing a move from TAU to SAS to analyse the datasets.

In 1994, I became involved in providing Home Office data on deaths of drug addicts notified to the Home Office Addicts Index to members of the Centre for Addiction Studies (later to evolve into the International Centre for Drug Policy) at St George's Hospital Medical School (now St George's, University of London). Through this connection, I was invited to give lectures on my work to students on taught Diploma and MSc courses in Addictive Behaviour at St George's; these subsequently became regular occurrences and evolved into sessions on substance epidemiology. Subsequently I was made an Honorary Research Fellow, and in January 2001 an Honorary Senior Research Fellow, becoming involved in research on drug-related mortality, publishing academic papers, co-editing international research monographs, etc. However, I think the most important aspect of my connections with St George's was being a prime mover in the establishment of the National Programme on Substance Abuse Deaths (NPSAD) at St George's, following the closure of the Home Office Addicts Index in April 1997. Subsequently, when Department of Health funding was obtained for the Programme, I was persuaded to become the NPSAD Programme Manager, remaining in that capacity until funding for that post ceased in late 2010.

The annual statistical bulletins on the Addicts Index contained information not only on notifications of individuals seeking treatment for drug addictions, drugs used in their treatment, but also loss to treatment - including death. Statistics on the deaths of the notified addicts were presented, together with information on HIV/AIDS deaths caused through injecting drug use. The Home Office also published information (covering the period from 1979) on deaths with an underlying cause described as drug dependence or non-dependent abuse of drugs, based on information from ONS and its Scottish equivalent. In 1996 I managed to get data from Northern Ireland and

was thus the first person to produce UK-wide drug-related deaths statistics. These statistics and information fed into the official reports from the UK to the United Nations and EMCDDA, and I was responsible for preparing the relevant parts of the reports over a couple of decades or so.

These official connections, responsibilities and expertise led to my role as the UK expert on drug-related mortality for the EMCDDA from 2000 to 2015, after which the current Focal Point (based in Public Health England) took this task in-house. However, I continued to provide a consultancy (in a private capacity) to the Focal Point on Northern Ireland deaths for several years. I continue to provide advice to the Vital Statistics section of the National Records of Scotland.

My knowledge of official statistics, especially on addict deaths, led to my appointment as a Home Office official on the ACMD Working Group on drug-related deaths (1998-2000) where I was responsible for overseeing the out-sourced research conducted by ONS. When a new working group on drug-related deaths was established by the ACMD in 2016 I was the only member who had been part of the original group.

My knowledge and expertise of drug indicators (treatment, mortality, seizures, offences, prices and purity) through my Home Office and St George's roles led to me being a member of a number of subsequent ACMD working groups and committees looking at specific substances, e.g., cannabis reclassification, ketamine, GHB, GBL, feeding in relevant statistics, information and advice. This continues: a Novel Psychoactive Substances Committee was set up in 2009 and I have been a member since it started. In 2016, I became co-opted member of the ACMD's Technical Committee. In recent years I have contributed to many working groups (see Appendix D).

For the last 20 years or more, I have collaborated in drug-related research with academics, particularly at St George's and UH, and subsequently with others in the UK and Europe as well as with other institutions and agencies through various networks. This has led to numerous academic papers, several book chapters, as well as invited lectures and conference presentations.

Over the last decade or so, I have put my own experience as a 'hands on' researcher to practical use, supervising research projects (undergraduate and Masters') at St George's and UH, as well as taking on responsibility for running research project modules, usually delivering most of the materials. In recent years, I have been part of three successful PhD supervisory teams and also

an advisor to other teams, to gain an understanding of what is required at a doctoral level from a supervisor's perspective. I also act as a mentor to early career researchers and colleagues starting to supervise research projects. These activities and roles have helped me realise that I have relevant experience to successfully undertake and complete a doctoral research programme.

It seems appropriate to me to bring together my practical experience of research, my expertise in the epidemiology of UK drugs, especially mortality-related dimensions, and my extensive range of publications by pursuing a PhD programme, principally based on existing and planned publications which I have written and/or to which I contributed. In a sense, this resultant product is an encapsulation of my academic and scholarly writing in this field to date.

I hope this thesis is of interest to those who read it and inspires them to know more about drug-related mortality in the wider context of psychoactive substance epidemiology. This area is ever-changing, as the reader will discover … and with it will come new challenges.

Holland, Surrey

1 June 2024

ACKNOWLEDGEMENTS

The research reported in this thesis has been undertaken with the assistance of a great many institutions and individuals. Apologies are extended to all those whom I may have overlooked; any omissions are unintentional.

An immeasurable, eternal debt of gratitude is owed to my foremost academic mentor and inspiration in the field of drug addiction - the late Professor Abdol Hamid Ghodse CBE - for his continual encouragement, critical comments, and faith in me as a researcher. With his guidance I made the transfer from civil servant to academic, and finally teacher. The experience of working for and with him has left an indelible mark on my life; one of which I am honoured and proud.

My thanks then go to my Doctoral supervisors at the University of Hertfordshire (UH) Professor Fabrizio Schifano and Professor Giovanni Martinotti for their guidance, chasing, and encouragement over the past six years.

Financial support for this programme of research was generously provided by the Department of Clinical, Pharmaceutical and Biological Sciences, School of Life and Medical Sciences, University of Hertfordshire.

Appreciation is also due to the staff of the following institutions, organisations and agencies for providing data or access to them: Office for National Statistics; National Records of Scotland; Northern Ireland Research and Statistics Agency; His Majesty's Coroners; Police Scotland; Home Office; Ministry of Justice; Public Health England; Publish Health Scotland; Public Health Wales; Department of Health & Social Care (Northern Ireland); National Drug Treatment Monitoring Service; StatsWales; Mr Stephen Ream, Director of Re-Solv; and Professor Simon Thomas, National Poisons Information Service (Newcastle).

Thanks also go my former Home Office colleagues who played a part in my development as a drugs expert, particularly the following: Miss Joy Mott, Mrs Patricia Dowdeswell, Mrs Ann Barber, Mrs Ann Wass, Dr Les King (former head of the Drugs Intelligence Unit of the Forensic Science Service), Mr Graham Wilkins, Mr Alan Macfarlane (former Chief Inspector of Drugs Inspectorate). A special mention too for Mr Michael Burgess CVO, OBE (former Coroner for Surrey and the Royal Household) in his role as former Honourable Secretary of the Coroners' Society and advisor

to what became the National Programme on Substance Abuse Deaths. A well-deserved mention also for Mr Geoff Monaghan, independent consultant and former Detective Sergeant in the Metropolitan Police Service, for help in tracking down old Home Office statistical bulletins and other statistical sources, general feedback, and encouragement.

In addition to my thanks for the input at St George's University of London of the late Professor Ghodse, I would like to recognise the contributions made to my career by Professor Carmel Clancy, Dr Adenekan Oyefeso, Dr Caroline Copeland, Mr Hugh Claridge, Mrs Christine Goodair, Ms Vinesha Naidoo, and Ms Thomy Tonia. In addition, my appreciation goes to those who helped to collect, enter and analyse data: Dr Lucy Webb, Mr Richard Goldfinch, Mr Mike Pollard, Miss Jackie Lind, Miss Mary Hunt, Ms Debbie Bannister, Dr Kathryn Cobain, Miss Ruth Dryden, and Dr Kapil Ahmed. Also involved in the latter activities at St George's were Dr Barbara Loi and Dr Stefania Chiappini, both of whom I had the honour and privilege of co-supervising with Professor Schifano and Dr Amira Guirguis during their successful PhD programmes at UH.

In respect to the running and administration of my doctoral programme, I would like to thank the UH Doctoral College and staff, especially Mrs Kathy Lee and Mrs Elizabeth (Liz) Day. Gratitude is also due to the UH library staff for assistance in tracking down and providing publications, Dr Keith Sullivan for statistical advice, and others who helped by reading various drafts of papers submitted for publication, discussing work in progress, and making valuable suggestions. Warm encouragement and plenty of coffee, biscuits and chocolate bars have been provided by Dr (now Professor) Amira Guirguis.

My thanks go to the External Assessors who assessed my competence and progress in this PhD endeavour and gave invaluable feedback and advice: Professor Susanne MacGregor (London School of Hygiene & Tropical Medicine), External Assessor for my Initial Registration on the PhD Programme in April 2019; and Professor Alessandro Vento (Università degli Studi Guglielmo Marconi, Rome) External Assessor for my Progression on a Doctoral Programme in November 2021. Further thanks are due to Professor MacGregor and Professor Matteo Marti (Department of Translational Medicine, University of Ferrara) for acting as the External Examiners for my thesis and final viva. Your comments and feedback are most helpful. I am grateful to the Independent Chair, Dr Loic Coudron, for the some running of the viva and associated administrative tasks.

Thank you to my 'critical friends' who read the full draft thesis for their dedication and support. Any mistakes are purely attributable to the author, and all views expressed are his alone.

Finally, but far from least, my thanks are given to my family for their patience and forbearance over the many years it has taken to carry out this programme of research and to write it up. Unfortunately, neither of my parents are around to see me finally complete this odyssey.

DECLARATION OF AUTHORSHIP

This dissertation was written solely by the PhD candidate, John Martin Corkery, in partial fulfilment of the requirements for the degree of Doctor of Philosophy. He declares that that this thesis and the work presented in it are his own and has been generated by him as the result of his own original research and endeavours. No generative Artificial |intelligence was employed. All data analyses were undertaken and interpreted by the candidate alone. Where the published work of others has been consulted, this is always clearly attributed, and where the candidate has quoted from the work of others, the source is always stated.

The work has not been submitted elsewhere in any other form for the fulfilment of any other degree or qualification. The thesis does not contain any material or content previously written in another publication except for where such work has been used and referenced as appropriate in the present work**.** Most of the publications and other outputs (e.g., posters and oral presentations) produced by the candidate during the course of his doctoral programme of research involve co-authors, whose contributions are clearly stated in the relevant section of each publication.

John Corkery, 1 June 2024

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reference compounds (amphetamine, cannabis, cocaine, heroin, ketamine, MDMA and mephedrone).

SELECTED ABBREVIATIONS AND ACRONYMS

ACDD	Advisory Committee on Drug Dependence
ACMD	Advisory Council on the Misuse of Drugs
BCS	British Crime Survey
CDC	Centers for Disease Control
COPFS	Crown Office and Procurator Fiscal Service
CSEW	Crime Survey for England and Wales
DH	Department of Health
DHNI	Department of Health (Northern Ireland)
DHSC	Department of Health and Social Care
DHSSPS	Department of Health Social Services & Public Safety
DRD	Drug-Related Death
ECCAS	European Collaborating Centres on Addiction Studies
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
ESLD	End-stage liver disease
EU	European Union
EU-MADNESS	EUropean-wide, Monitoring, Analysis and knowledge Dissemination on Novel/Emerging pSychoactiveS
FAI	Fatal Accident Inquiry
FOI	Freedom of Information
FSS	Forensic Science Service
GBL	Gamma-butyrolactone or γ-butyrolactone
GDPR	General Data Protection Regulation
GHB	Gamma-Hydroxybutyric acid or γ-hydroxybutyric acid
GBD	Global Burden of Disease
GMR	General Mortality Register
GRONI	General Register Office for Northern Ireland
GROS	General Register Office for Scotland
HCC	Hepatocellular carcinoma
HIV/AIDS	Human Immunodeficiency Virus infection and Acquired Immunodeficiency Syndrome
HM	Her/His Majesty
HSA	Health Security Agency
HMSO	Her/His Majesty's Stationery Office

ICD	International Classification of Diseases
IDU	Intravenous drug user
IOPC	Independent Office for Police Conduct
IPED	Image or Performance Enhancing Drug
ISD	Information Services Division
ISDD	Institute for the Study of Drug Dependence
MBDB	Benzodioxolyl-N-methylbutanamine
MCCD	Medical Certificate of Cause of Death
MDA	3,4-Methylenedioxyamphetamine
MDEA	Methyldiethanolamine
MDMA	3,4-Methylenedioxymethamphetamine
MHRA	Medicines and Healthcare products Regulatory Agency
MSM	Men having sex with men
NACDA	National Advisory Committee on Drugs and Alcohol (Ireland)
NDEC	National Drug Evidence Centre
NDRDD	National Drug-Related Deaths Database (Scotland)
NDTMS	National Drug Treatment Monitoring System
NFCC	National Fire Chiefs' Council
NHS	National Health Service
NISRA	Northern Ireland Statistics and Research Agency
NPCC	National Police Chiefs' Council
NPIS	National Poisons Information Service
NPS	Novel Psychoactive Substance
NPSAD	National Programme on Substance Abuse Deaths
NRS	National Records of Scotland
NTA	National Treatment Agency for Substance Misuse
OHID	Office for Health Improvement and Disparities
ONS	Office for National Statistics
OPCS	Office of Population Censuses and Surveys
PhD	*philosophiae doctor* [Doctor of Philosophy]
PHE	Public Health England
PHIRB	Public Health Information and Research Board (Northern Ireland)
PHLS	Public Health Laboratory Service
PHS	Public Health Service
PSNI	Police Service of Northern Ireland
PWID	People who inject drugs
RCP	Royal College of Pathologists
RTA	Road traffic accident
SCDEA	Scottish Crime and Drug Enforcement Agency
SCRA	Synthetic cannabinoid receptor agonists

SDMD	Scottish Drug Misuse Database
SFIU	Scottish Fatalities Investigation Unit
SMR	Special Mortality Register
SPSS	Statistical Package for the Social Sciences
Std Dev	Standard Deviation
UH	University of Hertfordshire
UK	United Kingdom
UKFP	United Kingdom Focal Point
UNODC	United Nations Office on Drugs and Crime
USA	United Stated of America
WHA	World Health Assembly
WHO	World Health Organization

SELECTIVE GLOSSARY

Addicts' Index	see page 109
Channel Islands	Crown Dependencies (Bailiwicks) of Guernsey and Jersey
Covid-19	coronavirus disease caused by the SARS-CoV-2 virus
Coroner	see page 88
Drug	see page 9
Drug abuse	habitual taking of illegal/illicit drugs
Drug addiction	chronic, relapsing disorder characterised by compulsive drug seeking and use despite adverse consequences
Drug dependence	chronic, progressive disease characterised by significant impairment that is directly associated with persistent and excessive use of a psychoactive substance
Drug misuse	use of a substance for a purpose not consistent with legal or medical guidelines
Drug/substance use	use of selected substances with possible dependence and other detrimental effects
Epidemiology	see page 9
Fatal Accident Inquiry	see page 95
General Mortality Register	see page 97
Great Britain	England, Wales, and Scotland
Inquest	see page 94
Medical Examiner	senior medical doctor trained in the clinical and legal elements of death certification processes
Metabolism	life-sustaining chemical reactions in the body
Novel Psychoactive Substance	"psychoactive drugs which are not prohibited by the United Nations Single Convention on Narcotic Drugs or by the Misuse of Drugs Act 1971, and which people in the UK are seeking for intoxicant use" (ACMD)
'Over the Counter'	medicine that can be bought without a doctor's prescription
Pathology	diagnosis and study of disease
Pharmacodynamics	biochemical and physiological effects of substances
Pharmacokinetics	processes by which the body affects a substance after its administration

‘Popper’	sub-class of volatile substances of the alkyl nitrite chemical family
Psychoactive substance	see page 9
Procurator Fiscal	see page 89
Special Mortality Register	see page 97
Surveillance	"the continuous, systematic collection, analysis and interpretation of health-related data needed for the planning, implementation, and evaluation of public health practice." (WHO)
Tolerance	reduced reaction to a drug following its repeated use
Toxicology	diagnosis and study of the adverse effects of chemical substances on living organisms
United Kingdom	England, Wales, Scotland, and Northern Ireland
Volatile substance use	purposeful inhalation to experience intoxicating effects of substances which, at room temperature, produce a gas or vapour
‘Z’ drugs	hypnotic drugs, including zolpidem, zopiclone, zaleplon, and eszopiclone

PART 1 – CONTEXT SETTING

Structure of the thesis

The following areas are examined:

- Context setting: context and scope of the work, overarching themes, rationale, aims and objectives;
- Defining drug-related deaths and drug-related mortality;
- Data sources, methods and analyses in general terms;
- Improvements in: identifying substances through toxicological screening; recording of substances on death certificates; identification of cases; understanding of mechanisms of death; and death coding;
- Improved reporting and publishing of drug-related death statistics;
- Changes over time in the types and nature of drugs involved in drug-related deaths;
- Identification of typologies of decedents and drugs;
- The relationship(s) of the drug-related death indicator for a range of index drugs/drug classes to other drug indicators;
- Impacts on policy, law and practice;
- An overview of past, present and future drug-related deaths and associated needs.

These have been grouped together into five (5) parts:
Part 1 - Context setting - Chapter 1;
Part 2 - Processes - Chapters 2-5;
Part 3 - Epidemiology - Chapters 6 and 7;
Part 4 - DRDs and other drug indicators - Chapters 8-12;
Part 5 - Decision-making and the way forward - Chapters 13 and 14.

CHAPTER 1 - INTRODUCTION

"Drugs cost lives."
Waly (2021)

"Methadone heals, but it also harms. It is life-saving treatment, but it is also a life-threatening poison. The challenge is how to confer the benefit without incurring the damage …"
Strang and Tobar (2003:3)

"There is a range of problems for those who use drugs; death is by far the least likely. But it is the issue that attracts most attention and causes most concern."
Corkery (2008)

Origins of the study

The present study has evolved from the author's professional and academic activities, endeavours and roles, as outlined in the Preface. Given this, it is necessary to incorporate some elements of the author's earlier and on-going work. Some aspects of this earlier work and research are discussed and developed more fully below.

Background

For thousands of years, humans have been experimenting, exploring and employing plant-based substances (e.g., cannabis, opium, coca leaf, khat), then creating new substances, i.e. pharmaceutical products (such as morphine and other opioids, barbiturates and benzodiazepines), and as understanding of the nature of such materials and their mechanisms of action has developed, often through advances in chemistry and technology, the release of Novel Psychoactive Substances (NPS).

The development of science ensured that the observation of animals in certain settings (including experimental) has continued. Animal models are still a fundamental part of the pre-clinical phase in the development of pharmaceuticals (Russell and Burch, 1959). Animal models, however, have their limitations and are not necessarily translatable to humans.

Although human clinical trials are important in the development of therapeutic drugs, this is not typically the case with NPS. Here the emphasis of their creators is speed in getting products on sale rather than safety, and the effects (if any) of products are predicted on the basis of their

chemical structure. It is unlikely that even computer modelling (*in silico* research), let alone *in vitro* or *in vivo* testing has taken place (Orsolini et al., 2019).

Reasons for using drugs

An individual may have a very simple reason for using a psychoactive substance (see below for definitions of this term and 'drug') or they may have several motivations (including desires, wants, and needs) that are multidimensional or complex (Corkery et al., 2018). These can be described along several dimensions (Table 1.1).

Table 1.1: Classification of motivational dimensions for drug use

Dimension	*Example*
Religious/spiritual	As part of a religious ritual (to celebrate 'sacraments' as in 'taking 'communion' using wine or marijuana); to be 'cleansed' or 'purified' (e.g., ayahuasca); to accompany reading a Holy Book; to enhance 'enlightenment', to commune more directly with deities or other spiritual forces;
Exploratory/experimentation/curiosity	This can range from scientists (such as the late research chemist Alexander Shulgin) designing new molecules, self-experimenting with them and recording their effects, to 'e-Psychonauts' who intentionally experience drug-induced altered states of consciousness so as to try investigating their minds, and possibly address spiritual questions, through such direct experiences, through to 'creatives' such as artists, designers, musicians, writers, philosophers, thinkers and even academics using psychoactive substances to be more original, innovative and 'thinking outside the box' to achieve new insights or understandings of phenomena in the world(s) around them;
Social/cultural	Being part of a social (including religious) group will lead to expectations on the part of others that individuals will conform to particular norms, practices and customs (e.g., peer pressure), thereby confirming their allegiance or belonging to that group; symbolic evidence of this relationship may have to be demonstrated through the consumption of a psychoactive substance, such as at an initiation ceremony, or a 'rite of passage'. Regular consumption, at regular intervals and settings, may help to reinforce this sense of belonging, e.g., "going out with the boys/girls" to the local bar or pub on a Friday or Saturday night. Loyalty to a group, a nation or its leader may be customary at formal occasions, e.g., 'toasting the bride and groom' or 'toasting the Queen/King';
Recreational	Drug use is often associated with particular types of music scene, with specific drug classes being linked to individual genres of music, e.g., 'dance club' drugs; these scenes and their associated drug repertoires can be fluid and evolve;
Employment/occupational	It may be necessary to taste psychoactive substances as part of one's occupation, for example wine-taster, brewer, whisky-blender; to consume it as a religious leader or practitioner (e.g., priest or shaman) during a religious service/rite, e.g., a 'sacrament' such as 'communion' or performing an exorcism; to facilitate business transactions;
Therapeutic	Preventative or to cure (e.g., ibogaine to treat and even cure addiction to drugs), to deal with symptoms of a disease or mental health problem (whether prescribed by a health professional or self-medicated), to enhance the effects of another psychoactive substance, to ameliorate the side-effects of another psychoactive substance e.g., during 'come-down' or to facilitate withdrawal;
Addiction/dependence	Physiological/chemical dependence as well as psychological dependence on, 'craving' for a substance may develop; the abrupt cessation of use may be potentially life-threatening in some extreme cases;
Functional	Searching for energy; to be alert/stay awake; to stave off hunger, suppress appetite, and weight-loss; passing time/ avoiding boredom; dealing with trauma, adverse events/experiences; etc.
Source: Derived from Corkery et al., 2018, pp. 166-7.	

As the drug using career/history of an individual evolves, these dimensions may well overlap, boundaries can become blurred and intersect with one another, and have different significances (Corkery et al., 2018).

Extent and impact of drug use

Data from the United Nations Office on Drugs and Crime (UNODC) on the global extent of drug use are reported in its *World Drug Report*. The most recent publication (UNODC, 2023) indicates that in 2021 an estimated 284 million people worldwide aged 15-64 years had used drugs in the previous year; this is about 5.6% of the population in the age range. More than 1% in this age-group had a drug use disorder. Estimates of the number of people using the main classes of drugs in 2021 were as follows: cannabis 219 million; opioids 60 million; cocaine 22 million; amphetamine-type 36 million, and 'ecstasy'-type 20 million.

The Global Burden of Disease (GBD) Study reported that, in 2019, an estimated 494,000 deaths and 30.9 million years of "healthy" life were lost as a result of premature death and disability could be attributed to drug use. The past three decades (1990-2019) saw an increase of 110% in the number of deaths due to drug use, including 18% in the last decade. However, the increase for deaths attributable to drug use disorders rose by 45% (41% for opioids) in that same decade, 2010-2019, whilst deaths from HIV/AIDS acquired through injecting drug use fell by 14% （GBD 2019 Diseases and Injuries Collaborators, 2020). Using data from the GBD 2019, Shen et al. (2023) estimate that the overall number of deaths from drug use disorders rose from 56,100 in 1990 to 128,100 in 2019. Deaths associated with amphetamine use disorder increased from 6,600 to 9,000 over this period, with cocaine use disorders accounting for an increase from 2,400 to 12,800, and opioid use disorders accounting for a rise from 36,800 to 88,400. No figures are offered for deaths due to cannabis use disorders.

In 2019, at the European Union (EU) level about 83 million people had ever taken drugs; 28.9% of 15-64 year-olds. Around 17.4 million (16.9%) of young adults aged 15-34 years had used drugs in the previous year. There were 5,769 drug-induced deaths in the EU (27) plus Norway and Turkey in 2019; this is a rate of 14.8 deaths per million population aged 15-64 years. Opioids were involved in 76% of such deaths. Overall, deaths have been increasing since 2012, with an increase of 74% in the over-50 years age-group (EMCDDA, 2021), mainly due to the increasing age profile of opioid (including heroin) users.

Prior to leaving the EU, the United Kingdom (UK) accounted for about one-third of all drug-induced deaths; the overall number for the EU (28) plus Norway and Turkey being about 9,500 in 2017 (EMCDDA, 2020). The estimated mortality rate per million population aged 15-64 years

old was 22.3 in 2018. However, the rate for Great Britain was estimated at about 76.2 in 2017; but Scotland had an estimated rate of 295 (Figure 1.1).

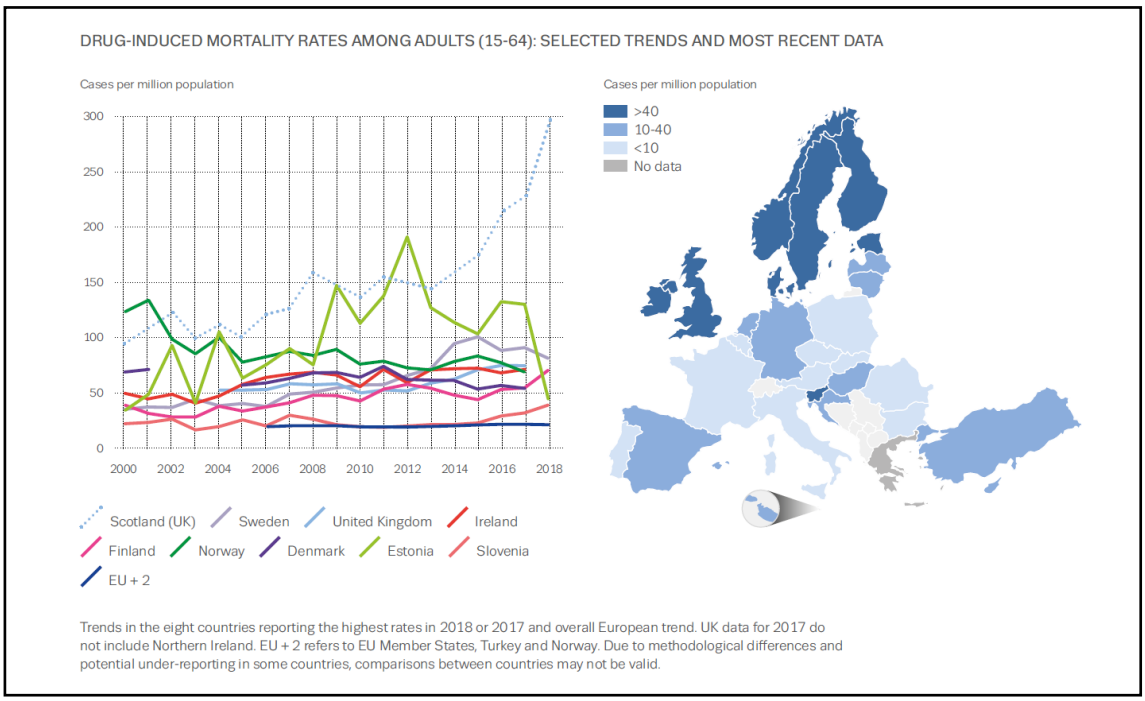

Figure 1.1: Drug-induced mortality rates among adults (15-64): selected trends and most recent data.

Source: Figure 38 in EMCDDA (2020). Reproduced with permission of the EMCDDA.

To provide some context of the relative contribution to the mortality burden in the UK, it is appropriate to compare drug-related deaths to alcohol-related, transport accident and 'all cause' deaths as was previously done for deaths related to volatile substance abuse (e.g., Ghodse et al., 2012). Here, the author has extended that principle to include smoking-related deaths.

As can be seen from Table 1.2, the use of substances can result in a range of outcomes. These results may range from no effect through desired effects to unforeseen and unwanted/adverse ones. There are many ways in which these can cause chronic health conditions and reduce life-spans (Glei and Preston, 2020). That said, drug overdose counts provide a useful yardstick to measure the lethality of substances (Newman et al., 2021). The ultimate negative outcome is, of course, death, whether accidental or intentional. Drug-related deaths (using the widest definition of drug poisoning), although accounting for about one per cent of all deaths in the UK in 2019, still impact individuals and society as a whole.

Table 1.2: Relative contributions to deaths, selected causes, United Kingdom, 2019

Cause of death	*Number*	*Percentage of all deaths*	*Rate per million population*	*Source(s)*
Road traffic accident	1,808	0.30	27.07	Department for Transport, 2023; PSNI, 2023;
Drug misuse	4,328	0.72	64.79	NISRA, 2024; NRS, 2023; ONS, 2023;
Drug poisoning	5,990	0.99	89.67	NISRA, 2024; NRS, 2023; ONS, 2023;
Alcohol-specific	7,565	1.25	113.25	ONS, 2021a
Smoking-related	91,860	15.19	1,375.22	ASH, 2021
All cause(s)	604,707	100.00	9,052.93	Statistica
UK population	66,796,800			ONS, 2021b

The latest available data show that in 2022 the number of deaths attributed to road traffic accidents fell to 1,766 (Department for Transport, 2023; PSNI, 2023). Alcohol-specific deaths rose to 9,641 in 2021 (ONS, 2022) and 10,048 in 2022 - a new record (ONS, 2024). Data presented in Chapter 6 indicate that the number of drug misuse deaths registered in 2022 was 4,305, and the number of drug-poisoning deaths was 6,254 (NISRA, 2024; NRS, 2023; ONS, 2023).

The research problem

It is this final consequence - death - which is the primary focus of this thesis. This sub-section outlines why this merits attention.

The societal imperatives for investigating the reasons behind the upward trends in drug-related deaths in the UK are obvious. As noted by the ACMD (2000:1) “Society expends a good deal of effort in preventing premature deaths from all causes. That is a characteristic of a caring and civilised society, and should apply no less to drug misusers than it does to other classes of people.” Moreover, many drug-related deaths are unintentional and thus preventable (Shah et al., 2001). Many of them are premature (Flanagan and Rooney, 2002) and, as was noted above, lead to many years of (healthy) lives lost. The latter, in turn, means that nations lose productive lives which could contribute to the greater wealth, health and well-being of their populations.

The last point has consequences in terms of economic costs to the family of decedents, communities, and the wider economy; costs are incurred by public health service providers in terms of treatment and care for drug users prior to their deaths, as well as in terms of interventions to prevent future deaths (Godfrey et al., 2002; Gordon et al., 2006). Interventions by first responders, ambulance personnel, and paramedics and possible subsequent hospital treatment to stop overdoses proving fatal should also be considered. Further costs are also going to be incurred because of investigations into (suspected) drug-related deaths by police, pathologists,

toxicologists, Medical Examiners, Coroners, Procurator Fiscals, etc. Deaths in police custody and penal establishments have to be investigated, resulting not only in extensive and thus expensive Coronial inquests and Fatal Accident Inquiries but also inquiries by Prison Ombudsmen and bodies such as the Independent Office for Police Conduct.

The emotional, psychological and psychiatric impacts of drug-related deaths on relatives and friends of decedents are immeasurable, but no less important (da Silva et al., 2007; Titlestad et al., 2021). Indeed, it is suggested that at least ten next of kin will experience the effects of bereavement following a single drug-related death (Dyregrov et al., 2018). Those health, emergency service and penal establishment personnel directly involved in dealing with such cases are also adversely affected (McAuley and Forsyth, 2011; Saunders et al., 2019; Barry, 2020).

Finally, there are good scientific reasons to investigate what has and is going on, so as to deepen knowledge and understanding, which in turn can be applied in theoretical and practical ways to reduce and mitigate the above negative consequences. It is hoped that this thesis will help in these respects and lead to positive benefits arising from such unwanted events.

Rationale for the study

A lot of effort and resources have gone into tackling drug-related mortality over time in the UK, especially during the last two decades. Although there was previous research into the deaths of addicts notified to the Home Office (Oyefeso et al., 1999a, 1999b), arguably, the seminal events in relation to this issue were the publication of the first UK Drug Strategy (H.M. Government, 1998) and a report by the Advisory Council on the Misuse of Drugs' (ACMD) Working Group on Drug-Related Deaths (ACMD, 2000); both of which the author was involved with as a Home Office official. However, the number of deaths is still climbing across the UK (NISRA, 2024; NRS, 2023; ONS, 2023). This is against a background of improvements in case identification, investigation, and reporting; with associated public health and law enforcement prevention, treatment and care programmes, and other initiatives.

So far as the author can establish, there are no other PhD theses that have used the approach(es) deployed here to look at drug-deaths or drug-related epidemiology, either in the UK or worldwide. There is only one thesis that relates closely to this topic in any way. Morgan (2007) looked at the epidemiology of drug poisoning mortality in England and Wales, using data provided by the Office for National Statistics from the Drug Poisoning Mortality Database, and the impact of harm reduction initiatives between 1993 and 2004. Data for hospital admissions, prescriptions, pharmacy drug sales, and the availability of illicit drugs were used to interpret mortality trends. These are similar to some of the sources the researcher has previously used in research

(Schifano et al., 2005, 2006; Schifano and Corkery, 2008). Pierce (2006) looked at the nexus between opioid mortality, crime and treatment in England and Wales. There is a (non-doctoral) dissertation which has taken a brief or superficial look at part of the UK drug-related deaths scene; Koch (2018) summarises the drug-related death phenomenon in the UK focusing on England and Wales, and compares the figures with international development, particularly in the EU. Three decades ago, a Master's thesis looked at deaths attributed to benzodiazepines in Great Britain during the decade 1980-1989 (Serfaty, 1992).

There has been no overview or in-depth study of the drug-related deaths in the UK and associated issues. To date, there has been no detailed description of the processes underlying how such deaths have been identified, investigated, recorded, analysed and information about them disseminated. Furthermore, no comprehensive study has been undertaken of what has been going on, what insights we now have that we did not have 30 years ago, and what we have been doing with that knowledge. This programme of research aimed to provide not only that overview, but also an in-depth exploration of the aspects outlined above, drawing on the researcher's unique knowledge, understanding, expertise and working directly on these topics as a substance epidemiologist in the Home Office and academia since 1987.

The intention was to provide a framework/structure that enables the researcher to give a narrative of what has happened in the UK over the last three decades or so in respect of the mortality of drug users and deaths related to drugs. Therefore, the approach and structure are unique; it is customised to take account of the aspects investigated by this programme of research.

Definitions

Before attempting this task, it is necessary to clarify some basic terms. Specialist terminology is explained, where appropriate, in the relevant sections of the following chapters. A glossary is also provided to assist the reader.

Epidemiology - a widely accepted and simple definition of this terms is "the study of the distribution and determinants of health related states or events in specified populations, and application of this study to control of health problems" (Last, 2001).

Drug - "a medicine or other substance which has a physiological effect when ingested or otherwise introduced into the body" (https://languages.oup.com/google-dictionary-en/). This is a wide-ranging definition which catches substances such as alcohol, nicotine, volatile solvents, and gases, as well as prescribed and over-the-counter medications, 'street' or illegal (i.e.,

'controlled') drugs, and natural/herbal products or derivatives. Some substances may fall into several of these categories at the same time.

Psychoactive substance - the term is being used here in respect of a drug (as set out in the previous paragraph) or other substance that affects how the brain works and causes changes in awareness, behaviour, feelings, mood, sensations, or thoughts. Where the term has a more specific meaning, e.g., legal, this will be provided.

Delimitation of scope

This thesis is not an exhaustive examination but is comprehensive and broad-based through focusing on a select range of groups/classes of drugs: 'established' recreational drugs e.g., heroin, cocaine, amphetamine, MDMA (ecstasy); 'legal highs'/Novel Psychoactive Substances (NPS) e.g., synthetic cannabinoids, synthetic cathinones; natural products e.g., khat, ibogaine, kratom; prescribed medications e.g., methadone, benzodiazepines, ketamine. To keep the research programme at a manageable level, it did not cover: drugs used for image or performance enhancement (IPEDs) e.g., anabolic steroids; nicotine; volatile substances; gases (such as nitrous oxide and helium); or caffeine - substances on which the researcher has also worked in relation to deaths.

General approach to the thesis

The theme for this doctoral programme was: "Developments in the epidemiology of drug-related mortality in the United Kingdom over the last three decades". This was operationalised as the following research question: Have there been changes in the nature, extent and understanding of drug-related mortality in the United Kingdom over the past 30 years?

Aim

The aim of this thesis was to describe and understand developments in the epidemiology of drug-related mortality in the UK over the last three decades, and how that knowledge has been disseminated and impacted policy and practice.

Objectives

The main objectives were to:

- Tell the story of drug-related deaths during this period.

- Look at how understanding of the phenomenon has improved.
- Illustrate how drug-related deaths can be understood in the wider context of other drug indicators.
- Attempt to provide approaches to identify 'at-risk' populations.
- Consider how improvements in knowledge and understanding of the phenomenon can contribute to: decision-making; policy advice and formulation; legislation; law enforcement policies and practices; clinical treatment and service provision; education; etc.
- To take a look forward to what the future may look like, and what will be needed in terms of epidemiological information, and to make appropriate suggestions.

The narrative is presented by referencing relevant publications and peer-reviewed literature, including publications which the researcher wrote or to which he contributed. This uses a range of publications, including Home Office Statistical Bulletins and Research Findings, UK Focal Point reports to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), reports from the National Programme on Substance Abuse Deaths (NPSAD); National Records of Scotland statistical reports on drug-related deaths; Hamid Ghodse's text book on Drugs and Addictive Behaviour (Ghodse, 1995, 2002, 2010); International Narcotics Control Board and United Nations Office for Drugs and Crime publications; book chapters; peer-reviewed and journal articles; EMCDDA publications; ACMD reports; conference posters and presentations, etc. The narrative, of necessity, draws on published data and information from others.

Original research by the author is also included in several chapters. Some of this has been published.

Approaches

Given the breadth of the data being investigated, generated and analysed, a range of methodologies have been utilised. These draw on a range of disciplines and perspectives, including: criminology, epidemiology, netnography, pathology, pharmacoepidemiology, pharmacovigilance, sociology, surveillance, toxicology, and toxicovigilance.

This chapter would appear to be the most appropriate place, rather than in a separate chapter on methods, to outline the philosophical approaches or paradigms that have been considered. In passing, the author notes that other University of Hertfordshire (UH) PhD theses undertaken on psychoactive substances from a chemical or pharmacological perspective have not included such information, whereas those with a clinical focus have done so. As this programme of research has largely been undertaken from an epidemiological perspective, reflecting the author's professional experience and expertise, and has been used, in part, to inform clinicians, it is relevant to

rehearse these paradigms here.

Philosophical and paradigmatic perspectives

The English word ‘philosophy’ derives from the Greek *φιλοσοφία [philosophia]* meaning ”love of wisdom” but has come to be used to describe “The study of the nature, causes, or principles of reality, knowledge, or values, based on logical reasoning” (Merriam-Webster, 2023) or “the study of the theoretical basis of a particular branch of knowledge or experience” (oup.com, 2023). The Latin word *paradigma* means "pattern” or “example”. Similarly, the Greek *παράδειγμα [paradeigma]* translates not only as “pattern” or “ example” but also as “model” or “precedent”. However, within scientific communities, the term ‘paradigm’ is usually construed as a type of framework that brings together underlying assumptions, styles of thinking, different theories (not just one) and methodologies. It is true to say that these terms are often used interchangeably. Theoretically, a research paradigm comprises several elements (Teddlie and Tashakkori, 2008) and provides a justification for them (Creswell, 2009): epistemology; ontology; axiology; methodology.

Epistemology

Epistemology is concerned with theories of knowledge and how it is acquired. This approach maintains that knowledge derives from four principal sources; in descending order of level, from divine revelation, through experience, logic and reason, to intuition. It is further bounded or delimited by its nature, methods, possibilities, scope, and validity (Oxford Languages, 2023; Rehman and Alharthi, 2016). There are a range of positions or stances within epistemology each of which posits what type(s) of knowledge can be generated by conducting research, how information is garnered, collated, and presented (Griz, 2001; Üztemur, 2020): constructivism, empiricism, instrumentalism, interpretivism, objectivism, operationalism, positivism, pragmatism, rationalism, realism, referentialism, subjectivism, etc.

The two broad positions that cover the main paradigms and their variants commonly discussed in PhD dissertations are positivism and interpretivism. Positivism advocates a ‘deductive’ approach, with an emphasis on quantitative methods and testing hypotheses.

Positivism

The positivist approach is widely used within the natural sciences as it is based on the premise that true knowledge comes from observation and experiment experienced by the senses (Guba and Lincoln, 1994). These deterministic and empiricist roots means that positivism seeks to

investigate cause and effect relationships. This can be carried out through quantitative measurement, observations, and predictions of relationships between the observed phenomena or variables (Cook et al., 2015). Biases are minimised and researchers are as objective as possible (Guba and Lincoln, 1994). The determination of 'facts' is guided by the external reality in which the researcher exists; a 'deductive' approach.

Interpretivism

By contrast, social scientists tend to employ an interpretivist approach to knowledge. This proposes an 'inductive' approach, stressing qualitative methods derived from ideas or concepts that have given rise to hypotheses. In this view, individuals' views of the world are derived by their concepts, ideas and language concerning it. Researchers are a part of the research process through their interactions with who and what is being investigated. The aim is to understand rather than to predict. The researchers' conclusions are based on their own observations, typically using qualitative methods.

Table 1.3: Principal paradigms

Paradigm	*Core elements/characteristics*	*Methodological approach*
Positivism	Quantitative methods such as experiment and observation to test hypotheses.	Quantitative
Constructivism/ Interpretivism/ Social Constructivism	Qualitative methods to generate hypotheses, based on the notion that participants' views and experiences are constructed by multiple realities.	Qualitative
Critical Theory/ Transformative/ Advocacy/ Participatory	Researchers aim to improve social conditions via political debate and actions, seeking different perspectives on a particular issue.	Mixed methods
Pragmatism	Focuses on a specific issue, related situations and actions, usually a range of approaches to understand the issue in hand and achieve a resolution. Researchers' priorities are: what works, what approach is most appropriate for understanding particular circumstances or to resolve an issue.	Mixed methods
Phenomenology	In this constructivist approach, observation precedes theory. Researchers look at individuals' interactions in their everyday lives (and deaths).	Qualitative

Some writers consider positivism more as a paradigm in itself. Other paradigms mentioned in the literature considered relevant to the present programme of research are presented in Table 1.3 (Crotty, 1998; Mackenzie and Knipe, 2006; Creswell, 2009; Bowling, 2014). Paradigms such as functionalism are not considered appropriate to investigate drug deaths, although this example might be useful in exploring suicides involving drugs.

Ontology

Ontology is concerned with reality and beliefs and how to view it/them. The role of ontology is to classify and explain entities, whether individuals or processes, that exist within our experience, their properties/characteristics, and their inter-relationships. Relative differences and similarities are categorised as part of the process of understanding these elements.

How these are determined depends on whether an objectivist or a subjectivist approach is taken (Bryman, 2008; Charlwood et al., 2014). Objectivism, based on assumptions used in the natural sciences, maintains that the social reality which researchers investigate is outside (external) to social actors (Goldkuhl, 2012), including researchers themselves. In this view, "social and physical phenomena exist independently of individuals' views of them and tend to be universal and enduring in character. Consequently, it makes sense to study them in the same way as a natural scientist would …" (Saunders et al., 2019:135). Researchers can do so either directly or indirectly, typically using quantitative methods, to answer 'what' questions.

Subjectivism, often associated with the social sciences, argues that social reality is constructed from the beliefs/perceptions of social actors (individuals) and their consequent actions, but at the individual (hence subjective) level. Interactions between social actors are ongoing in nature and in a state of constant evolution. Therefore, the researcher has to "study a situation in detail, including historical, geographical and socio-cultural contexts in order to understand what is happening or how realities are being experienced" (Saunders et al., 2019:137). Therefore, such understandings or theories as are developed are dependent upon those conducting the research (Bryman, 2008).

Axiology

This can be defined, in the context of research design, as the art and science (both are involved from the author's own perspective) of deploying methods used in a research programme/study so as to obtain the correct information/data (Creswell, 2009). Axiology is primarily concerned with the aims of research and appropriate methods. This constituent part of the philosophical approach to research endeavours to clarify if the researcher is attempting to explain (a part of) the world or predict where it is going (Bryman, 2008).

Saunders et al. (2019) argue that this philosophical element is also concerned with values and ethics. This is an important consideration, not least for the researcher! One needs to be able to gauge how and to what extent research is affected, coloured, impacted, impinged, and influenced by one's own beliefs and values; and whether this is beneficial or disadvantageous.

Even the choice of topic investigated reflects, to some extent at least, what the researcher considers important. Although, the field of research may be externally determined (e.g., by funders' needs and interests, or challenges to practitioners), the philosophical stance adopted will reflect the researcher's values; the data collection/generation and analysis methods will likewise mirror these values.

Statement of the author's philosophical position on the investigated topic

Researchers can enhance their awareness of whether their own personal values are influencing the interpretation of data and consequent conclusions they make by writing a 'statement of personal values'. This articulation means one has a clearer understanding of one's own value position on the topic under investigation, decide what is ethically appropriate, and be able to explain decisions if asked or challenged (Saunders et al., 2019:134).

The author's professional background and experience have led to him to become not only interested in but also to develop a desire to understand as fully as possible substance-related deaths and mortality of substance users. Although he has no direct personal experience of losing friends or immediate family due to the acute consequences of substance use, over the past three decades the author has met several parents whose teenage children died because of consuming stimulants and seen the devastation caused by their children's premature demise. From a much closer position, he has witnessed the fatal consequences of chronic substance use, and its continuing effects on loved ones.

Whilst recognising that substance use, misuse and abuse will undoubtedly continue, no matter what the legislative or regulatory environment, the researcher believes that understanding these mainly preventable events can provide insights into how and why they happened, and thereby inform approaches to education, prevention, and clinical interventions. Hopefully, by doing this, some deaths may be avoided. However, it is naïve to assume that they will ever drop to zero. An excess of any substance, psychoactive or otherwise, is potentially lethal.

The present researcher likes to regard himself as both objective and pragmatic. In order to conduct the programme of research reported here, an overall 'hybrid' approach was necessary for a comprehensive and cohesive exposition of the research topic. There are also elements of positivism, in that quantitative methods were used to capture and measure death data, and looking at the relationships between variables/parameters at a national level. On the other hand, taking an in-depth look at individual fatalities so as to understand singular sets of circumstances and extrapolate back to aggregated data involved qualitative approaches, such as 'psychological autopsies', or a constructivist perspective.

It is worth noting that some drug-related 'paradigms' have emerged over the last few decades. Some of these the author has absorbed during the course of his drug-related research career and to which he subscribes. Room provides a useful summary of these:

"Five paradigms of current social research in the field are described: ethnographic research; survey interviewing and research; social psychological questionnaires and experiments; social and health indicator studies; and policy, cultural and historical document-based studies. Three current trends in the social research literature are noted: a tendency for studies to draw on more than one paradigm; a greater emphasis in study designs and analyses on time and change; and a trend toward bringing drug phenomena which have been studied separately -- licit and illicit drugs, drug use and drug dependence -- into a common analytical frame."
Room (1992).

Although written over three decades ago, these words still resonate with the author and what he teaches, writes and practices. The use of both quantitative and qualitative approaches ('mixed methods') was born out of the need to identify and employ methods that were appropriate for the conduct of a range of activities, and to achieve the author's research programme's aims and objectives (Teddlie and Tashakkori, 2008), as reported in this thesis.

The nature of the topic investigated, its dimensions, and data availability meant that a pragmatic approach was necessary. In other words, the methods had to be both ethically and methodically appropriate and feasible. Whilst Chapter 2 looks at definitions (e.g., 'drug misuse', 'drug-related', etc.) that are 'socially constructed' in the sense that they have been created by a range of stakeholders (including data generators and analysts, policy- and law- makers, and researchers from a range of disciplines), Chapters 3 to 5 look at data generation, analyses, dissemination and application (Chapter 13), as part of a process. A public health (positivist) perspective underlies an examination of patterns and trends using aggregated data (Chapters 6 and Chapters 8 to12). A more granular (interpretivist) approach, based on examining individual deaths, forms the basis of Chapter 7.

Methodologies

The research journey is mapped out by means of setting out the methodology. The first step of the journey cannot be taken without a clear idea of what is being investigated, why and how the destination (goal) is going to be reached.

Materials and methods are detailed in relevant chapters rather than in a discrete methodology section or chapter. The choice of methods has been informed by the author's knowledge, experiences, expertise with regard to sources, and the availability of methods. These factors have been influenced or 'coloured' by what the author regards as relevant, appropriate and feasible. In other words, a 'pragmatic' approach to method selection. Suffice it to say, here, that a range of

methods have been used both quantitative and qualitative; thus, the methodology could be described as a ‘mixed methods’ one.

The ‘mixed methods’ approach has several benefits: the use of both quantitative data and qualitative information to provide a more comprehensive and in-depth understanding of the topic being investigated; it mitigates the weaknesses inherent in methods using just one perspective; the integration of methods provides more confidence in understanding and interpreting findings; this, in turn, can be underscored by the triangulation of results; it can provide more enhanced granularity than a single method; and it is well suited to studying organisational issues, phenomena and processes (Molina-Azorin et al., 2017).

There are limitations with the ‘mixed methods’ approach. Clearly it is more complex, and due to employing several methods together it may require more resources, especially time (and perhaps funding). A wider range of expertise is called on to collect/generate, curate, analyse and interpret data. The need for training in such methods can be time-consuming; this is not relevant in the present case as the author is very experienced in both types of methods and indeed teaches them at post-graduate level to clinical and public health professionals.

Validity, reliability and objectivity

The use of different approaches comprising several methods enhances the degree to which a study’s results and interpretations accurately echo or mirror the entities themselves and the milieux/contexts in which they exist, thereby improving validity (Bryman, 2008).

Internal validity, which considers causal relationships between variables, is at the core of Chapters 8 to 12 which look at the relationships of drug-related deaths to nine other ‘drug indicators’. ‘Construct validity’ is concerned with the extent to which the methods employed have actually measured what the research set out to investigate, including present-day (concurrent), content and predictive validity (Bryman, 2008). Generalisability or external validity is dependent on a number of factors in order for a study’s findings to be extrapolated outside the confines of the particular context investigated. These factors include: completeness and representativeness of data (e.g., databases); sampling frames, sampling procedures (and hence representativeness); sample sizes; and response rates (e.g., surveys, interviews, focus groups, audits/service evaluations). Taken as an overall concept, validity enables the researcher to confidently present conclusions that have a high degree of integrity.

The reliability of a research study is dependent on the degree to which it is possible to replicate, reproduce or repeat it using the methods, procedures, instruments, measure and data described.

The main test for the present programme of study would be internal consistency. In addition, the use of inter-rater reliability could be used for some aspects of the research, e.g., qualitative methods such as netnography (the study of communities with a presence on the Internet/social media, or using the Internet as a research resource).

There is a possibility that unconscious bias may have occurred in the selection of materials selected for presentation in this thesis due to the author's long and extensive experience of and expertise in many of the areas covered. However, the author has tried to mitigate this possibility by being as objective as possible, viewing all issues from more than one perspective, and applying self-criticality.

Ethics

On 23 July 2018, the researcher made enquiries via e-mail as follows of the University of Hertfordshire's Health, Science, Engineering and Technology Ethics Committee with Delegated Authority (ECDA):

"So far as ethics is concerned, at present we only foresee using data relating to deceased individuals (which does not require ethics approval in the UK) and undertaking analysis of data/statistics either already in the public domain and/or which are provided by the relevant generating/providing organisations/government departments that relate to drug indicators (e.g. treatment; inpatient and Emergency Department admissions; drug offences; drug seizures/confiscations; price; purity; prevalence; prescriptions; etc.). So far as I am aware, none of these activities would require ethics approval by UH or any other institution. Where named data is provided on deceased individuals, appropriate measures will be adopted to maintain anonymity, confidentiality, etc. as already required by and documented with the data providers (e.g., National Records of Scotland, Northern Ireland Statistics & Research Agency, National Programme on Substance Abuse Deaths) for previous, on-going and planned research activities. The information on deceased individuals is derived either from death certificates and/or coroners' paper/electronic files; information on death certificates is available to any member of the public, e.g., genealogists. There is no interaction with the deceased relatives, friends, witnesses, etc. In effect, the research does not involve human subjects - only documents relating to them.

I have used the Doctoral College EC9 form/decision tool … and have concluded that UH ethics is not needed. I have also used the online decision-making tool provided by the Health Research Authority, which you mentioned this morning, to check on whether NHS ethics approval is required: my conclusion is that I do not require such approval in any part of the UK …"

An e-mail in response sent by Professor Barry Hunt, the then ECDA Chair, on 7 August 2018 confirmed that “we don’t need to give ethical approval to this study”.

Themes

The above-outlined topics can be subsumed within three major themes: context, change, and challenge. However, linking these themes together is the essential ‘golden thread’ for understanding mortality from an epidemiological perspective - cohesion, provided by comparators. Thus, continuity of indicators related to vital events and associated dimensions is also key to unlocking the mysteries of drug-related deaths.

These themes are elaborated conceptually in the core constructs mapped in Figure 1.2 (“Corkery’s conceptual constructs for coherence in communicating epidemiology”). The author has attempted to use this schema to provide links within and between chapters in this thesis to present a coherent narrative.

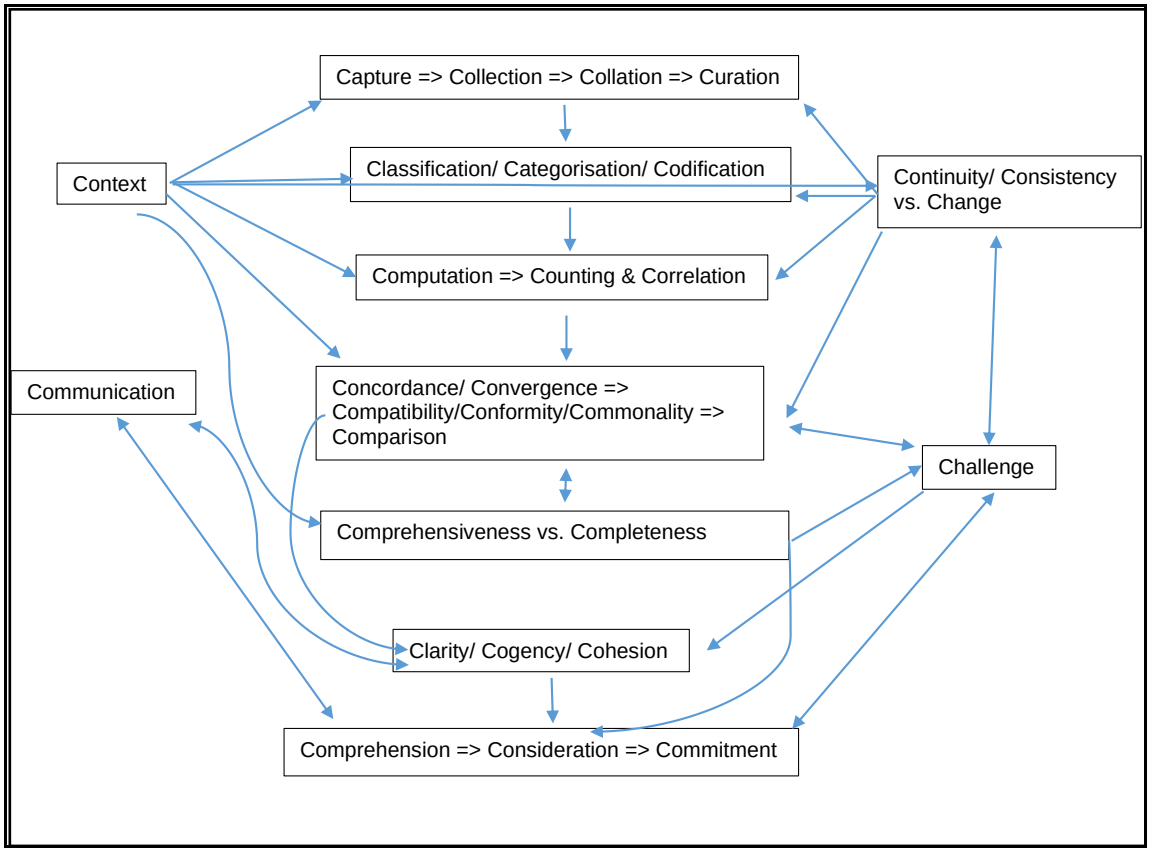

Figure 1.2: Construct map

Chapter overview

This chapter has introduced the themes to be explored and the nature of the general research problem. The researcher's philosophical approach has been outlined. Research questions and specific dimensions of the phenomenon to be explored through a range of methods, including statistical and other quantitative techniques as well as qualitative ones, have been presented. The arguments for the particular methodologies utilised are addressed in relevant chapters. The reasons for this particular research project have been given. The scope and limitations of the study have been outlined, together with the structure of the thesis.

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PART 2 – PROCESSES: FROM INVESTIGATION TO DISSEMINATION

This Part consists of four chapters (2 to 5) that provide a description and critical evaluation of drug-related deaths (DRDs) in general before taking a 'deep dive' into the situation in the United Kingdom (UK) in respect of the processes involved in identifying potential DRDs all the way through investigation, recording, analysis and use as data to inform procedure, policy and practice.

Chapter 2 explains the key concept underlying this thesis, namely the different ways of defining deaths associated with the use of drugs. Thereby, it provides a solid foundation on which the other chapters in this Part build.

Chapter 3 describes the materials used for constructing the present narrative, including the scope of sources relating to information about drug-related deaths and other drug indicators in the UK context. The methods of data generation, curation, and analyses are described.

Building on the two preceding chapters, Chapter 4 provides a narrative description of developments in the investigation and recording of DRDs which have helped to provide a better understanding of the extent of this phenomenon. Here the focus is on process rather than a chronological account. Aspects covered include: scene investigation; identification of potential cases; toxicological investigation; autopsy/postmortem examination; understanding mechanisms of death; recording of substances on medical death certificates; coding of DRDs; and counting cases.

However, the final chapter in this Part (Chapter 5) does employ a chronological approach to present a narrative description of developments in what has been reported and published concerning DRDs in respect of drug-related deaths (DRDs). Here the focus is on improved reporting, publishing and dissemination of DRD statistics at the sub-national, UK national and international levels.

CHAPTER 2 – DEFINING DRUG-RELATED DEATHS AND DRUG-RELATED MORTALITY

"Mortality and fatal overdose death is an essential proxy of the drug abuse problem. Decline and rise in the number of drug related deaths and fatal overdose will easily be interpreted in that perspective. However, variation in the number of such deaths might be due to factors not necessarily linked to the size of the drug problem as such. Understanding of the epidemiological processes which might influence change in mortality rate and number of fatal overdose [sic] is therefore important."
Ødegård et al. (2007)

"Drug-related mortality is a definitive index of the severity of drug abuse and dependence from both clinical and public health perspectives. It provides information about the natural history of addiction, emergence of, and increase in, drug abuse-related problems."
Oyefeso et al. (2002:3)

This chapter explains the key concept underlying this thesis, namely the plethora of ways in which terms used to refer to deaths associated with use of drugs have been and are being used. It also covers mortality arising from drug utilisation, which may not be directly due to, say, an overdose. Finally, it provides a solid foundation on which the next few chapters build, especially Chapter 3 which, in part, describes the materials used for constructing the present narrative. The building blocks laid out here have been reclaimed from earlier works (Oyefeso et al., 2002; Corkery, 2008), but also contain new materials so that the whole is as up-to-date as possible. Thus, the basic approach used was to sift through and identify relevant literature. This has led, in some cases, to primary research based on death certification.

The challenge of defining terms

At the outset, a few points need to be made. Firstly, a series of questions must be posed: "Once a person is certified dead, the question arises, what is the main or underlying cause of death? Is the death caused directly or indirectly by ingestion of a particular drug? In other words, is the death drug-related?" … Secondly, there is a general acknowledgement that the term 'drug-related death' is overinclusive. Consequently, most studies have often defined the term operationally, depending on the focus of inquiry, the population of interest and the drug categories being investigated." (Oyefeso et al., 2002:3). Thirdly, a range of dimensions are used in determining and defining drug-related deaths (DRDs). An appreciation of these issues is fundamental to understanding the phenomenon of DRDs and what has been written about them.

International approaches to defining deaths associated with drug use

Differences in approach to determining what constitutes a death associated with the use of a drug or polysubstance use can be seen by reference to some national, regional and global examples.

Two decades ago, the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA, 2000) defined two types of Drug-Related deaths. The first form is where death is directly attributed or linked to an acute adverse reaction i.e., overdose, poisoning, toxicity. That is, where death occurs as an immediate consequence of the use of illegal substances or the misuse/abuse of licit drugs. The second form is used for deaths indirectly associated with drug abuse; ones occurring as a result of having a drug habit that exposes individuals to the risk of dying in some other way. These risks can be defined (Corkery, 2008) as:

- An infectious disease acquired through a drug (mis)using habit/way of life e.g., HIV/AIDS, leading to death by natural causes;
- Complications arising from an infection acquired through long-term drug misuse e.g., hepatitis (especially hepatitis C) causing liver failure, cirrhosis through the use of infected/contaminated drugs e.g., *Clostridium novyi*;
- Violent deaths related to the supply and/or use of illegal drugs;
- Accidents (including road traffic ones) arising from impaired judgement as a result of consumption of drugs, whether prescribed or illicit; and
- Suicide.

At the same period, in the United States of America (USA), the Drug Abuse Warning Network (US Department of Health and Human Services, 2000) had developed a somewhat different perspective. They used an over-arching term of ‘drug-abuse death’, which refers to death resulting from a drug used for psychic effect, dependence, or suicide. However, this term encompasses two other categories – drug-induced and drug-related deaths: (a) a ‘drug-induced death’ is one where the death was caused by a specific drug, through overdose; whereas (b) a ‘drug-related death’ is one where the medical examiner was convinced that a specific drug was implicated but was not the sole cause (US Department of Health and Human Services, 2000).

Various chapters in a monograph on European perspectives on drug-related mortality (Ghodse et al., 2002) present different criteria for defining a DRD, thereby underlining the difficulty in adhering to a standard definition across national boundaries. The problems this causes in making international comparisons was recognised by the World Health Organization (WHO). They recommended that the term ‘drug abuse-related death’ should be used in place of ‘drug related

death' or 'drug abuse death' (WHO, 1993:7). The term was defined as: "fatal consequences of the abuse (non-medical use, misuse) of internationally controlled substances and/or of non-medical use of other substances for psychic effects" (p7). This definition includes the following categories of death: acute intoxication or poisoning; polysubstance abuse and influence of adulterants/additives; poisoning due to accidental exposure; chronic intoxication; suicides; drug abuse-related accidents; and drug abuse-related diseases. These WHO categories are used below to explore different forms of drug-related deaths. However, we must not forget homicides involving drugs.

Acute intoxication or poisoning (overdose)

A large proportion of drug-related mortality is attributable to this category of death. Historically, for example, during the period 1967-1993 two-thirds (68%) of deaths of addicts notified to the Home Office fell into this class (Ghodse et al., 1998), opioids accounting for 65% of these deaths. Exactly the same proportion, i.e., 68%, of United Kingdom (UK) drug-related deaths occurring in 2012 reported to the National Programme on Substance Abuse Deaths (NPSAD) was due to accidental poisoning as the underlying cause of death (Corkery et al., 2014). Many overdose deaths may be due to: (a) sudden variations in drug purity or strength; (b) loss of or reduced tolerance after periods of enforced or voluntary abstinence. Finally, some acute poisonings may result from deliberate administration, whether suicidal or homicidal in nature.

Polysubstance abuse and influence of adulterants/'cutting' agents

Contrary to what most drug commentators might expect, most drug users in the UK do not use other substances (including alcohol, gases, volatile substances as well as drugs) in combination at the same time. Indeed, although the last time the Crime Survey for England and Wales asked about this topic (in 2013/4 and 2014/5) a statistically significant increase was reported, the rise was only from 7% (in 2010/11 and 2011/12) to 9% (Lader, 2015). This does not contradict findings from the Global Drug Survey, where latent class analysis showed that the highest level of polysubstance use (23.6%) was likely to occur where users took cannabis and ecstasy (Morley et al., 2015).

However, as we will see in a later chapter (Chapter 6), most drug poisoning deaths involve the administration or consumption of several substances, even if not all have contributed to causing death. For example, NPSAD data have consistently shown this to be the case (Ghodse et al., 2000; Corkery et al., 2014). The consumption of drugs is likely to be sequential rather than concurrent, i.e., simultaneous.

The largest proportions of drug fatalities are due to the combined central nervous system depressant effects of opiates/opioids with other drugs. The principal substances known to interact with opioids in a synergistic fashion are alcohol and benzodiazepines. Although these substances are weak respiratory depressants on their own (van de Borne et al., 1997), they potentiate acute intoxication due to opiates/opioids (White and Irvine,1999).

Complications may arise from undisclosed or unknown adulterants, contaminants, diluents, cutting agents, etc. being contained within products purchased (or otherwise acquired). An adulterant may be defined as an undeclared ingredient which is added to a product, or a substance included accidentally as a result of the manufacturing, packaging, or storage processes. 'Cutting' agents are also sometimes, confusingly, described as substances that either enhance or imitate the effects of controlled substances. Diluents are substances (typically inert) which are added to add weight or bulk out products.

In recent years, these have included: heroin cut with fentanyls (Carroll et al., 2017; Tupper et al., 2018); 'street' benzodiazepines containing 'designer benzos' (Tobias et al., 2021); or even heroin/opioids cut with benzodiazepines (Mahintamani et al., 2021). Since 2019 there have been increasing numbers of deaths in the USA where opiates/opioids such as heroin or fentanyl have been adulterated with xylazine (a sedative with muscle relaxant and analgesic properties used in veterinary medicine); see for example (Cano et al., 2023). The first such death in the UK has now been reported by NPSAD (Rock et al., 2023). No wonder drug users are exposing themselves to a form of 'Russian roulette' (Harris et al., 2015).

Poisoning due to accidental exposure

This category clearly overlaps to some extent with the previous one as many 'street' drugs, contain unstated constituents. Some of these adulterants may be pharmacologically active; and they may give rise to harmful or even toxic side-effects. Two decades ago, common pharmacologically active adulterants included caffeine, dextromethorphan, lidocaine, procaine. quinine, scopolamine, and even strychnine. [The pharmacological reason for the use of the last-named substance is questioned by the author and some of his external co-researchers, including former law-enforcement officers.] These substances are still being employed today; but have been joined by a range of others including lignocaine, paracetamol, and those mentioned in the previous paragraph. For a recent comprehensive review see Solimini et al. (2017); however, the picture continues to evolve. Novel Psychoactive Substances are also appearing as cutting agents

(Minutillo et al., 2019); so, clinicians, forensic toxicologists, pathologists and death investigators need to keep up to date with such developments.

Also captured by this category are deaths involving ‘body packers’, drug ‘mules’, ‘stuffers’ and ‘swallowers’, closely linked with the smuggling of illicit drugs, the decedents acting as couriers. Fatalities result from the rupture of drug packages inside the body, typically within the gastrointestinal tract although some may have been concealed in other body cavities, i.e., rectum or vagina. In the European and UK contexts, the numbers of such incidents have been increasing over the past two decades or so, often where ‘body packers’ have died of cocaine intoxication after the rupture of the package in the gastrointestinal tract (Anders et al., 2000). Sometimes, death is due to the wrapping acting as a semipermeable membrane (Beck et al., 1993).

The author noted about 30 drug ‘swallower’ cases occurring across the 2000-9 period during his own data-collection activities for NPSAD; these were chiefly cocaine-related, but some involved other substances such as heroin. Unsurprisingly, most such deaths occur in or near international airports. The true extent of such incidents in the UK is difficult to gauge as Her Majesty’s Customs and Excise/Border Force have not published any data on this phenomenon for many years. In addition, some incidents may arise from individuals trying to conceal small bags of drugs by swallowing them before being arrested by police (e.g., amphetamine and ecstasy (MDMA)). A study of 148 drug overdose inquests conducted in 2003 across seven of the eight coroner’s jurisdictions in Greater London found that two related to cocaine body ‘packers’/’stuffers’ (Hickman et al., 2007). They are rare events but do occur. It is also of note that, occasionally, ‘body packers’ have also been known to re-ingest the content of excreted drug packages to commit suicide (Stichenwirth et al., 2000).

Also, into this category can be placed cases of DRDs of infants and children resulting from neglect. (Intentional fatal poisonings do also occur but are considered below.) There is a greater likelihood that such events happen to the children of drug-abusing parents who may be careless or neglectful (Hunter et al., 2021) in the way(s) in which they store their illicit drugs or prescribed medications, or indeed because their judgement is clouded from ‘being under the influence’ (Welch and Bonner, 2013). Fatalities most commonly arise from the accidental ingestion of drugs. A typical example would be a child managing to access methadone from an unsecure container (such as a child’s beaker (e.g., Traynor, 2014) stored in a fridge) or within easy reach of a toddler (e.g., Thomas, 2009). The introduction of ‘child-proof’ lids and ‘child-resistant’ containers for ‘Over-the-Counter’ medicines has led to significant reductions in accidental poisonings of children (Li et al., 2009). However, this appears to be limited to non-opioid analgesics in the UK context (Mbeledogu et al., 2015).

In the USA, most drug poisonings involve ‘regulated oral drug preparations’, which include “oral prescription drugs and commonly used non-prescription pain relievers, such as acetaminophen [paracetamol], ibuprofen, aspirin, and naproxen sodium” (Franklin and Rodgers, 2008). Fatalities arising from adult formulations of cough and cold medications containing diphenhydramine have been reported (Halmo et al., 2021). Where intent is unclear with regard to the fatal administration of drugs to children aged under 10 years in the USA, opioids are the most commonly reported, along with diphenhydramine and recreational drugs such as cocaine and methamphetamine (Hunter et al., 2021).

Chronic intoxication

The WHO (1993:6) state: “It is known that chronic intoxication by drugs could result in fatality. Although it is unlikely that the dependence syndrome alone could cause death, long-term exposure to drugs could lead to other potentially fatal disorders (including toxic organ damage).” They “agreed that deaths due to chronic intoxication or harmful long-term use of drugs would be included in the data collection system for drug abuse-related deaths.” The second interpretation is being adopted here by the author. This definition could be considered to overlap with that of ‘drug abuse-related diseases’ which is considered below.

A couple of decades ago, UK commentators were observing that “In general, addicts die at a rate that is often much higher than that of the general population. A lifestyle of addiction predisposes the addicts’ population to premature mortality as a consequence of generally poor health status.” (Oyefeso et al., 2002:6). At that point in time, research based on 92,802 addicts notified to the Home Office Addicts Index (5,310 of whom were deceased) showed that mortality amongst this cohort was about seven times higher than in the general population (Ghodse et al., 1998); amongst teenage addicts this differential rose to about 15 times that of individuals of the same age in the wider community (Oyefeso et al., 1999a). Although death rates had declined over the study period, addicts < 45 years were six times more likely than older addicts to die of a drug-related cause, especially since non-therapeutic addicts were 20 times more likely to die from such a cause. This higher risk was attributed to non-therapeutic addicts consuming illicit drugs and thus increased exposure to adulterants and other impurities in ‘street’ drugs (Ghodse et al., 1998). Oppenheimer et al. (1994) reported an excess mortality ratio of 11.9 in a 22-year follow-up study of 128 heroin addicts first attending London clinics in 1969.

Some insight into deaths of notified addicts can be gleaned from the last Home Office statistical bulletin (compiled by the author) to contain detailed breakdowns of deaths in this population

(Home Office, 1995). The majority (four-fifths) of therapeutic addicts (i.e., whose addiction arose from medical treatment) who died during the 1988-1993 period were aged 50 years or more. By contrast, the average age of non-therapeutic addicts was almost 33 years in 1993; 43% being aged under 30 and only 3% over 50 when they died. Across the period 1983-1993 around 60% of addict deaths had drugs attributed as causing or contributing to these outcomes. In 1993 only 53% of addict deaths were drug-related, mostly overdoses; three-quarters of these involved 'notifiable' drugs, chiefly heroin, morphine, methadone or unspecified opiates. Natural causes accounted for most deaths of therapeutic addicts.

An overall Standardised Mortality Ratio (SMR) of 5.7 was found in a very large cohort (198,247) of opioid users in England in 2005-9 (Pierce et al., 2015). A study of a cohort (n = 456) of ever-injecting drug users in Glasgow (Scotland) over a 30-year period found that mortality within this population was almost nine times greater than in the wider population, with an SMR of 31.6 in those aged 15–24 years (Nambiar et al., 2015).

The above-mentioned findings of excess mortality in the UK addict population were in accord with a couple of earlier and smaller scale studies conducted in Australia (Caplehorn et al., 1994) and Sweden (Engström et al., 1991) amongst opiate/heroin addicts. More recently, Hazard Ratios for those reporting lifetime use of heroin or cocaine were 2.40 and 1.27 respectively in a cohort followed up over 20 years in the USA (Reisinger Walker et al., 2017). Increased SMRs of 14.3 for cocaine and heroin users and 5.1 for cocaine users were reported in a cohort of Spanish cocaine users in treatment (de la Fuente et al., 2014). Taking a worldwide view, the 2010 Global Burden of Disease estimated that more than 700,000 excess deaths occurred involving dependent illicit drug users compared to the 44,000 cases (43,000 opioids) where drugs were recorded as the cause of death (Charlson et al., 2015).

Suicides

About 703,000 individuals die from suicide each year across the world; an age-standardised rate of about 9.0 per 100,000 population in 2019 (WHO, 2021). In those aged 15-29 it was the fourth leading cause of death. The Global Burden of Disease 2016 estimated the global age-standardised rate of years of life lost from this cause of death to be 458.4 per 100,000 - accounting for 2.18% of total years of life lost (Naghavi, 2019).

The latest national UK data on suicides are for 2018; 6,057 were registered in that year (ONS, 2019). This is an overall age-standardised rate of 11.2 (males 17.2, females 5.4) deaths per 100,000 population. Following a review of the suicide statistics for Northern Ireland, these rates

for 2020 are now reported as follows: England & Wales 10.0, Northern Ireland 13.3, and Scotland 15.0 (NISRA, 2022b). Poisoning was the second most common method for committing suicide across the UK in 2018 (ONS, 2019); it accounted for 17.9% (n = 877) of male suicides and 36.2% (n = 580) of female suicides. Poisoning was the most common suicide method among females in England and Wales between 2001 and 2007; however, since 2013, this changed to hanging, suffocation or strangulation. Intentional self-poisoning by drugs, medicaments and biological substances accounted for 16.0% of all drug-related deaths in Northern Ireland in the period 2011-21 (NISRA, 2022c).

In a study of successive cohorts of 69,880 addicts in the UK, Oyefeso et al. (1999b) reported an annual suicide rate of 62.9 per 100,000 person-years (excluding undetermined deaths). Overdose accounted for the largest proportion (45%) of suicides. Methadone and antidepressants were the drugs most frequently implicated in suicide. Altogether, suicide was six times more likely to occur among addicts than in the general population. By contrast, in deaths of undetermined intent, overdose accounted for 67% of fatalities; four times the rate in the general population. A study involving 69,457 individuals reported to the Scottish Drug Misuse Database between April 1996 and March 2006 found that 10% had undergone a non-drug-related suicide, a suicide rate of 0.8% (Merrall et al., 2013).

Drug abuse-related accidents

Intoxication can lead to accidental deaths in some instances. Although, most of these are commonly associated with road traffic accidents (RTAs) or accidents in a place of employment, they can occur in other situations (Oyefeso et al., 1999a). The common causal element in such instances is that intoxication impairs judgement, including the perception of risk.

In the UK context, based on deaths reported to the NPSAD that occurred in 1999, Ghodse et al. (2000) noted that about one per cent of these deaths was as a result of asphyxiation, accidental drowning and multiple injuries. Using the same source of information, but using a study panel of coroners in England, Oyefeso et al. (2006) examined the nature, extent and pattern of fatal injuries under the influence of psychoactive drugs (FIUI) between January 1999 and December 2001. The principal mechanism for intentional FIUI was suffocation while the predominant mechanisms in unintentional FIUI were RTAs and falls. More recently, NPSAD has reported similar incidents involving antihistamines (Oyekan et al., 2021). The author and colleagues have also commented on deaths due to exposure and drowning following the consumption of recreational drugs, including: ecstasy (MDMA) (Schifano et al., 2003), GHB/GBL (Corkery et al., 2015), ketamine

(Schifano et al., 2008; Corkery et al., 2021), methoxetamine (Chiappini et al., 2015), and mephedrone (Corkery et al., 2012; Loi et al., 2015).

A study of fatal vehicle occupant fatalities dealt with by ten UK police forces between 1994 and 2005 found that 4% of cases involved drugs (Clarke et al., 2010). Eight per cent (n = 18) of drivers were found to be under the influence of drugs but not alcohol, with a further 6% being positive for both drugs and alcohol. Males were more likely than females to be involved in such deaths. Although cannabis was, predictably, the drug found most often, other substances such as amphetamines, cocaine, ecstasy (MDMA) and heroin were also found in post-mortem toxicology.

A study of a wider range of 1,047 victims of UK fatal RTAs during the period 2000-6 found that 54% of all victims were positive for drugs and/or alcohol, but with a higher rate of 63% for pedestrians (Elliott et al., 2009). The most likely victims were males aged 17-24. One-third (32%) of car drivers testing positive for drugs and/or alcohol had only drugs implicated, whilst a further 26% involved both drugs and alcohol; the proportion for drugs alone was 44% for motorcyclists. A wide range of substances were detected, including: “opiates, cannabinoids (as THC-carboxylic acid), cocaine, anti-depressants, benzodiazepines, amphetamines, barbiturates and “others” … (prescription medications (e.g., anti-convulsants, anti-histamines, anti-inflammatories, anti-psychotics, cardiac drugs and diabetic drugs), over-the-counter products (e.g., paracetamol) and some other drugs of abuse (e.g., benzylpiperazine and ketamine)” (Elliott et al., 2009). The researchers concluded that their findings mean that drugs were implicated in the RTAs, probably affecting driving ability and impairment of individuals.

The latter point is also made by Hamnett et al. (2017). Their study of 118 motor vehicle crash victims during the period 2012-5 found that 36% were positive for drugs and a further 13% for drugs and alcohol. The majority (88%) were male, with a mean age of 41 years, compared to 44 years for females. Cannabinoids were present in 20% of cases, followed by opioids (14%), benzodiazepines (12%), prescription medications (10%), Over-the-Counter medications (8%), and stimulants (8%).

The Royal Life Saving Society UK (RLSS UK) report that on average 73 individuals die each year due to a substance-related drowning; this is more than one-quarter of all accidental drownings (RLSS UK, 2021). The latest statistics from the National Water Safety Forum’s (NWSF) WAID database indicates there were 58/226 (25.7%) accidental drownings in 2022 with a reported presence of alcohol and/or drugs (where known) across the UK (NWSF, 2023), of which 26 (44.8%) were aged under 35 years. Most accidental deaths involving drugs/alcohol were in England (44/151; 29.1%), followed by Scotland (8/45; 17.8%), Wales (5/22; 22.7%; and Northern

Ireland (1/8; 12.5%). The corresponding total figure in 2020 was 69 deaths (NWSF, 2021); in 2015 it was 65; of which 55 had alcohol detected, three with alcohol and drugs and seven with only drugs (NWSF, 2016).

A range of recreational drugs have been implicated in drownings in the UK, including ecstasy (MDMA), GHB/GBL, ketamine, methoxetamine and mephedrone (see above). Evidence from other countries suggests that psychotropic drugs may play a significant role in drowning, whether on their own or in conjunction with alcohol, particularly due to their effects on cognition and psychomotor function (Pajunen et al., 2017).

As part of his PhD research programme, the author identified that there has been no in-depth research drilling down into UK cases. To start rectifying this situation he initiated a research activity. An examination of anonymised drug-related poisoning deaths registered in Scotland between 1996 and 2020, provided to the author by the National Records of Scotland as part of an EU-funded research project (EU-MADNESS) has now been undertaken as part of the author's doctoral research programme. A paper based on this study has been published (Corkery et al., 2023). Some of the key findings are reproduced here.

Less than one per cent (0.9%; 160/18,277) of such cases had 'drowning' or 'immersion' mentioned in the 'cause of death' field(s) on the death certificate. Nearly seven-tenths (n = 110) were males. The mean age of those drowning was 39.84 (range 16-81, Std Dev. = 15.02) years: males tended to be younger (mean 38.12, range 16-80 years, Std Dev. = 14.45) than females (mean 43.64, range 21-81 years, Std Dev. = 15.70).

There is year-on-year variation between 1997 and 2017, with a rapid increase in recent years: from 7 deaths in 2017, to 12 in 2018, to over 20 in 2019 and 2020. There does not appear to be any seasonality in terms of months of the year when deaths occur; the number per month ranges from 10 to 19, with two peaks in February and April.

The most common substances implicated were: drugs alone or in combination (95); drugs and alcohol (50). In addition, there were 15 cases where no specific substance was mentioned in the cause of death, but 12 of these had 'drug abuse/drug misuse' mentioned as a contributory cause. The maximum number of substances implicated was 7, the mean was 1.97. In descending order, the drug classes implicated were: opiates/opioids (65); benzodiazepines (49); stimulants (30); antidepressants (23); 'Z' drugs (zolpidem, zopiclone) (6); antipsychotics (5); gabapentinoids (3); antiepileptics (2); antihistamines (2). There were also 15 cases in which the drugs were described as 'unspecified'. No volatile substances were specified. Over one-half (28/49; 57%) of drownings

involving benzodiazepines mentioned NPS or ‘designer’ benzodiazepines, particularly etizolam (23 cases). No other NPS were mentioned. NPS or ‘designer’ benzodiazepines are a principal contributing factor to the increase in drug-related poisoning deaths observed in Scotland during the last few years (Corkery et al., 2020) and may well be responsible, in part, for the increased numbers of drug-poisoning related drownings.

The most common combinations of drug classes implicated were: opiates/opioids + benzodiazepines (28); benzodiazepines + stimulants (11); benzodiazepines + antidepressants (7); opiates/opioids + stimulants (6); opiates/opioids + antidepressants (5). Alcohol was implicated in 50 deaths, most commonly with the following drug classes: alcohol + benzodiazepines (20); alcohol + opiates/opioids (19); alcohol and stimulants (16). At least one central nervous system depressant (alcohol, benzodiazepine, diphenhydramine, opiate/opioid) was implicated in 106/160 (66.25%) deaths.

Based on ICD-9 (WHO, 1978) and ICD-10 codes (WHO, 1992), just under two-fifths (n = 61; 38.23%) of all deaths were accidental in terms of intent, whereas about one-third (n = 52; 32.50%) were intentional, and about one-quarter (n = 44; 27.50%) were of undetermined intent. Two cases were deemed homicide, and one natural causes.

For the 110 males, the most common intent was accidental (n = 49), followed by undetermined intent (n = 32) and intentional (n = 27), along with one homicide and one natural causes. For the 50 females, the most common intents were: intentional (n = 25), accidental (n = 12), and undetermined intent (12); there was one homicide. Of the 67 deaths in those aged under 35 years, accidental accounted for 22, undetermined intent for 25 cases, intentional for 19, and homicide for one case. For the 93 cases aged 35 years or more, the most common intent was accidental (n = 39), followed by intentional (n = 33), undetermined (n = 19), homicide (1), and natural causes (1).

Very little information can be gleaned from the ‘cause of death’ death and/or the ICD codes used with respect to the circumstances of the death. ‘Drug abuse’, ‘drug abuser’ or ‘drug misuse’ was mentioned in 65 (40.63%) of the cases. In the majority of cases (n = 129; 80.63%) the type of water is unspecified; in 16 cases the body of water is simply referred to as ‘natural water’, and there are four instances of ‘fresh water’. However, “bath” is mentioned nine times and “cold water” twice. The terms ‘cold’ and ‘hypothermia’ are mentioned in a total of six case, as are ‘falls’ or ‘jump from height’. To get a better insight into such issues, it would be necessary to undertake record linkage, such as is undertaken by NPSAD and the Scottish National Drug-Related Deaths Database (Public Health Scotland, 2022).

As noted above, the author and colleagues have found, through examination of coroners' records, that drowning fatalities following consumption of drugs (with or without alcohol) occur both at home (in a bathtub) and in 'natural water', whether flowing (sea, rivers, canals, and streams) or static (reservoirs, swimming pools, lakes and ponds). In the home environment, individuals have become sleepy or lost consciousness under the effects of drugs, many of which have sedating properties, and their heads have subsequently slipped under the water, cutting off their oxygen supply, leading to death. In terms of 'natural water', the typical scenario is that of an individual under the influence of drugs (and alcohol) decides to go for a swim without appreciating the risks involved. These risks might include the presence of fast currents and undertows, coldness of the water, their own lack of swimming ability, undertaking these activities at night/in the dark, etc. Exposure to cold temperatures is common in drownings but also in deaths which have occurred as a result of individuals becoming disorientated due to the effects of drugs (and alcohol), getting lost, finding themselves without shelter and falling asleep with fatal consequences e.g., hyperthermia. An unusual case reported is that of an 18-year-old male who consumed a high-strength ecstasy tablet, began acting strangely and wandered away from his friends, and was found lying in a puddle or damp grass. He suffered a cardiac arrest on the way to hospital in an ambulance and was pronounced dead on arrival. His death was regarded as a drug-related drowning (Courtney-Guy, 2021).

Drug abuse-related diseases

According to the UK Health Security Agency (HSA) (2021b), an estimated 106,890 individuals were living in the UK with HIV in 2020, of whom about 97,740 were in England. New HIV diagnoses in England peaked around 2005 and have since shown an overall fall, to 2,630 in 2020 (54% lowered compared to 5,780 in 2014). Over the past decade the all-cause mortality rate in England of persons with diagnosed HIV has been stable (c. 630/100,000 population in 2020).

Up to 2011 there were 114,608 new cases of HIV diagnosed across the UK. The probable exposure categories were: heterosexual contact 52,102 (45.46%); sex between men 50,549 (44.11%); injecting drug use 5,278 (4.61%); vertical transmission 2,233 (1.95%); and other 1,826 (1.59%). During the decade 2011-2020, out of an overall total of 52,554 diagnoses the categories accounted for the following contributions: heterosexual contact 20,047 (38.15%); sex between men 25,107 (47.78%); injecting drug use 1,257 (2.39%); vertical transmission 659 (1.25%); and other 384 (0.73%). The respective numbers and proportions in 2020 (total = 2,766) were: heterosexual contact 1,067 (38.58%); sex between men 995 (35.97%); injecting drug use 59 (2.13%); vertical transmission 24 (0.87%); and other 32 (1.16%). These statistics indicate that the

transmission of HIV has increased amongst males having sex with males (MSM) but fallen by more than half within the injecting drug use community.

Deaths of intravenous drug users (IDUs), including MSM, AIDS victims accounted for 7.9% (1,269/16,102) of the total number of AIDS deaths in England and Wales up to the end of December 2007. In Northern Ireland, the figure was 5.1% (4/79), but in Scotland it was 50.6% (727/1,438). The proportion for the Channel Islands and Isle of Man was 1/9. The UK figure of 58 for 2006 was about 28% of the peak level of 208 in 1995. The decline in the number of deaths of IDU (including MSM) AIDS victims saw a levelling off in the mid-2000s. The latest UK figures, during the period 1981-2020 (personal communication from UK HSA to author, 1 February 2022), for all AIDs deaths show that 10.59% (2,750/25,979) of deaths was related to IDUs (including MSM); the respective proportions for the individual countries are: England 7.46% (1,699/22,775); Scotland 44.53% (985/2,212); Wales 7.06% (32/453); Northern Ireland 0.52% (8/155). Here it can be seen very pronounced differences in both numbers and rates exist between Scotland, England and Wales, and Northern Ireland. Such regional differences will be also remarked on in Chapter 6 in respect of drug poisoning related fatalities.

To obtain accurate figures on HIV/AIDS deaths associated with IDU (including MSM), it is necessary that relevant information is captured on the death certificate. However, as an HIV/AIDS diagnosis as the main cause of death may be accidentally or even deliberately remain undisclosed or concealed (Hickman et al., 1999; Copeland et al., 2004), the true impact of the HIV epidemic may be underestimated (Copeland et al., 2004). Therefore, record linkage as used in cohort studies is the best way to overcome such shortcomings.

Another common infection acquired through IDU is hepatitis C. This is a blood-borne virus that damages the liver. Chronic infection can cause hepatic cancer (hepatocellular carcinoma or HCC), cirrhosis and liver failure. There were an estimated 174,000 individuals living in the UK with a chronic hepatitis C infection in 2005; this was believed to have fallen to 118,900 in 2019 (PHE, 2020c), and to 92,900 in 2021 (UK HSA, 2023). In England, the relevant numbers were 129,000 in 2015 and 74,600 in 2021, a fall of 57.8% (UK HSA, 2022). IDU accounts for 90% of disclosed risk factors in UK laboratory reports (PHE, 2020a; Health Protection Scotland, 2018) and 59% in Northern Ireland (Northern Ireland Hepatitis B & C Managed Clinical Network, 2020). UK surveys of people who inject drugs (PWIDs) indicate that in 2019 just over a half of PWIDs had ever been infected (55% in Scotland, 54% in the rest of the UK), and that about one-fifth were currently testing positive (19% in Scotland, 23% in the rest of the UK (PHE, 2020b). The most recent figures, for 2021, indicate that, overall, in the UK 58.6% of PWIDs had ever been infected (UK HSA, 2023).

The number of UK deaths associated with hepatitis C-related end-stage liver disease (ESLD) and HCC in 2005 was 209, but more than doubled to 464 in 2015. However, there are signs of a reduction in such deaths in the period up to 2019 (PHE, 2020c). Identification of such cases is through identification of the hepatitis C virus on the death certificate in England, Wales and Northern Ireland. In Scotland the process is somewhat more complex: “In Scotland, data on deaths from ESLD/HCC are obtained via record-linkage of Scotland’s National Hepatitis C Diagnoses Database to the national deaths register; thus, ESLD/HCC deaths for all individuals diagnosed with HCV (antibody positive) infection in Scotland are reported (including those with, but also those without, hepatitis C recorded on their death record)” (Notes to Figure 9, PHE, 2020c). ESLD is “Defined by codes or text entries for ascites, bleeding oesophageal varices, hepato-renal syndrome, hepatic encephalopathy or hepatic failure” (Notes to Figure 9, PHE, 2020c). However, there are difficulties in determining the route through which hepatitis was contracted if reliance is made on the death certificate alone. In many instances, those with HCV are unaware of their diagnosis and, thus, how they acquired the infection. Moreover, the person completing the death certificate, even if they have such information as to the aetiology of the condition, may not include it on the death certificate. Furthermore, information regarding aetiology may be accidentally or deliberately concealed, as happens with HIV/AIDS (see above). Record linkage and cohort studies are robust methods of mitigating, to some extent, such shortcomings.

Cases of acute severe illness involving bacterial infection resulting in at least 40 deaths were reported in Scotland, Ireland and England between April and August 2000 (see, for example, (Jones et al., 2002; McGuigan et al., 2002; Murray-Lillibridge et al., 2006). These deaths were linked to the *Group A Streptococcus, Staphylococcus aureus, Clostridium* and *Bacillus* species. The condition resulting in death was characterised by extensive local inflammation at injection sites, followed by hypotension and circulatory collapse (CDC, 2000). Further investigation of some of these cases revealed an alarming trend in wound infection among injecting drug users, by *Clostridium botulinum* and *Clostridium novyi* (PHLS, 2000). Another included Streptococcus pyogenes (Lamagni et al., 2008). Such infections, especially amongst opiate injectors are still a current concern (Lewer et al., 2020; Robertson et al., 2021).

Chronic drug use can present with life-threatening issues. These can include the effects of infections, such as HIV/AIDS and hepatitis, but also the consequences of growing older whilst continuing to use drugs. Phenomena, such as ageing cohorts of opioid, cocaine and methamphetamine users are looked at in Chapter 7.

Violent deaths associated with drugs

As far as the author is aware, there are no definitions of violent drug-related deaths. There are, however, a range of types of death that are violent in nature which can be associated with the use, effects of and trade in drugs. These will now be briefly outlined. Again, the reader will note that some of these types overlap, in part, with some of the classifications covered earlier in this chapter.

One type of such death is where administration of drugs by one party to another (whether at the request of the recipient or not) results in the latter's death (for the statutory definition of 'administer' see s. 130(9) of the Medicines Act 1968 as amended). Under this heading could be included a range of deaths: from accidental overdose, assisted suicide, manslaughter (see, for example, *R v Cato, Morris and Dudley* (1976) 62 Cr. App. R. 41 and *R v Dalby (1982)* 74 Cr. App. R. 348), murder or even judicial execution, i.e., implementation of the death penalty through the administration of drugs. Such drug administration, especially the latter example, has given rise to ethical debates (for example, Denno, 2007; Gibson and Barrett Lain, 2015) and morally-based export bans on the drugs typically used e.g., in the USA (e.g., Alper, 2014; Dresser, 2014; Booth, 2018).

In the UK context, however, any inquest or Fatal Accident Inquiry would usually take place after any criminal court cases arising from the supply and/or administration of substances have been completed. In England and Wales, where an inquest has been opened relating to a homicide, the coroner is most likely to adjourn it *sine die* (without fixed date) under paragraph 1(6) of Schedule 1 of the Coroners and Justice Act 2009, which effectively means that the facts established by the criminal court are those that pertain to the death. The intent (*mens rea*) is critical in this context as it can determine how the death is dealt with by law enforcement and criminal prosecution agencies. In some jurisdictions, it will be assumed initially to be a homicide and dealt with accordingly, unless deemed otherwise e.g., manslaughter or accident. However, it is important that pathologists and toxicologists involved in investigating such deaths focus objectively on explaining the death and leave legal issues to the relevant agencies.

A further type of death that could be encompassed within this category are those that occur when the killer or perpetrator (person responsible for causing death) was under the influence of drugs. This latter category can overlap with cases examined above, e.g., RTAs. There is no systematic data collection on such fatalities.

So far as the author is aware, statistical series on drug-related offences, i.e., committed as a result of consuming substances (apart from drug- or drink-driving) or in order to procure substances as opposed to drug offences such as possession, supply, importation, have not been collated or published by the Home Office for more than four decades. However, some limited information can be derived from the Homicide Indexes maintained by the Home Office and the Scottish Government, where such data on drug and alcohol use is derived from data generated by police from toxicology reports and suspect and witness statements. The Statistics Branch within the Police Service of Northern Ireland (PSNI) do not hold details on whether homicide victims or suspects were thought to be under the influence of illicit drugs at the time of the homicide, or if they were known to be drug users/drug dealers (personal communication to author from Gillian Hunter, PSNI Statistics Branch, 15 February 2022).

For the three-year period April 2020 to March 2023, data from the Homicide Index covering England and Wales (ONS, 2024) indicates that about 33% of victims were believed to be under the influence of alcohol and/or illicit drugs at the time of the homicide; 6% were under the influence of drugs and 8% under the influence of drugs and alcohol. A slightly lower proportion (30%) of homicide suspects were under the influence of alcohol and/or illicit drugs; 7% were under the influence of drugs and 8% under the influence of drugs and alcohol. Also, a slightly lower proportion (29%) of homicide suspects were under the influence of alcohol and/or illicit drugs; 6% were under the influence of drugs and 10% under the influence of drugs and alcohol.

There are some gender differences apparent with respect to both victims and suspects. Males as victims were more likely to be under the influence of drugs compared to females (8% vs 3%) or under the influence of drugs and alcohol (9% vs. 5%). The picture for suspects is somewhat reversed: 6% of male and 9% female suspects were under the influence of drugs, and female suspects were more likely than their male counterparts to be under the influence of drugs and alcohol (11% vs. 8%).

Drug users accounted for 32% and drug dealers for 15% of victims; amongst suspects the respective figures were 48% and 27%. Females accounted for lower proportions than males in respect of the following parameters: victim being a drug user (39% vs. 14%); victim being a drug dealer (20% vs. 3%); suspect being a drug user (49% vs. 37%); suspect being a drug dealer (29% vs. 8%). Motives were ascertainable by police in a low proportion of cases: stealing drug proceeds (4%); obtaining drugs (5%). These motivations were higher for males (5%) than for females (2% and 3%, respectively).

Over the past 16 years (April 2007 - March 2023) the proportion of homicides that have involved drug users or dealers or have been related to drugs in any way ranged mostly between 36% and 45% (in 2017-18) but increased to 55% in 2020-21, although falling to 53% in the two most recent years. In 2020-21, there were 306 homicides that fell into this group. This was 33 fewer than in 2019-20. ONS (2022) suggested that "this fall was driven by the number of drug-related homicides that took place in a public place and therefore may be because of coronavirus (Covid-19) restrictions imposed in the latest year." There was a steep rise in 2021-22 to 361, the highest number ever recorded by the Home Office in this data series. However, this fell back to 310 in 2022-23.

Secondary analysis of data shows that in Scotland, during the decade April 2013 - March 2023, the proportion of homicide suspects under the influence of drugs was 3.8% compared to 7.5% under the influence of drugs and alcohol and 23.3% under the influence alcohol alone (Scottish Government, 2023a). However, it should be noted that such status was unknown in 52.0% of cases. Making appropriate adjustments for the 'unknowns', the proportions of male and female suspects known to be under the influence of drugs were dissimilar (8.4% vs. 3.0%); but note the number of females was low. The proportions under the influence of drugs and alcohol were 29.6% and 12.1% for females and male suspects respectively; this is the opposite for cases in England and Wales.

In this specific Scottish context 'drug-related' is defined as "a homicide motivated by a need to obtain drugs or money for drugs, a homicide of or by a consumer or supplier of drugs, a homicide committed in order to steal proceeds of the drugs trade or a homicide as a consequence of rivalry between users and/or dealers within the drug trade" (Scottish Government, 2023b, Note 4.13). In terms of victims where the motive was 'drug-related' in the last decade, the overall proportion of solved cases that was drug-related was 40.5%; that for male victims was 43.6% compared to 31.5% for female victims. Previous years had seen an increase in the number of drug-related homicide cases; however, in 2021-22 there was a fall to 36 (from 40), and a further fall to 34 in 2022-23.

At the European level, publicly available information on drug-related homicides focussing on specific countries is very limited (de Bont and Liem, 2017; de Bont et al., 2018). Several (semi-) closed homicide monitoring systems also exist outside of the UK, but as can be seen in the case of Great Britain, they do have some problems. These issues include: difficulty in ascertaining whether a homicide is related to drugs, police and/or pathology reports normally provide the needed in-depth data; suspects' characteristics derived from criminal justice sources are typically

not linked to those of victims coming from health sources; and cross-national differences in defining and counting homicides hinders comparison (EMCDDA, 2019).

An audit, undertaken for the EMCDDA, of relevant data sources and a review of the available data considered homicide as drug-related when:

"(a) the homicide occurred while either the perpetrator or the victim or both were evidently under the influence of drugs; (b) the homicide was motivated by a need to obtain drugs, or money to buy drugs; or (c) the homicide was related to the various characteristics of the drug market. In this context, drugs are defined as cannabis, opioids (heroin, morphine, etc.), stimulants (cocaine, amphetamine, etc.), hallucinogens (LSD, tryptamines, etc.) and misused and abused prescription medicines. The … term related [was used] loosely, not implying causation but merely pertaining to the involvement of drugs in the crime."
EMCDDA (2019:11)

Homicides in Finland (2014-15), Sweden (2013-14) and the Netherlands (2012-16) were examined. Overall, half of all homicides were drug-related, although the nature of these varied from country to country; thus, Dutch cases were typically 'systemic' (occurring during the sale and distribution of drugs) whilst in Finland and Sweden they were largely 'psychopharmacological' (committed while either perpetrator or victim is under the influence of drugs) in nature. Economic-compulsive (economically oriented violence in order to support costly drug use) homicide was relatively uncommon in all three countries compared with the other two types of drug-related homicides. Both suspects and victims were mostly males and aged 25 to 45. Further detailed analyses are presented.

The richness of data captured in this pilot study, despite its limitations, demonstrates that more aspects could be potentially investigated in the UK if primary sources and record-linkage were to be employed. Such research could be based on a data protocol for drug-related homicide developed by the EMCDDA (2020).

As we have seen above, violence between individuals/organisations involved in drug supply and/or use can result in deaths. These 'drug-trade' related fatalities or 'economic-compulsive' drug-related homicides can result from: 'turf-wars' (fighting over territory or 'turf'); refusal to do business; thefts/robberies going wrong; disputes over drug prices; violence/terrorism in drug markets; and even imposition of drug controls (Corkery et al., 2011a), leading to judicial executions for committing drug offences. The latter group typically include 'trafficking' offences, such as 'transporting', 'possession with intent to traffic', acting as a courier, etc., but also for drug manufacture. In recent years, there have also been extrajudicial killings in the context of anti-drug operations in several countries (Girelli et al., 2024; SGGPO, 2023). At the other extreme, the

author has previously reported that, in at least one country, capital punishment had been imposed in the past on a woman who was in possession of, and had used, khat (Corkery et al., 2011a).

Some instances of the types of violent death outlined in the previous paragraphs have occurred in the UK. However, so far as the author is aware, no information is collated on such events. Three decades ago, the Government 'Green Paper' on "Tackling Drugs Together" noted:

"There are no reliable figures for England and Wales of the annual number of deaths caused by drug-related crime. Individual figures have been quoted which give a partial indication of the problem. For example, the United Kingdom Written Statement to the 37th session of the UN Commission on Narcotic Drugs referred to ten crack-related murders in London in 1993. Home Office addicts statistics quote the number of previously notified addicts who were murder victims, but their deaths need not have come about through drug-related crime. The figures for England and Wales by year of death were one in 1990, two in 1991, and two in 1992."
HMSO (1994:87)

The availability of reliable statistics is still an issue. However, recent examples can be classed as follows: homicide whilst under the influence of drugs and alcohol (Loweth, 2022) or 'high on drugs' (Naylor, 2021); drug gang rivalry, e.g., 'hit' on competitor (Sky News, 2022), arson (Barlow, 2021); drug deal going wrong, e.g., counterfeit bank notes used to pay for drugs (BBC Kent, 2021) or in revenge for being 'short-changed' when being paid for drugs (BBC Cambridgeshire, 2021); unpaid drug debt (Evans and Evans, 2021); theft of drugs (BBC Essex, 2021; Davies, 2021); theft from drug dealer (Corkery et al., 2012; BBC Berkshire, 2021); involvement in drug production, e.g., caught in a fire in premises where cannabis cultivation was taking place (Bryant, 2022), explosion whilst making methamphetamine (BBC London, 2020); counterfeit products, e.g., containing no active ingredient (Dalby, 2021).

Suicide/violent deaths

Within this category, one might include suicides/intentional deaths using violent means, such as hanging, use of firearms or jumping from a height, leaping in front of a train or other mode of transport, but where there was sufficient levels of a drug or drug combination in the decedents' system to have caused death in its own right.

A further variation on this theme is where a substance (or combination thereof) has triggered suicidal thoughts or ideation, leading to a successful attempt to take one's own life. As Mino et al. (1999) pointed out two decades ago, suicidal ideation is associated with severity of psychosocial dysfunctionning, lack of family support and polydrug abuse. Substances that could fall into this category include: cannabis (van Ours et al., 2013; Bolanis et al., 2020), amphetamine (McKetin et al., 2019), methamphetamine (Darke et al., 2009; Marshall et al., 2011; Han et al.,

2021), methylenedioxymethamphetamine (MDMA) (Kaye et al., 2009; Mithoefer et al., 2019), cocaine (Cottler et al., 2005; Mustaquim et al., 2021), mephedrone (Elliott and Evans, 2014; Dolengevich-Segal et al., 2016), opiates/opioids (Brown et al., 2020; Schepis et al., 2019), and even benzodiazepines (Schepis et al., 2018). These drugs are mainly stimulants in terms of their mode of action. As some of these molecules are relatively new (i.e., NPS such as mephedrone and other synthetic cathinones) additions to the menu of substances that are combined together by drug users, it is important to monitor their longer-term effects (Mead and Parrott, 2020). The author's research unit has reported that many NPS (especially synthetic cathinones, synthetic cannabinoids, and new synthetic opioids) appear to have the potential to cause suicidal ideation and related deaths (Chiappini et al., 2021).

The nexus/combination of (lethal levels of) drugs and violent modes of death can be illustrated by reference to several papers examining the characteristics of deaths involving specific drugs. The author and colleagues have previously noted with respect to synthetic cathinones, that hangings and firearm injuries have frequently been reported to have been used in suicides (Schifano et al., 2020), including coronial cases examined by the author (Corkery et al., 2012; Schifano et al., 2012; Loi et al., 2015). In one of these cases the decedent cut his own throat, and in another jumped from a bridge (Corkery et al., 2012). Other researchers have also reported a large proportion of suicides involving cathinones employing hanging as the mechanical means of death, e.g., 75% in a study by Pieprzyca et al. (2022). Jumping from a height also featured as a cause of death in cases involving consumption of khat (Corkery et al., 2011b). Cutting one's own neck whilst under the influence of GHB has also been reported (Corkery et al., 2015). We have also reported 15 deaths in England which could be deemed violent following ketamine use: six falls, four hangings, three road traffic accidents, one person being hit by a train and one instance of intentional self-harm by use of a knife (Corkery et al., 2021). Firearm injuries and hangings have also been reported for kratom-related deaths (Corkery et al., 2019). Amphetamine/ methamphetamine deaths are more likely than MDMA ones to involve mechanical asphyxia, whereas suicides are more likely to occur in MDMA-related deaths than those associated with amphetamine/methamphetamine (Schifano et al., 2010).

Deaths of neonates and infants

Some discussion has already been presented about accidental deaths of young children exposed to drugs. However, the author, whilst working as part of the NPSAD programme, came across examples of drug-related deaths which often go unreported or, at least, unremarked. Although probably few in number, they do merit a brief mention.

Two instances involved pregnant women using opiates/opioids. Case 1: The mother was seven months pregnant when found collapsed in a town-centre public toilet following an intra-venous heroin overdose. The baby was delivered by emergency Caesarian section but died 5 days later having been “irreversibly damaged intrapartum”. Cause of death was given as: “1a: global hypoxic-ischaemic damage; 1b: maternal circulatory insufficiency.” The neonate only weighed 2.05 kg (The Argus, 2002). The mother was still in a coma more than 6 years after the event, despite waking from the coma, she remained in a persistent vegetative state until her death in October 2009 (Willey, 2009; Sussex Express, 2011). The mother’s boyfriend died a week after the birth from a heroin overdose (The Argus, 2002). Case 2: the mother was on a methadone programme. The cause of death was given as “1a: Hyaline membrane disease; 1b: Prematurity; 2: Maternal substance abuse”. The neonate died within 4 days of birth. No inquest was held as the coroner considered it not to be in the public interest to do so.

A third case to note is one that involved a baby who was found dead unresponsive face-down in its cot when the father awoke at noon. The mother had fed the infant at 7:00 am prior to going to work at 8:30 am. The coroner found that the deceased child had died of a “Sudden Unexpected Death in Infancy”. However, what was noteworthy was the quantifiable level of cannabis metabolites found in the baby’s post-mortem blood (THCC (11-nor-delta-9-tetrahydrocannabinol-9-carboxylic acid) 0.02ng/ml, tetrahydrocannabol 0.20ng/ml). These levels were consistent with recent atmospheric exposure rather than ingestion or chronic inhalation exposure. Cannabis was smelt in the bedroom which was shared with the baby; the cannabis was kept underneath the bed. The coroner returned an “open” verdict.

Non-accidental fatal poisonings of infants and children

Neglect of children by drug-using parents can lead to death, often via drug poisoning. A US study categorised such events into three broad patterns: “i*ntentional administration without documented benign intent* (e.g., the perpetrator intentionally administered the substance with intent to cause harm or without documented intent to relieve child suffering)”; “*intentional administration with benign intent* (e.g., the perpetrator intentionally administered the substance with intent to relieve child suffering)”; and “u*nclear administration* (e.g., no clear evidence that the child was intentionally provided the substance)” (Hunter et al., 2021).

The drugs implicated in the first group were mostly opioids, followed by other prescription drugs, then recreational drugs (e.g., stimulants). Substances administered to induce sleep in the second group were mostly methadone and diphenhydramine. Opioids figured prominently in the third group, together with diphenhydramine and recreational drugs (e.g., stimulants). Issues raised by

the authors echo those in the earlier description of accidental poisoning fatalities: parents/carers being ignorant of the toxicity of the medications when administered to young children, and unsafe storage of prescribed drugs and illicit substances.

These cases are redolent of historical incidences of laudanum being administered to infants to help with teething, stop them crying, quieten them down (Berridge and Mars, 2004), many resulting in death. More recent UK examples include: the administration of methadone and diazepam (Ryan, 2007); methadone (BBC Bristol, 2012); and cocaine (Lennon, 2017).

United Kingdom drug-related mortality definitions and classifications

Up until 'Brexit', when the UK left the European Union on 31 December 2020, there were five definitions of drug-related deaths (DRDs) (excluding long-term consequences of drug using behaviour such as hepatitis and HIV/AIDS) used in the United Kingdom for 'official' purposes. These will now be briefly described.

ONS 'standard' definition

The Office for National Statistics (ONS) 'standard' definition essentially relates to deaths from drug poisoning. It looks at the underlying cause of death according to ICD criteria. It is the broadest of the official definitions, covering anything from heroin to aspirin, from volatile substances to NPS.

"Drug poisoning deaths involve a broad spectrum of substances, including controlled and non-controlled drugs, prescription medicines (either prescribed to the individual or obtained by other means) and over-the-counter medications. As well as deaths from drug abuse and dependence, figures include accidents and suicides involving drug poisonings, and complications of drug abuse such as deep vein thrombosis or septicaemia from intravenous drug use. They do not include other adverse effects of drugs, for example, anaphylactic shock, or accidents caused by an individual being under the influence of drugs."
ONS (2021:11)

Table 2.1 provides details of the relevant ICD codes used for the ONS 'standard' definition.

Table 2.1: International Classification of Diseases codes used for ONS 'standard' definition of drug poisoning deaths

Description	ICD-9 codes	ICD-10 codes
Mental and behavioural disorders due to drug use (excluding alcohol and tobacco)	292, 304, 305.2–305.9	F11–F16, F18–F19
Accidental poisoning by drugs, medicaments, and biological substances	E850–E858	X40–X44
Intentional self-poisoning by drugs, medicaments, and biological substances	E950.0–E950.5	X60–X64
Assault by drugs, medicaments, and biological substances	E962.0	X85
Poisoning by drugs, medicaments, and biological substances, undetermined intent	E980.0–E980.5	Y10–Y14

ONS 'drug misuse' definition

The 'drug misuse' definition is also sometimes referred to, incorrectly, as the 'UK Drug Strategy' definition. As such, it is relevant to set out its origins. In November 1997, the Advisory Council on the Misuse of Drugs (ACMD) decided to focus its resources on producing a report on preventing drug-related deaths (DRDs). Its Prevention Working Group (PWG) was charged with this task. Composed of Council members, co-opted experts, and government officials (including the author as a Home Office official - see ACMD, 2000:103), the Group held 17 full day meetings, heard from 14 invited witnesses, reviewed five specially commissioned background reports, reviewed the literature base, and commissioned research of its own (overseen by the author). The outcome of this labour was presented to the full Council in November 1999 and sent in its final form to Ministers in December 1999. The report was published six months later (ACMD, 2000).

Despite strong encouragement from the PWG's chair, the late Professor Griffith Edwards, and others to suggest a definition of 'drug-related death' that could be used for monitoring progress against the performance indicator of reducing DRDs that had been set out in the National Plan of the UK's Anti-Drug Co-ordinator, published in April 1999 (Cabinet Office, 1999), this idea was strongly opposed by key PWG members. Therefore, no definition was set out in the report. The ACMD report did, however, state that policies

"must be supported by a clearer definition of data needs and by reliable data which can help monitor policy effectiveness and focus their application. We see a strengthening in the data base as vital to the policy frame both in terms of national action, and action within communities, where ways of using the data effectively will need increasingly to be explored." ACMD (2000:96)

This omission necessitated the Department of Health convening an *ad hoc* "forum" or Technical Working Group (TWG) comprised of experts from relevant fields to consider how best the ACMD's recommendations on information needs could be taken forward and to produce a definition of

DRD for the UK Drug Strategy. (The author was a member of the TWG which met during 2000 and 2001.) There were four principal areas in which the TWG recommended that surveillance activities might be considered: (a) a headline indicator, i.e., 'acute' DRDs; (b) secondary data on blood-borne diseases, drug-related homicide, etc.; (c) making funding available for enhanced data such as that produced by NPSAD; and (d) local confidential inquiries. The TWG's DRD definition endorsed by the full ACMD and officially adopted for use in the Government's Action Plan (Department of Health, 2001) concentrated on direct unintentional deaths - “Deaths where the underlying cause is poisoning, drug abuse or drug dependence and where any of the substances scheduled under the Misuse of Drugs Act 1971 were involved” (Corkery, 2002).

Thus, the ONS ‘drug misuse’ definition is somewhat narrower than the ‘standard’ definition in terms of the range of substances covered, for example it excludes non-opioid analgesics (as well as co-proxamol). However, it looks at both the underlying cause in terms of ICD codes and the status of the drug i.e., controlled under the Misuse of Drugs Act 1971 (see Table 2.2).

“Death classified as drug misuse must be a drug poisoning and meet either one (or both) of the following conditions; the underlying cause is drug abuse or drug dependence, or any of the substances controlled under the Misuse of Drugs Act 1971 are involved.”
ONS (2021:11)

Table 2.2: Cause of death categories included in the ONS 'drug misuse' definition

(a) deaths where the underlying cause of death has been coded to the following categories of mental and behavioural disorders due to psychoactive substance use (excluding alcohol, tobacco, and volatile solvents):	
(i)	Opioids (F11)
(ii)	Cannabinoids (F12)
(iii)	Sedatives or hypnotics (F13)
(iv)	Cocaine (F14)
(v)	Other stimulants, including caffeine (F15)
(vi)	Hallucinogens (F16)
(vii)	Multiple drug use and use of other psychoactive substances (F19)
(b) deaths coded to the following categories and where a drug controlled under the Misuse of Drugs Act 1971 was mentioned on the death record:	
(i)	Accidental poisoning by drugs, medicaments, and biological substances (X40–X44)
(ii)	Intentional self-poisoning by drugs, medicaments, and biological substances (X60–X64)
(iii)	Poisoning by drugs, medicaments, and biological substances, undetermined intent (Y10–Y14)
(iv)	Assault by drugs, medicaments, and biological substances (X85)
(v)	Mental and behavioural disorders due to use of volatile solvents (F18)
Notes	
1: Deaths coded to opiate abuse which resulted from the injection of contaminated heroin have been included in the indicator. This differs from the approach taken in Scotland, where these deaths have been excluded. This is because the General Register Office for Scotland (GROS) is able to identify deaths which occurred as a result of the use of contaminated heroin, whereas in England and Wales, these deaths cannot be readily identified. In practice, in England and Wales, they will only be included where the drug was mentioned on the death record and the death was coded to one of the ICD codes on the ONS database of drug-related poisonings and not to an infection code.	
2: Specific rules were adopted for dealing with compound analgesics which contain relatively small quantities of drugs listed under the Misuse of Drugs Act, the major ones being dextropropoxyphene, dihydrocodeine and codeine. Where these drugs are mentioned on a death record, they have been excluded if they are part of a compound analgesic (such as co-proxamol, co-dydramol or co-codamol) or cold remedy. Dextropropoxyphene has been excluded on all occasions, whether or not paracetamol or a compound analgesic was mentioned. This is because dextropropoxyphene is rarely, if ever, available other than as part of a paracetamol compound. However, codeine or dihydrocodeine mentioned alone were included in the indicator. This is because they are routinely available and known to be abused in this form. This approach is the same as that taken by GROS.	
3: ICD-10 codes are given in brackets. Information ICD-9 codes are in Health Statistics Quarterly 13. Available at: www.ons.gov.uk/ons/rel/hsq/health-statistics-quarterly/no--13--spring-2002/index.html	
Adapted from ONS (2021)	

European Union definitions

The EMCDDA has two definitions (EMCDDA, 2009): one for 'general mortality registers' (GMRs) such as ONS, and another for 'special mortality registers' (SMRs) such as that maintained by NPSAD.

The GMR definition (Selection B – see Table 2.3), while looking at the same range of underlying causes as the UK 'drug misuse' definition further refines them by applying a complex filter, which looks at the substances involved. Only deaths due to drugs typical of abuse like opiates, cocaine, amphetamines, cannabis, and hallucinogens are included; psychoactive medicines are excluded (see EMCDDA (2009) for further details).

This produces similar numbers to the UK 'drug misuse' definition but with a different drug profile. The degree of overlap between the first three of these definitions is illustrated graphically in Figure 2.1. There is close correspondence between the two ONS definitions over the timeframe presented. There is also a closer association of numbers between the ONS 'drug misuse' and the EMCDDA DRD definitions to about 2013, when there is a sharp divergence.

Table 2.3: Summary of ICD-10 codes used for EMCDDA Selection B for General Mortality Registers

Underlying cause of death	***Selected ICD-10 code(s)***
Disorders	F11-F12, F14-F16, and F19
Accidental poisoning	X42[1], X41[2]
Intentional poisoning	X62[1], X61[2]
Poisoning undetermined intent	Y12[1], Y11[2]
Notes: (1) In combination with the T-codes: T40.0-T40.9; (2) In combination with the T-code: T43.6.	
Adapted from EMCDDA (2009:16).	

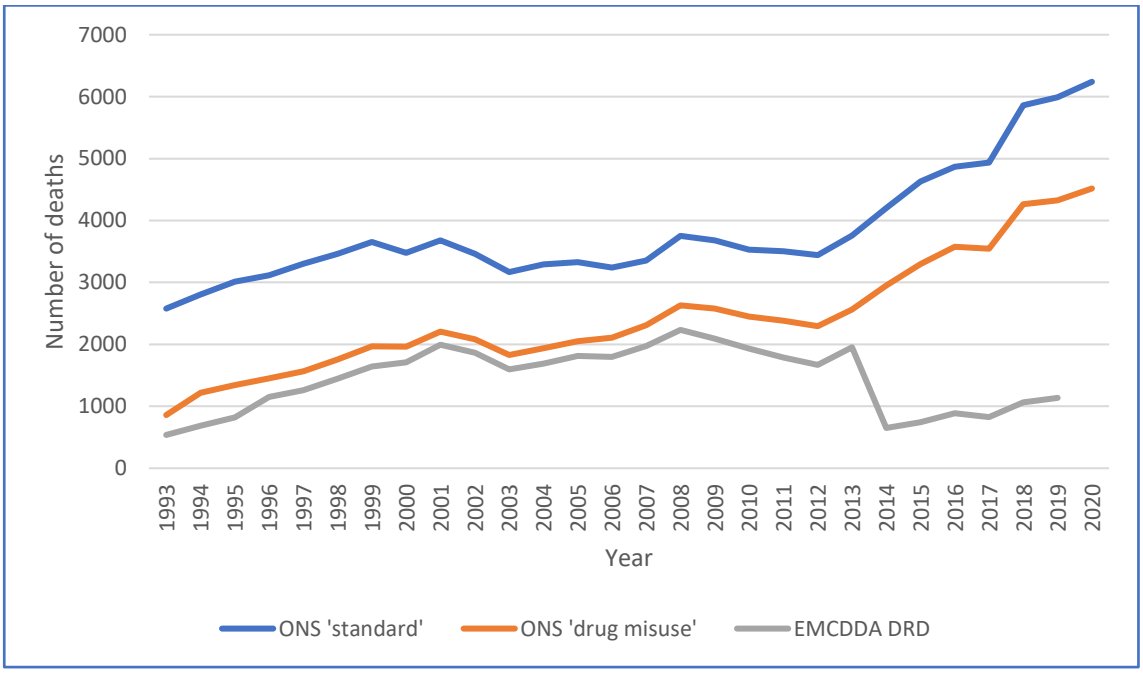

Figure 2.1: Comparison of total numbers of United Kingdom drug-related deaths reported to the EMCDDA using three definitions, by year of registration, 1993-2020

Sources: UK Focal Point annual reports to EMCDDA, NRS (2021), ONS (2021), NISRA (2022a)

The degree of overlap and difference between the two ONS definitions and the EMCDDA definition can be best illustrated graphically. A recent example is provided by NRS (2022:8) - see Figure 2.2.

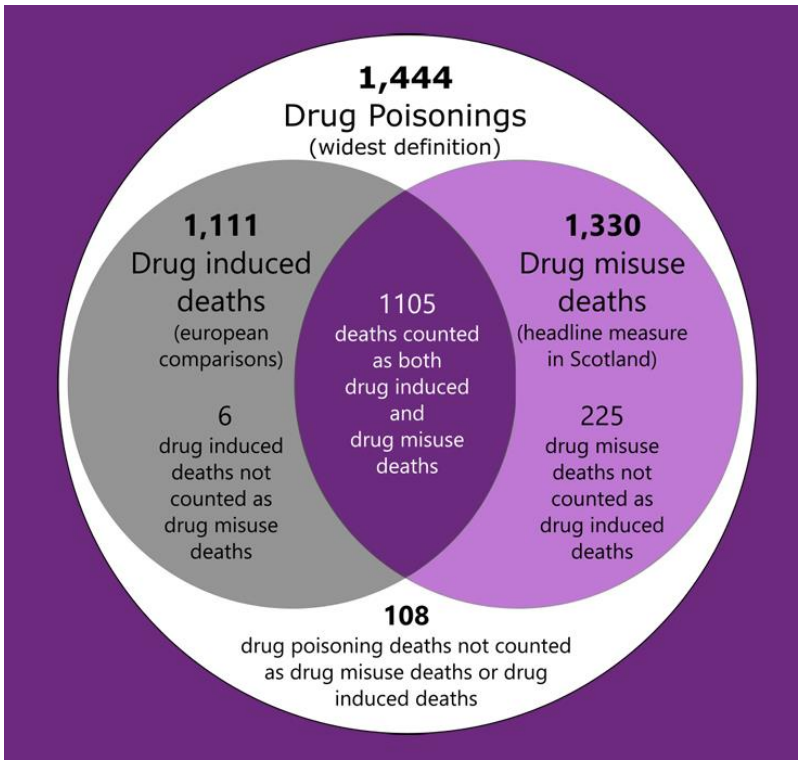

Figure 2.2: Extent of overlap of three main definitions used for drug deaths, Scotland, 2021

The EMCDDA definition for 'special mortality registers' looks at a smaller range of underlying causes in combination with a narrower coverage in terms of the substances considered i.e., 'drugs of abuse' them (Selection D - see Table 2.4). Complex rules are used to further filter them (see EMCDDA (2009) for further details).

Table 2.4: Summary of groups of deaths used for EMCDDA Selection D for Special Mortality Registers

Underlying cause of death	***Further breakdown***
Poisoning by: accident suicide undetermined intent	Poisoning by the substances: opioids methadone (only) poly-substances[1] including opioids poly-substances[1] excluding opioids unspecified[2] substances
Notes: (1) 'poly-substances' should include at least two of the above mentioned substances, or at least one, in addition to alcohol, or psychoactive medicine; (2) 'unspecified/unknown' will be included when it is assumed to include one of the above mentioned substances (i.e., based on other data without toxicological confirmation).	
Adapted from EMCDDA (2009:16).	

NPSAD definition

The final definition of drug-related and mortality commonly used in the UK is that of NPSAD (National Programme on Substance Abuse Deaths). The NPSAD case definition is one where any one of the following criteria is met at an inquest or fatal accident inquiry or similar investigation (Ghodse et al., 2000):

- one or more psychoactive substances directly implicated in death;
- history of dependence or abuse of psychoactive drugs;
- presence of controlled drugs at postmortem;
- cases of deaths directly due to drugs but with no inquest.

Thus, this definition is a hybrid one; it does not use the underlying cause of death as the principal criteria for inclusion, looking instead at psychoactive substances (including non-controlled substances such as 'poppers') directly implicated in death, a history of dependence or abuse of psychoactive drugs, and the presence of 'controlled' drugs at postmortem. Underlying cause of death is then used in combination with the coroner's verdict or finding to determine intentionality.

Choice of definition

The choice of definition employed can be related to the purpose(s) and role(s) of individual agencies and to the nature of the definition(s) used. These relationships, therefore, determine what can and cannot be used for specific investigations. Furthermore, the nature of the data sources themselves needs to be taken into consideration when deciding what type(s) of investigations into drug-related deaths are feasible - see Chapter 3.

The ONS definitions are typically used for 'official' purposes, especially as they and their equivalents in Scotland and Northern Ireland have complete coverage of all deaths registered in the UK. However, as will be seen in Chapter 3, they are limited in terms of being able to provide in-depth insights into cause of death and substances implicated, especially regarding toxicology. The ONS definitions do not allow comparisons with other countries.

By contrast, the EU definition(s) allow some comparison across countries, but they too have limitations with regard to, for example, the nature of the registers and their coverage, the data-collection processes and purposes, etc. A working group (which included the author) set up by the EMCDDA investigated such issues in depth (EMCDDA, 2009). Despite Brexit, if UK agencies continue to use/present data using the EMCCDA 'standard' definition, comparisons could

continue. Indeed, such comparisons are necessary to see how the UK, and its constituent countries, is faring alongside its European counterparts.

On the other hand, within the UK we have internationally recognised and well-respected special drug-related databases, especially the NPSAD. Its definition is, by comparison with the GMRs, more inclusive, but not over-inclusive. There is a degree of overlap between deaths involving several aspects of drug use: illicit and licit drugs, controlled and prescription drugs, etc. It is, therefore, useful to have the capacity to look at specific sub-samples, which other data sources might find more difficult to undertake.

The types of definitions and (some of) their uses are summarised in Table 2.5. A useful discussion of these and other UK variations of drug-related death definitions can be found in Annex B of the NRS annual drug-related deaths reports (e.g., https://www.nrscotland.gov.uk/files//statistics/drug-related-deaths/22/drug-related-deaths-22-annex-B.pdf).

Table 2.5: Definitions of acute/direct drug-related deaths employed in the United Kingdom and their uses

Use	***Definition***				
	ONS 'standard'	ONS 'drug misuse'	EMCDDA selection B (GMR)	EMCDDA selection D (SMR)	NPSAD
For EU monitoring purposes	✓	✓	✓	✓	✓
For UK Drug Strategy monitoring		✓			✓
GMR publications	✓	✓			
NPSAD publications	✓	✓	✓		✓
Local confidential inquiries		✓			✓
Validation of other DRD datasets	✓	✓	✓	✓	✓
Academic/scientific publications	✓	✓	✓	✓	✓
Abbreviations: DRD – Drug-Related Death; EMCDDA - European Monitoring Centre for Drugs and Drug Addiction; EU – European Union; GMR – General Mortality Register; NPSAD – National Programme on Substance Abuse Deaths; ONS – Office for National Statistics; SMR – Special Mortality Register; UK – United Kingdom.					
Note: Based on Corkery (2008)					

Chapter overview

The chapter commences with outlining the challenges of defining ‘drug-related deaths’, including over-inclusivity, overlapping conceptual frameworks, etc. To overcome such issues, in many instances definitions are operationalised by researchers to suit the needs of their specific studies.

The reader is guided through the plethora of definitions which have been used over the past three decades, including international, EU and UK approaches. These are illustrated with detailed comments reflecting on practical issues such as what index or classes of substances should be covered, relative contributions of drugs to fatalities, differing interpretations of commonly used definitions, and coverage of different data sources.

Such challenges are further examined later in this Part; for example, Chapter 3 looks at the various UK data sources in the light of the latter two themes, whilst Chapter 4 considers the interpretation of toxicology, drug combinations, etc, and Chapter 5 examines how these factors affect the statistics produced on deaths associated with drugs.

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CHAPTER 3 - DATA SOURCES, METHODS, AND ANALYSES

"Like all data about illegal drug use, information about deaths comes from a variety of sources, which, together, present a picture that is still incomplete, although improving all the time."
Corkery (2008)

"From Death to Death Certificate: What do the Dead say?"
Gill (2017)

The range of sources relating to information about drug-related deaths and other drug indicators in the UK context are described here, together with methods of data generation, curation, and analyses in general terms. The research method used here is that of the literature review.

How and when deaths are reported

England and Wales

In England and Wales, all deaths have to be registered, in the district where they occurred and within five days, unless the Registrar (of Births, Deaths, Marriages and Civil Partnerships) says this period may be extended. The event must be registered by a relative or someone present at the death.

If an individual dies at home and the death was expected (e.g., from a terminal illness) the family doctor or General Practitioner (GP) should be notified. The doctor will then be able to issue a Medical Certificate of Cause of Death (MCCD) to allow the death to be registered at the relevant Register Office. The latter will then be able to issue a Death Certificate. Relevant details as well as additional statistical information will also be sent electronically to the General Register Office, which is part of the Office for National Statistics (ONS). If an individual dies in hospital, it is the hospital which will usually issue a medical certificate. The same process as above is then followed.

The MCCD can be signed by any registered medical practitioner,

"even if the deceased was not attended during their last illness and not seen after death, provided that they are able to state the cause of death to the best of their knowledge and belief.
Once that MCCD reaches the registrar there are two possibilities depending on whether the deceased was seen before or after death. If a medical practitioner (who does not have to be the same medical practitioner who signed the MCCD)

attended the deceased within 28 days before death (a new, longer timescale) or after death, then the registrar can register the death in the normal way. Second, if there was no attendance either within 28 days before death or after death, then the registrar would need to refer that to the coroner.

The Notification of Deaths Regulations 2019 provide that a registered medical practitioner must notify the coroner where:
it is reasonably believed that there is no attending medical practitioner required to sign the MCCD; or
it is reasonably believed that the attending medical practitioner required to sign the MCCD is not available to do so within a reasonable time of death."
Ministry of Justice (2021)

If an individual dies unexpectedly at home, the death may have to be reported to a Coroner. The Coroner is usually either a doctor or a lawyer, but increasingly dually qualified, appointed and paid by a local authority. A Coroner investigates deaths which are violent, unnatural, unknown cause of death, or occurring in custody or state detention.

One of the conclusions of the Third Shipman Inquiry (The Stationery Office, 2003) was that there should not be separate processes for burials and cremations in respect of death certification. The Coroners and Justice Act 2009 introduced a system whereby all MCCDs would be subjected to independent medical review. The Health and Care Act 2022 enables NHS bodies in England and Wales to appoint medical examiners, thereby allowing them access to "the sensitive and urgent timescales required to register a death" (DHSC, 2024a). Changes being introduced, following a review of the death certification system completed by the Department of Health and Social Care (DHSC), will mean that from 9 September 2024 it will become a statutory requirement that "all deaths in any health setting that are not referred to the coroner in the first instance are subject to medical examiner scrutiny" (DHSC, 2024c). The relevant Regulations, which cover England and Wales, were laid before Parliament on 15 April 2024 (see DHSC (2024b) for further information). These new provisions will apply where:

"there is no attending practitioner
an attending practitioner is not available within a reasonable time
In either of these circumstances, the death is referred to the senior coroner by a referring medical practitioner (not a medical examiner) and the senior coroner decides not to investigate. In these circumstances only, the senior coroner should refer the case to a medical examiner to certify the death by completing a medical examiner MCCD."
DHSC (2024a)

These developments are

"designed to help strengthen safeguards and prevent criminal activity.
They will also consult with families or representatives of the deceased, providing an opportunity for them to raise questions or concerns with a senior doctor not involved in the care of the person who died."
DHSC (2024c)

Northern Ireland

Coroners in Northern Ireland are lawyers (solicitors or barristers) appointed by the Lord Chancellor.

The process of reporting a death in Northern Ireland is slightly different. Although a death has to be registered within five days, unless referred to a Coroner, it can be notified to any District Registration Office. Changes were made due to Covid-19 restrictions in the process which appear to have become permanent. The MCCD will be forwarded electronically by the relevant doctor or hospital to the General Register Office for Northern Ireland (GRONI), who will forward it to the registration office which covers the deceased's home address. The relevant relative or other person registering the death can then arrange to formally register the death. This has to be done within five working days from when the MCCD has been received from the hospital, rather than from when the death occurred - unless the event has been referred to a Coroner.

Typical reasons for referring a death to a Coroner are: "the deceased had not been seen by doctor within 28 days before death"; "the death was not caused by natural illness", or "the cause of death was unclear, sudden or suspicious" (nidirect, 2024a). A more complete list of scenarios is provided here:

"A death is reported to a Coroner in the following situations:
a doctor did not treat the person during their last illness
a doctor did not see or treat the person for the condition from which they died within 28 days of death
the cause of death was sudden, violent or unnatural such as an accident, or suicide
the cause of death was murder
the cause of death was an industrial disease of the lungs such as asbestosis
the death occurred in any other circumstances that may require investigation

A death in hospital should be reported if:
there is a question of negligence or misadventure about the treatment of the person who died
they died before a provisional diagnosis was made and the general practitioner is not willing to certify the cause
the patient died as the result of the administration of an anaesthetic

A death should be reported to a Coroner by the police, when:
a dead body is found
death is unexpected or unexplained
a death occurs in suspicious circumstances

A death should be reported by the Governor of a prison immediately following the death of a prisoner no matter what the cause of death is."
nidirect (2024b)

Scotland

There is a separate legal system in Scotland. Deaths have to be registered within eight days. If an individual dies at home the family doctor should be contacted. They should then be able to provide a MCCD which is needed by the Registrar to register the death or report the event to the Procurator Fiscal. Similarly, if an individual dies in hospital and the cause of death is quite apparent, the hospital can issue a MCCD or, if appropriate, report the occurrence to the Procurator Fiscal.

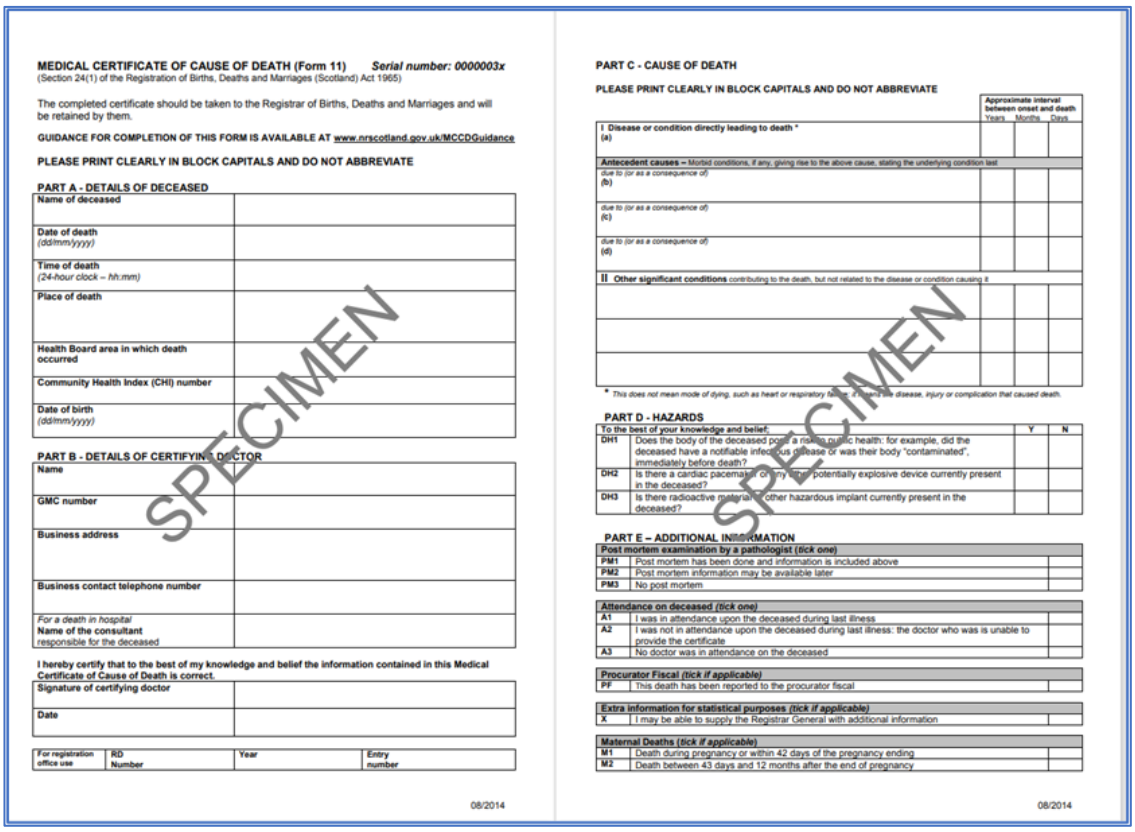
Procurators Fiscal are qualified lawyers who are employed by Crown Office and Procurator Fiscal Service (COPFS) and who act on the instructions of the Lord Advocate. It is the Lord Advocate's responsibility to investigate any death which requires further explanation.

The usual way in which a death comes to the Procurator Fiscal's attention is via a report from a GP, hospital doctor, Registrar, or the police. "Most sudden and unexplained deaths are reported to the Procurator Fiscal because a doctor is unable to confirm the cause of the death and is therefore unable to issue a death certificate" (COPFS, 2024). "However, anyone who has concerns about the circumstances of a death can report it to the Procurator Fiscal" (The Scottish Government Law Reform Division, 2017:7). Other categories of death that are investigated by a Procurator Fiscal include suspicious deaths, Fatal Accident Inquiries (FAIs) and disaster victim identification. Thus, the Procurator Fiscal may enquire into any death that is brought to his/her attention. According to Parks and Maskell (2022) this means that about 20% of deaths are considered 'reportable' to a Procurator Fiscal. The Crown Office and Procurator Fiscal Service (COPFS) delegates investigations to its Scottish Fatalities Investigation Unit (SFIU); SFIU has three teams that look after different parts of Scotland (East, North, and West).

There are specific categories of deaths that have to be investigated. In England and Wales this means where the deceased died while in custody or state detention as defined by section 1(2) of the Coroners and Justice Act 2009 (https://www.legislation.gov.uk/ukpga/2009/25/section/1). In Northern Ireland, if a death occurs in a prison. In Scotland, deaths of persons subject to compulsory treatment under mental health legislation (including detention or community based compulsory treatment order), or deaths of persons subject to legal custody, and any deaths thought to be the result of intentional (deliberate) self-harm are investigated by the COPFS (COPFS, 2024).

Medical Certificate of Cause of Death

The World Health Organization provides guidance for physicians on use of the international form of the MCCD; its 4th edition was published in 1979 (WHO, 1979). Individual countries also provide national guidance. This can lead to variations in approaches to not only completing the MCCD but also its content. Within the UK, the form for England and Wales (ONS and HM Passport Office, 2022) allows only three lines for Part I, as does that used in Northern Ireland (DHNI, 2022), whereas in Scotland (Scottish Government, 2018) there is provision for four lines - see Figure 3.1.



MEDICAL CERTIFICATE OF CAUSE OF DEATH (Form 11) ***Serial number: 0000003x***
(Section 24(1) of the Registration of Births, Deaths and Marriages (Scotland) Act 1965)

The completed certificate should be taken to the Registrar of Births, Deaths and Marriages and will be retained by them.

GUIDANCE FOR COMPLETION OF THIS FORM IS AVAILABLE AT www.nrscotland.gov.uk/MCCDGuidance

PLEASE PRINT CLEARLY IN BLOCK CAPITALS AND DO NOT ABBREVIATE

PART A - DETAILS OF DECEASED

Name of deceased	
Date of death *(dd/mm/yyyy)*	
Time of death *(24-hour clock – hh:mm)*	
Place of death	
Health Board area in which death occurred	
Community Health Index (CHI) number	
Date of birth *(dd/mm/yyyy)*	

PART B - DETAILS OF CERTIFYING DOCTOR

Name	
GMC number	
Business address	
Business contact telephone number	
For a death in hospital **Name of the consultant** responsible for the deceased	

I hereby certify that to the best of my knowledge and belief the information contained in this Medical Certificate of Cause of Death is correct.

Signature of certifying doctor	
Date	

For registration office use	**RD Number**	**Year**	**Entry number**

08/2014

SPECIMEN

PART C - CAUSE OF DEATH

PLEASE PRINT CLEARLY IN BLOCK CAPITALS AND DO NOT ABBREVIATE

	Approximate interval between onset and death: Years	Months	Days
I Disease or condition directly leading to death * (a)			
Antecedent causes – Morbid conditions, if any, giving rise to the above cause, stating the underlying condition last			
due to (or as a consequence of) (b)			
due to (or as a consequence of) (c)			
due to (or as a consequence of) (d)			
II Other significant conditions contributing to the death, but not related to the disease or condition causing it			

* This does not mean mode of dying, such as heart or respiratory failure, but the disease, injury or complication that caused death.

PART D - HAZARDS

To the best of your knowledge and belief:		**Y**	**N**
DH1	Does the body of the deceased pose a risk to public health: for example, did the deceased have a notifiable infectious disease or was their body "contaminated", immediately before death?		
DH2	Is there a cardiac pacemaker or any other potentially explosive device currently present in the deceased?		
DH3	Is there radioactive material or other hazardous implant currently present in the deceased?		

PART E – ADDITIONAL INFORMATION

Post mortem examination by a pathologist ***(tick one)***		
PM1	Post mortem has been done and information is included above	
PM2	Post mortem information may be available later	
PM3	No post mortem	

Attendance on deceased ***(tick one)***		
A1	I was in attendance upon the deceased during last illness	
A2	I was not in attendance upon the deceased during last illness: the doctor who was is unable to provide the certificate	
A3	No doctor was in attendance on the deceased	

Procurator Fiscal ***(tick if applicable)***		
PF	This death has been reported to the procurator fiscal	

Extra information for statistical purposes ***(tick if applicable)***		
X	I may be able to supply the Registrar General with additional information	

Maternal Deaths ***(tick if applicable)***		
M1	Death during pregnancy or within 42 days of the pregnancy ending	
M2	Death between 43 days and 12 months after the end of pregnancy	

08/2014

SPECIMEN

Figure 3.1: Example of Medical Certificate of Cause of Death used in Scotland

Source: https://www.nrscotland.gov.uk/files//statistics/death-certificates/f11-mccd-from-6-aug-14.pdf Accessed 31 March 2022. *Reproduced with the permission of the National Records of Scotland.*

The facts that Coroners and Procurators Fiscal seek to establish

The Coroner's role in England and Wales is defined under section 5 of the Coroners and Justice Act 2009 (https://www.legislation.gov.uk/ukpga/2009/25/section/5) as to ascertain: (a) who the

deceased was; (b) how, when and where the deceased came by his or her death; and (c) the particulars (if any) required by the Births Deaths and Registrations Act 1953 to be registered concerning the death. In Northern Ireland Coroners are concerned with establishing (a) and (b) above. In Scotland, the Procurator Fiscal has the additional responsibility of considering whether to investigate and prosecute any crime connected with a death.

How and when possible drug-related deaths are reported

As we have seen, Coroners and Procurators Fiscal are likely to be involved in investigating sudden, unexpected and suspicious deaths. Some of these events may have been the result of the administration of substances, whether psychoactive or not. For example, the latest coronial statistics for England and Wales show that out of 35,643 Inquest Conclusions handed down in 2022, there were 3,973 (11.15% compared to 12.04% the previous year) described as 'drugs/alcohol related' as well as others which would be covered by 'suicide' and other conclusions (Ministry of Justice, 2022, 2023).

In addition, Coroners and Procurators Fiscal (under the Fatal Accidents and Sudden Deaths etc (Scotland) Act 2016) also have a responsibility to investigate deaths of individuals 'in contact with the police', in 'police custody' or in 'state custody' e.g., penal establishments, immigration removal centres, secure training centres, Mental Health Act detentions, local authority secure children's homes.

Many deaths in police and prison custody involve drugs. For example, the Prisons and Probation Ombudsman (2023) investigated 404 deaths in 2022/23 that occurred in England and Wales, 65 of which were 'non-natural' ones (most of which were drug-related) but another 20 deaths currently remain unclassified (but most of which are expected, based on past experience, to be drug-related). This is a higher rate than the 88/1830 deaths that occurred in the period 2008-2016 (ONS, 2019).

"Deaths in, or following, police custody are defined as those deaths that happen whilst a person is under arrest, or detained under the Mental Health Act 1983, or where a person is no longer detained but their death arises from injuries or medical problems that developed or were identified during their detention. This includes deaths that occur within a police custody suite, but also on private or medical premises, or in transport to or from these premises, or in any other public place."
Home Office (2021)

Drugs and/or alcohol featured as causes in around half (49%) of such deaths in England and Wales during the period 2004/05 - 2014/15: about 27% were described as due to 'drug/alcohol overdose and approximately 23% as 'drug/alcohol related', i.e., where long-term abuse of drugs

or alcohol is associated with the cause of death (Lindon and Roe, 2017:32). In 2020-21, of 19 deaths in or following police custody, 14 (73.7%) involved individuals

"known to have a link to alcohol and/or drugs. This meant that at the time of their arrest they had recently consumed, were intoxicated by, in possession of, or had known issues with alcohol and/or drugs. Where cause of death is reported, a pathologist recorded that alcohol or drug toxicity, or long-term abuse, was likely to be a contributing factor in the deaths of eight people."
IOPC (2021)

The figures for 2021-22 also indicate that the majority of such deaths were associated with alcohol and/or drugs (9/11; 81.8%); three of those were "arrested for drug or alcohol-related offences (excluding drink driving)" (IOPC, 2022). In 2022-23 there was a total of 23 deaths in this category (IOPC, 2023), two of which involved individuals "arrested for drug or alcohol-related offences (excluding drink driving)". Overall, at least seven of the deaths in this category involved alcohol and/or drugs; many deaths were still undergoing investigation in February 2024.

According to data available in April 2024 on the website of the Scottish Prison Service (https://www.sps.gov.uk/about-us/transparency/death-custody) there were 40 deaths in Scottish prisons in 2023. At least 8 (20%) involved drugs; 12 were still under investigation. Six out of 44 deaths (14%) in 2022 involved drugs. At least 15 of out 53 deaths (28.3%) in 2021 involved drugs. The proportion in 2020 was 8/34 (23.5). Unfortunately, statistical information on drug-related deaths in police custody in Scotland does not appear to be available.

Processes for investigating drug-related deaths

Drug-related deaths are most likely to occur in sudden, unexpected or suspicious circumstances, and occasionally violent ones. However, not all drug-related deaths will be caught by the requirements regarding reporting to Coroners and Procurators Fiscal outlined above. The exceptions are deaths due to HIV/AIDS or hepatitis acquired through intravenous drug use.

England and Wales

When a suspected drug-related death is reported to a Coroner, their primary responsibility is to:

"• decide whether an investigation is needed; and if it is,
• investigate to establish the identity of the person who has died; how, when, and where they died; and any information they need to register the death; and,
• use information discovered during the investigation to help prevent other deaths."
Ministry of Justice (2020:8)

They will instruct (one of) their Coroner's Officer to initiate inquiries on their behalf. Coroner's officers may be civilian police staff, local authority staff, seconded serving police officers or retired police officers. Their tasks include liaison with bereaved families and witnesses, as well as to:

"get information from bereaved families, the police, doctors, mortuary staff, hospital bereavement staff and funeral directors. They will also get information and documents from those who may have been involved in the death, such as witnesses, or those a coroner decides is an 'interested person' in the investigation."
Ministry of Justice (2020:9)

If the Coroner decides that these initial inquiries indicate that a death was not due to natural causes or was natural with the cause unexplained they may request a pathologist to conduct an autopsy (postmortem examination). In turn, the pathologist may request histological and/or toxicological investigations. If these investigations provide evidence that the death was natural and there are no other factors, e.g., legal requirements, to hold an inquest, then a cause of death can be given, and the death registered in the normal way.

An inquest should be conducted within six months, or as soon as reasonably possible, following a death being reported to a Coroner. The hearing will normally take place in public in the Coroner's Court. The complexity of the case and whether it has to be held with a jury will determine how long the hearing may take. The Coroner determines what evidence is presented and by whom. After 'summing up' the evidence, the coroner or jury will deliver their Conclusion(s) or Verdict(s). This statement comprises: (a) the legal decision of what happened; (b) the cause of death; and (c) 'findings', i.e., what contributed to the death. A form will then be sent to the relevant Registrar to enable a cause of death to be assigned; this will be forwarded to the General Register Office (at ONS) for processing for statistical purposes.

Northern Ireland

As in England and Wales, the Coroner will get the police to gather information which will help establish if a death was natural and if a doctor can complete an MCCD. The procedures to be followed by the police are covered in detail in the Police Service of Northern Ireland (PSNI) Service Instruction on Death Investigation (PSNI, 2016). Investigation will involve speaking to the decedent's GP, relatives, those present at death, etc. If a doctor cannot sign an MCCD, the Coroner may request an autopsy, which may result in further histological and toxicological investigations. If the death is considered natural and there is no need for an inquest, the Coroner will issue a certificate for the death to be recorded by a Registrar.

The Coroner may decide if an inquest is needed, but will consult with the decedent's relatives. Suicides do not have to go to inquest in Northern Ireland. If an inquest is held, it follows the same process as outlined above for England and Wales.

In England and Wales, as well as Northern Ireland, the Coroner will await the outcome of any criminal proceedings before concluding their inquiries or inquest. Typically, the facts established in the criminal court are taken as the facts relating to death; inquests are then usually adjourned *sine die* (without a date, i.e., indefinitely).

Scotland

As noted above, in Scotland, the COPFS is home to the SFIU. This is a specialist unit responsible for investigating all sudden, suspicious, accidental, and unexplained deaths. There are three designated regional teams responsible for investigating such events. When the circumstances of a death are considered suspicious, the relevant Procurator Fiscal will request Police Scotland to look into these "circumstances and consider whether criminal charges should be brought which may lead to a prosecution" (COPFS, 2024).

Not all drug-related deaths will lead to an FAI, a judicial investigation presided over in public by a Sheriff (a type of judge allocated to a specific court). Leading evidence and calling witnesses is the role of the Procurator Fiscal; other interested parties may also be represented and ask questions. When the FAI is concluded, the Sheriff makes a determination setting out: (a) when and where the death occurred; (b) cause of death; (c) any precautions which may have prevented the death; etc. Such a hearing will only take place if the death occurred as: (a) the result of a work-place related accident; (b) in legal custody; or (c) COPFS consider it to be in the public interest. There are around 60 FAIs per year in Scotland (Parks and Maskell, 2022).

The police will gather information on the events leading up to and the circumstances of a death. This may involve interviews with relatives, friends, witnesses, and the decedent's GP. The latter may be able to provide a past medical history, including mental health and substance use, as well a medication history.

If a doctor can certify a cause of death, there may be no need for an autopsy. If a death is regarded as 'suspicious', an autopsy will be requested to make sure "all available evidence is gathered to assist with any criminal investigation, including identifying those persons responsible for the death" (COPFS, 2024). If an autopsy is conducted, the pathologist may request further investigations, including histology and toxicology.

The signing of an MCCD or a certificate from the Procurator Fiscal issued after appropriate investigation allows the registration of a death with the relevant Registrar, who will pass on the required information to the National Records of Scotland (NRS).

There have been recent calls to overhaul the way in which potential DRDs are investigated in Scotland. In particular, one commentator (Ward, 2024), suggests that the only public scrutiny of DRDs is the FAI. These are relatively few in nature and largely concern deaths in Government institutions. She further claims that only one-third of drug deaths are subject to post-term and toxicology screening. Consequently, under-reporting and misclassification of such events may occur, or even go unnoticed. The implication of this is that misleading statistics could be used by health professionals and policy-makers when making important decisions. Ward (2024) argues that much could be learnt from the Coronial System in England and Wales to improve the accuracy of statistics on drug deaths, particularly through "adopting a more immediate and detailed review process". In the author's view many of these criticisms arise from a lack of understanding of the relevant processes on the part of the commentator, rather than inherent shortcomings.

Sources of information for investigating drug-related deaths

As noted above, the Coroner or Procurator Fiscal has a range of information on which to base his/her conclusions: the statements of witnesses, emergency services, friends, and relatives collected by the Coroner's Officer and/or police; the results of any postmortem and toxicological examinations; and perhaps the medical, psychiatric, drug, and prescription history of the individual.

As with many other jurisdictions overseas, UK Coroner's Officers and police officers investigating suspected drug-related deaths can draw on a wide range of resources in collating their report to the Coroner or Procurator Fiscal. These can include information from the scene: description of the scene, including photographic, personal camera video footage, etc.; drug paraphernalia and medications found at the scene, both of which can be screened by forensic toxicologists (see also Chapter 4). Those responding to incidents, e.g., paramedics, first responders, ambulance personnel, fire service personnel, and police officers may have completed reports; they may also have body-worn video camera footage. Finally, hospital records may be available. covering admission and intervention/treatment relating to: vital signs; blood and urine samples; liver function and other tests; x-ray, ultra-sound, and magnetic resonance imaging (MRI) scans; etc.

Types of mortality registers

In the UK, there two main types of sources for collated information on drug-related deaths: (a) 'general mortality registers' (GMRs) such as ONS, NRS and NISRA; and (b) 'special mortality registers' (SMRs) such as the National Programme on Substance Abuse Deaths (NPSAD) and the National Drug Related Deaths Database (NDRDD) in Scotland (see also Chapter 5).

In the EU, GMRs are usually maintained by the national statistical offices (as in the UK) or Health Departments. SMRs have either been specifically developed to monitor drug-related mortality combining several sources (police, forensic, etc.) or are part of existing information systems maintained by forensic institutes, medico-legal bodies, coroners, poisons centres, etc. (EMCDDA, 2009). Whilst both types of sources have their strengths and limitations (see Table 3.1), they complement each other if existing in the same country: "Reporting and cross analysis of both sources will contribute to improve their quality and will improve also the understanding and interpretation of trends (in numbers and characteristics of victims)" (EMCDDA, 2009:10).

Table 3.1: Strengths and limitations of General Mortality Registers and Special Mortality Registers in the European Union context

	General Mortality Register	***Special Mortality Register***
Strengths	Solid indicator of the population impact of health problems Complete coverage (strong legal basis, death certification) International standards for procedures and classification (ICD) Guarantee of continuity	High detection rate (if good quality) More information per case, including toxicology Clearer causal relationship between drug use and death Timelier
Limitations	Important underreporting/low detection rate in some countries Limited information in death certificate per case (e.g., toxicology, circumstances of death) Divergence across countries in some procedures and application of ICD Slow process and delay	Limited coverage in many countries No standard international classification or procedures Less guarantee of continuity Some cases may not be detected (e.g., dying in hospitals, non-marginalised populations)
Notes: Adapted from table on page 10 of EMCDDA (2009); ICD = International Classification of Diseases.		

Sources of data on United Kingdom Drug-Related Deaths

United Kingdom GMRs

Technically speaking, the three General Register Offices covering the four UK countries have responsibility for registering all deaths that occur within their borders (as well as some that may occur overseas). However, in practice, the collection and analyses of information submitted as part of the death registration process is undertaken by the following agencies: the Office for

National Statistics (ONS), covering England and Wales; the National Records of Scotland (NRS); and the Northern Ireland Statistics and Research Agency (NISRA) (see also Chapter 5).

CORONER'S CERTIFICATE AFTER INQUEST
furnished under section 11(7) of the Coroner's Act 1988

To be completed by Registrar
Register No.
Entry No.

To the ____ Registrar of Births and Deaths

Inquest held on
at
Was a post-mortem held?

PART I PARTICULARS OF DECEASED (Not still born - see separate Form 99A)
1 Date and place of death
2 Name and surname
3 Sex
4 Maiden surname of woman who has married
5 Date and place of birth
6 Occupation and usual address

SPECIMEN

Cause of death I(a)
(b)
(c)
II
Verdict

PART II VISITING FORCES
The inquest was adjourned on
*under section 7 of the Visiting Forces Act 1952
*and has not been resumed

PART III BURIAL/CREMATION
†Enter Order for Burial/Certificate E for Cremation
I have issued†
on
to
of

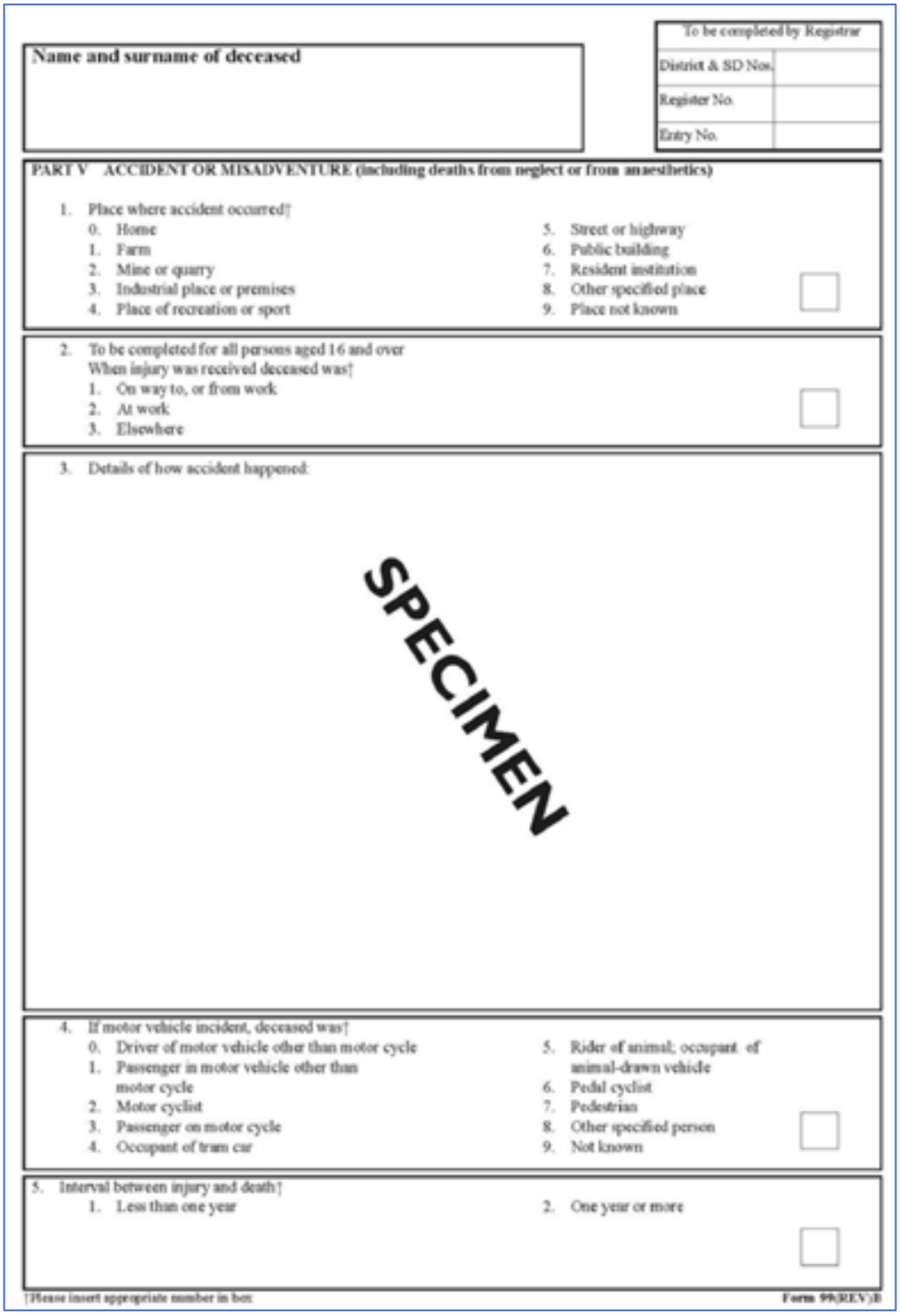
PART IV MARITAL CONDITION etc. All persons aged 16 and over
Insert appropriate number in box. 1 Single 2 Married 3 Widowed 4 Divorced 5 Not Known
If married enter date of birth of surviving spouse — Day / Month / Year

I certify that the findings of the inquest were as above.
Date Signed
Name
Appointment
Jurisdiction

*Delete as necessary
Form 99(REV)A
9817Ga 1/93

Figure 3.2a: Specimen of Part B of Coroner's certificate - page 1

Reproduced with the permission of the Office for National Statistics..



Name and surname of deceased

To be completed by Registrar

District & SD Nos.	
Register No.	
Entry No.	

PART V ACCIDENT OR MISADVENTURE (including deaths from neglect or from anaesthetics)

1. Place where accident occurred†
   0. Home
   1. Farm
   2. Mine or quarry
   3. Industrial place or premises
   4. Place of recreation or sport
   5. Street or highway
   6. Public building
   7. Resident institution
   8. Other specified place
   9. Place not known

2. To be completed for all persons aged 16 and over
   When injury was received deceased was†
   1. On way to, or from work
   2. At work
   3. Elsewhere

3. Details of how accident happened:

SPECIMEN

4. If motor vehicle incident, deceased was†
   0. Driver of motor vehicle other than motor cycle
   1. Passenger in motor vehicle other than motor cycle
   2. Motor cyclist
   3. Passenger on motor cycle
   4. Occupant of tram car
   5. Rider of animal; occupant of animal-drawn vehicle
   6. Pedal cyclist
   7. Pedestrian
   8. Other specified person
   9. Not known

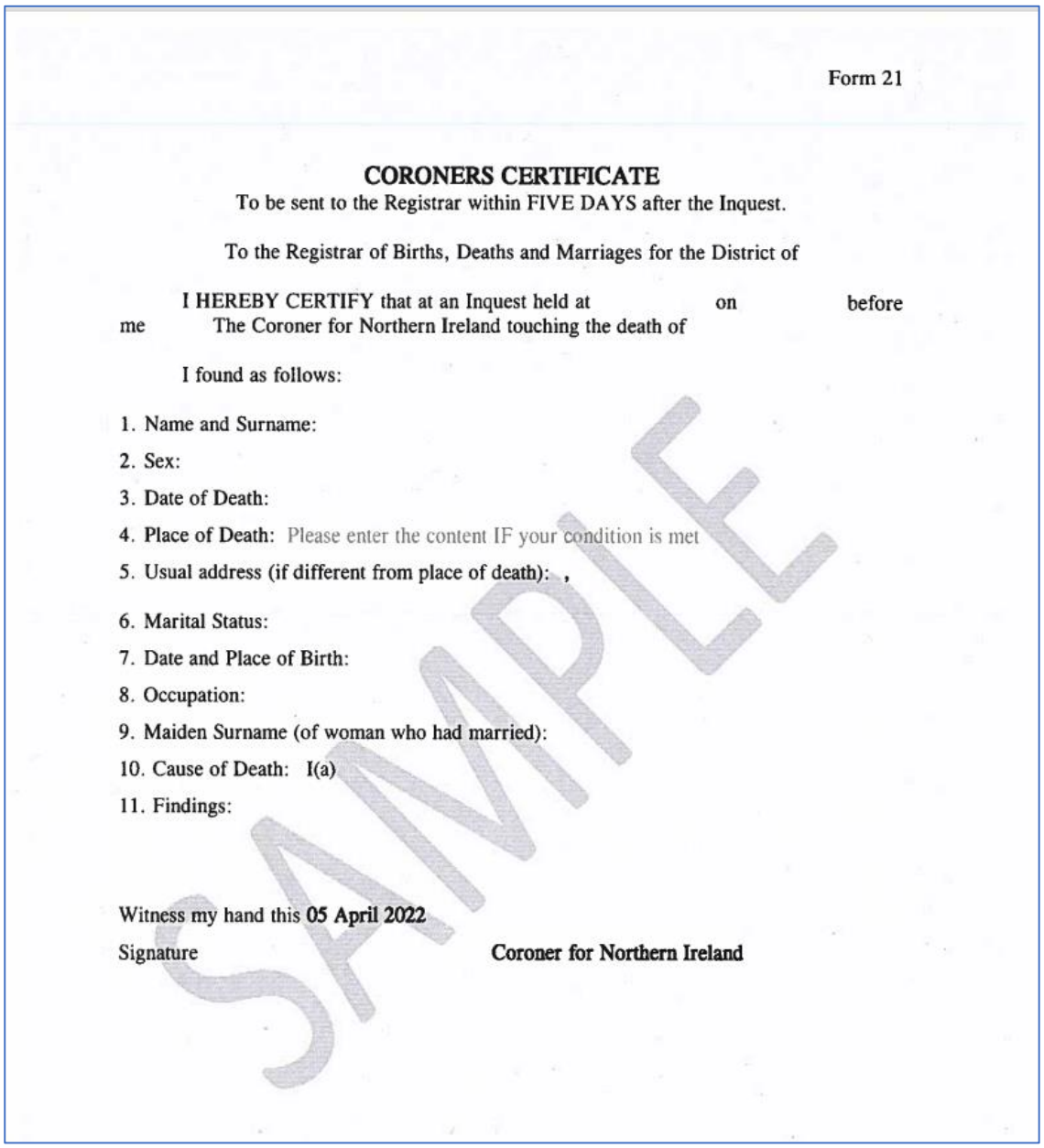
5. Interval between injury and death†
   1. Less than one year
   2. One year or more

†Please insert appropriate number in box

Form 99(REV)B

Figure 3.2b: Specimen of Part B of Coroner's certificate - page 2

Reproduced with the permission of the Office for National Statistics.



Form 21

CORONERS CERTIFICATE

To be sent to the Registrar within FIVE DAYS after the Inquest.

To the Registrar of Births, Deaths and Marriages for the District of

I HEREBY CERTIFY that at an Inquest held at on before me The Coroner for Northern Ireland touching the death of

I found as follows:

1. Name and Surname:
2. Sex:
3. Date of Death:
4. Place of Death: Please enter the content IF your condition is met
5. Usual address (if different from place of death): ,
6. Marital Status:
7. Date and Place of Birth:
8. Occupation:
9. Maiden Surname (of woman who had married):
10. Cause of Death: I(a)
11. Findings:

Witness my hand this **05 April 2022**

Signature **Coroner for Northern Ireland**

Figure 3.3: Specimen of Form 21 used by Coroners in Northern Ireland

Reproduced with permission of the Coroners' Service for Northern Ireland.

In England and Wales, most deaths are certified by a medical practitioner, using the MCCD (see above) which is then usually taken to the local Registrar by an informant, typically a relative of the decedent. However, if a Coroner has investigated a death, the information provided by him/her is used by the Registrar rather than that contained on the MCCD. Sometimes the Registrar forwards ONS additional information to ONS derived from Part B of the Coroner's certificate - (https://www.ons.gov.uk/file?uri=/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/methodologies/userguidetomortalitystatisticsjuly2017/annexc.pdf) see Figures 3.2a and 3.2b.

Thus, there are four information sources whence ONS mortality statistics are generated:

- details supplied by the doctor when certifying a death, for example, whether the body was seen after death, cause of death, when the deceased was last seen alive and whether a post-mortem was carried out
- details supplied by the informant to the registrar, for example, occupation of deceased, sex, usual address, date and place of birth, marital status, date of death and place of death
- details supplied by a coroner to the registrar following investigation, for example, cause of death (following post-mortem), place of accident (following inquest); in the case of deaths certified after inquest, the coroner supplies the registrar with all the particulars that would have been supplied by the informant
- details derived from information supplied by one of the other three sources, for example, age of deceased is derived from date of birth and coded cause of death

Details are also supplied by the informant on the spouse of the deceased (only if the deceased is either married or civil partnered), for example, name, date of birth, occupation and employment status. If the deceased was a child, the full names and occupation of the parents will be required. If these details are supplied by the coroner rather than the informant, then occupation and employment status will not be supplied."
ONS (2021:4)

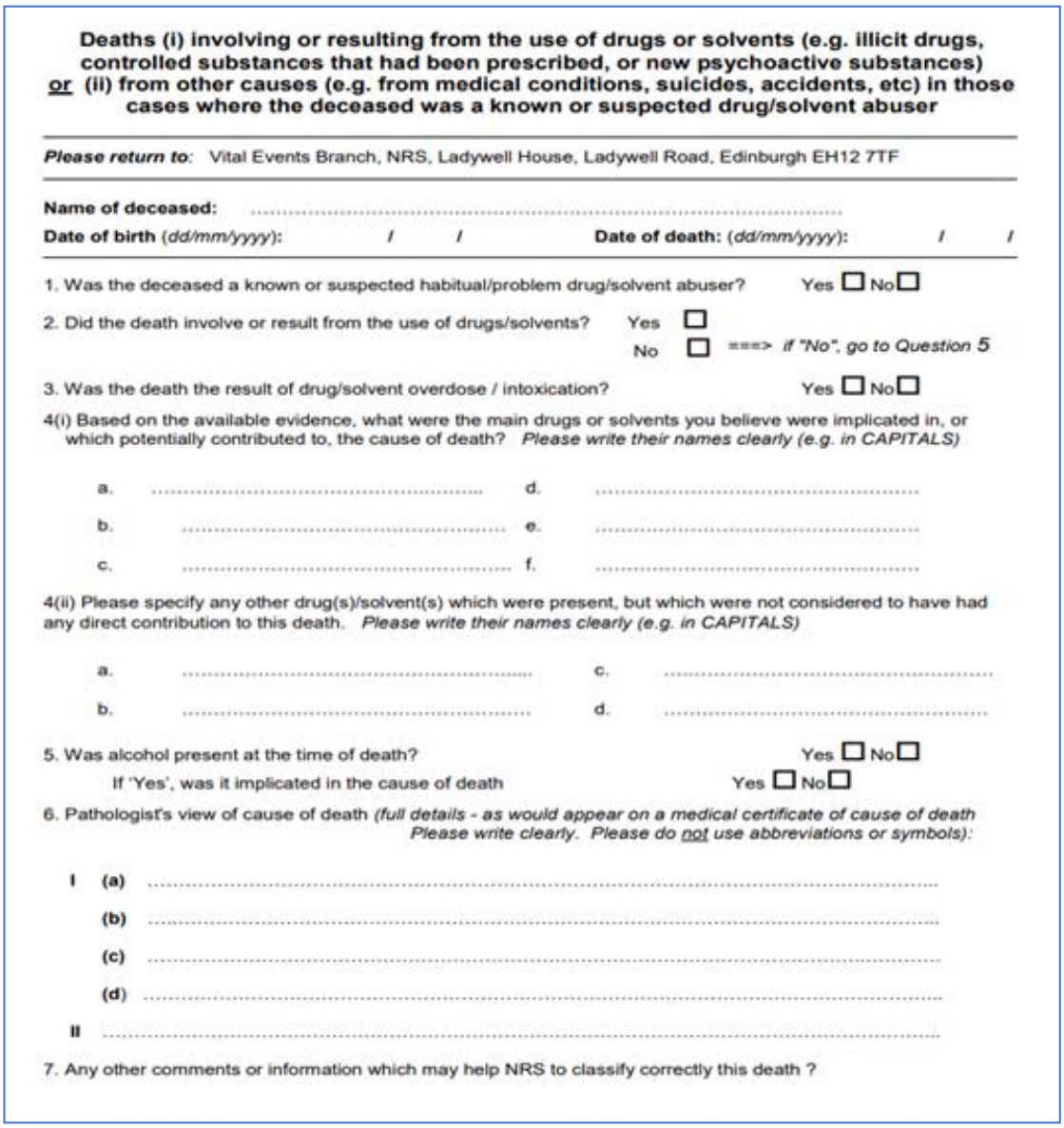
NISRA (2022a) receives information on deaths via completed MCCD forms or an interim certificate from the Coroner ('Coroner's Certificate of Evidence of Death') to allow administrative arrangements to be completed. Coroners In Northern Ireland can sign deaths off using one of three forms (personal communication to author from Claire Rocks, NISRA, on 4 March 2022): (a) Form 14 - used to certify death where a postmortem is not required; (b) Form 17 - used to certify death following a postmortem; and (c) Form 21 - used to certify death following an inquest – this form usually includes a narrative of the circumstances of the death outlined at inquest (see Figure 3.3). Thus, "All deaths statistics are sourced from two systems: i) NIROS: the Northern Ireland Registration Office System of the GRONI; and ii) CLEAR: The information management system of the Coroners Service for Northern Ireland (CSNI)." (NISRA, 2022b:8). The flow of data through the death registration system, the Coronial System and ultimately to the production and publication of death statistics is shown in Annexes 1 and 2 of the latest Quality Assurance

assessment of the process (NISRA, 2022b). The Agency does not receive any toxicological information from Coroners, other than the information contained in the 'cause of death' (personal communication to author from Claire Rocks, NISRA, on 4 March 2022).

NRS has four main sources of data on drug-related deaths: (a) the MCCD; (b) other information provided to Registrars when informants register deaths; (c) findings of the pathologist(s) – form ME4; and other information provided by other agencies, e.g., Procurators Fiscal (NRS, 2021). The ME4 form (see Figure 3.4) has been used since 2014 for deaths involving or resulting from use of controlled substances. It is completed by the 30 or so (June 2022) pathologists at the Forensic Medicine Units within Scotland who conduct investigations into drug-related deaths; each pathologist is likely to have their own way of working (see also Chapter 4).

From at least 1977 (Knight, 1977) up until 31 March 2013 there were 4 (four) toxicology providers: Glasgow (Forensic Medicine and Science, University of Glasgow) covered Glasgow and Strathkelvin, North and South Strathclyde, and Dumfries and Galloway from 2006; Edinburgh (Scottish Police Services Authority (SPSA)) covered Lothian and Borders; Dundee (Centre for Forensic and Legal Medicine, University of Dundee) covered Central, Tayside and Fife; and Aberdeen (Aberdeen Royal Infirmary) covered Grampian, Highlands and Islands .

Due to Government cutbacks this number fell to just two: the University of Glasgow took on responsibility for postmortems in the East of Scotland and part of the North of Scotland, thus looking after about 90% of cases; the remainder are dealt with by Aberdeen University who have sub-contracted the work to NHS Grampian. From 1 December 2022, the workload undertaken by the University of Glasgow transferred to the Scottish Police Authority (SPA) who are funded by direct grant from the Scottish Government. Up until mid-2022, there had been little co-ordination between the two toxicology providers. However, it is understood that discussions took place between NHS Grampian and the SPA ahead of the new arrangements (personal communication to author from Steve Scott, Crown Office & Procurators Fiscal Service, 9 June 2022). This augurs well for improved co-ordination and consistency in approach to investigating deaths (including those which are suspected to be drug-related. The SPA Forensic Service moved to a new laboratory with 'state of the art' equipment' (Forensic Services, 2023). This is underpinned by a Service Level Agreement between SPA FS and COPFS which came into effect, setting out Key Performance Indicators, the type of drugs to be examined, etc. (Scottish Police Authority, 2021).



Deaths (i) involving or resulting from the use of drugs or solvents (e.g. illicit drugs, controlled substances that had been prescribed, or new psychoactive substances) or (ii) from other causes (e.g. from medical conditions, suicides, accidents, etc) in those cases where the deceased was a known or suspected drug/solvent abuser

Please return to: Vital Events Branch, NRS, Ladywell House, Ladywell Road, Edinburgh EH12 7TF

Name of deceased: .....

Date of birth (*dd/mm/yyyy*): / / **Date of death:** (*dd/mm/yyyy*): / /

1. Was the deceased a known or suspected habitual/problem drug/solvent abuser? Yes ☐ No ☐

2. Did the death involve or result from the use of drugs/solvents? Yes ☐
No ☐ ===> *if "No", go to Question 5*

3. Was the death the result of drug/solvent overdose / intoxication? Yes ☐ No ☐

4(i) Based on the available evidence, what were the main drugs or solvents you believe were implicated in, or which potentially contributed to, the cause of death? *Please write their names clearly (e.g. in CAPITALS)*

a. ..... d. .....

b. ..... e. .....

c. ..... f. .....

4(ii) Please specify any other drug(s)/solvent(s) which were present, but which were not considered to have had any direct contribution to this death. *Please write their names clearly (e.g. in CAPITALS)*

a. ..... c. .....

b. ..... d. .....

5. Was alcohol present at the time of death? Yes ☐ No ☐

If 'Yes', was it implicated in the cause of death Yes ☐ No ☐

6. Pathologist's view of cause of death *(full details - as would appear on a medical certificate of cause of death Please write clearly. Please do not use abbreviations or symbols):*

I (a) .....

(b) .....

(c) .....

(d) .....

II .....

7. Any other comments or information which may help NRS to classify correctly this death ?

Figure 3.4: Extract from form ME4

Reproduced with permission of the National Records of Scotland.

The ME4 form includes the following information:

"whether the deceased was a known or suspected habitual drug abuser; the drugs or solvents which were implicated in, or potentially contributed to, the cause of death; any other drugs or solvents which were present but which were not considered to have had any direct contribution to the cause of death; whether alcohol was present and, if so, implicated; and the pathologist's view of the cause of death."

NRS (2022:2)

This additional information is used by the NRS Vital Events team to allocate more accurate International Classification of Diseases (ICD) codes and provides the basis for additional analyses (e.g., of the drugs involved in deaths, other substances reported in postmortem toxicology). For further information see NRS (2023).

United Kingdom SMRs

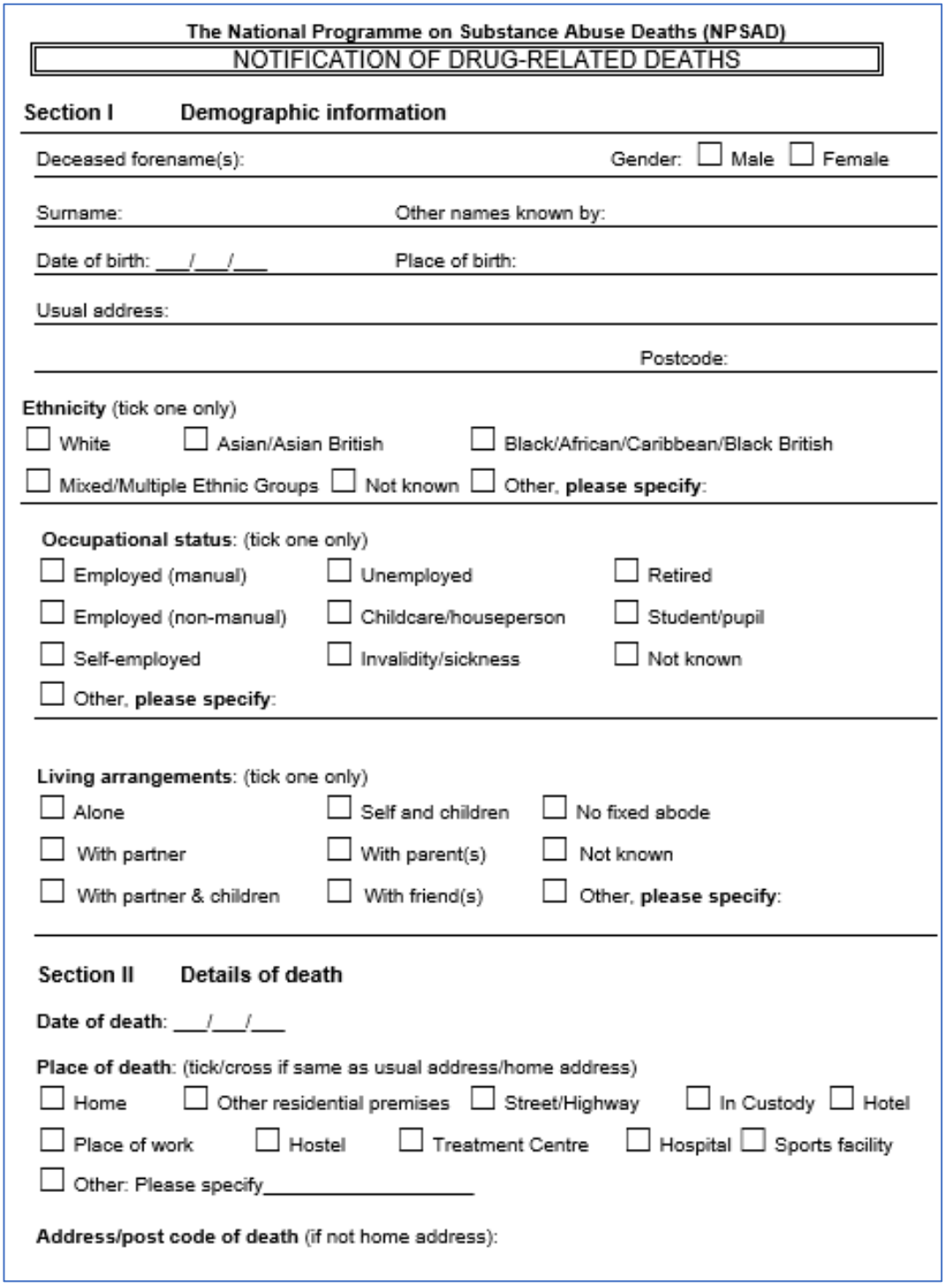
There are two principal SMRs in the UK: NPSAD based at St George's University of London (but recently transferred to King's College London) and NDRDD in Scotland (see also Chapter 5).

NPSAD receives information on a voluntary basis from Coroners in England and Wales, Northern Ireland, and the Crown Dependencies of Guernsey, Jersey, and the Isle of Man. Some information was received from several Procurators Fiscal in Scotland (1997-2003) and the Scottish Crime and Drug Enforcement Agency (2004-12). Coroners (or their staff on their behalf) are invited to complete a data-collection form and submit it by post or increasingly electronically.

The data collection form was largely developed by the author, including the piloting of an enhanced electronic version. In the past, NPSAD programme members, including the author, visited specific Coroner's office on a regular basis as these Coroners lacked resources to complete the forms. Team members extract(ed) information manually from the Coroners' files and enter(ed) them onto paper forms for later input into the database.

The data collected on the NPSAD collection form (see Figures 3.5a to 3.5c), originally prepared by the author, cover: socio-demographics, including name, usual residence, gender, date and place of birth, ethnicity, occupational and employment status, living arrangements; details of the death, including date and type of locus (place) of death; cause(s) of death as given on the death certificate; toxicology including blood, tissue and urine levels; Coroner's verdict – text; background information including recent history of drug abuse, prescribed psychoactive medication, etc.; and finally, details of the Coroner, including date of inquisition and jurisdiction.

Some Coroners also provide copies of autopsy/postmortem and toxicology reports. The form has changed very little since being first designed 27 years ago; some minor additions have been made regarding prescription history etc. No data item has been removed.



The National Programme on Substance Abuse Deaths (NPSAD)

NOTIFICATION OF DRUG-RELATED DEATHS

Section I Demographic information

Deceased forename(s): Gender: ☐ Male ☐ Female

Surname: Other names known by:

Date of birth: ___/___/___ Place of birth:

Usual address:

Postcode:

Ethnicity (tick one only)

☐ White ☐ Asian/Asian British ☐ Black/African/Caribbean/Black British

☐ Mixed/Multiple Ethnic Groups ☐ Not known ☐ Other, **please specify**:

Occupational status: (tick one only)

☐ Employed (manual) ☐ Unemployed ☐ Retired

☐ Employed (non-manual) ☐ Childcare/houseperson ☐ Student/pupil

☐ Self-employed ☐ Invalidity/sickness ☐ Not known

☐ Other, **please specify**:

Living arrangements: (tick one only)

☐ Alone ☐ Self and children ☐ No fixed abode

☐ With partner ☐ With parent(s) ☐ Not known

☐ With partner & children ☐ With friend(s) ☐ Other, **please specify**:

Section II Details of death

Date of death: ___/___/___

Place of death: (tick/cross if same as usual address/home address)

☐ Home ☐ Other residential premises ☐ Street/Highway ☐ In Custody ☐ Hotel

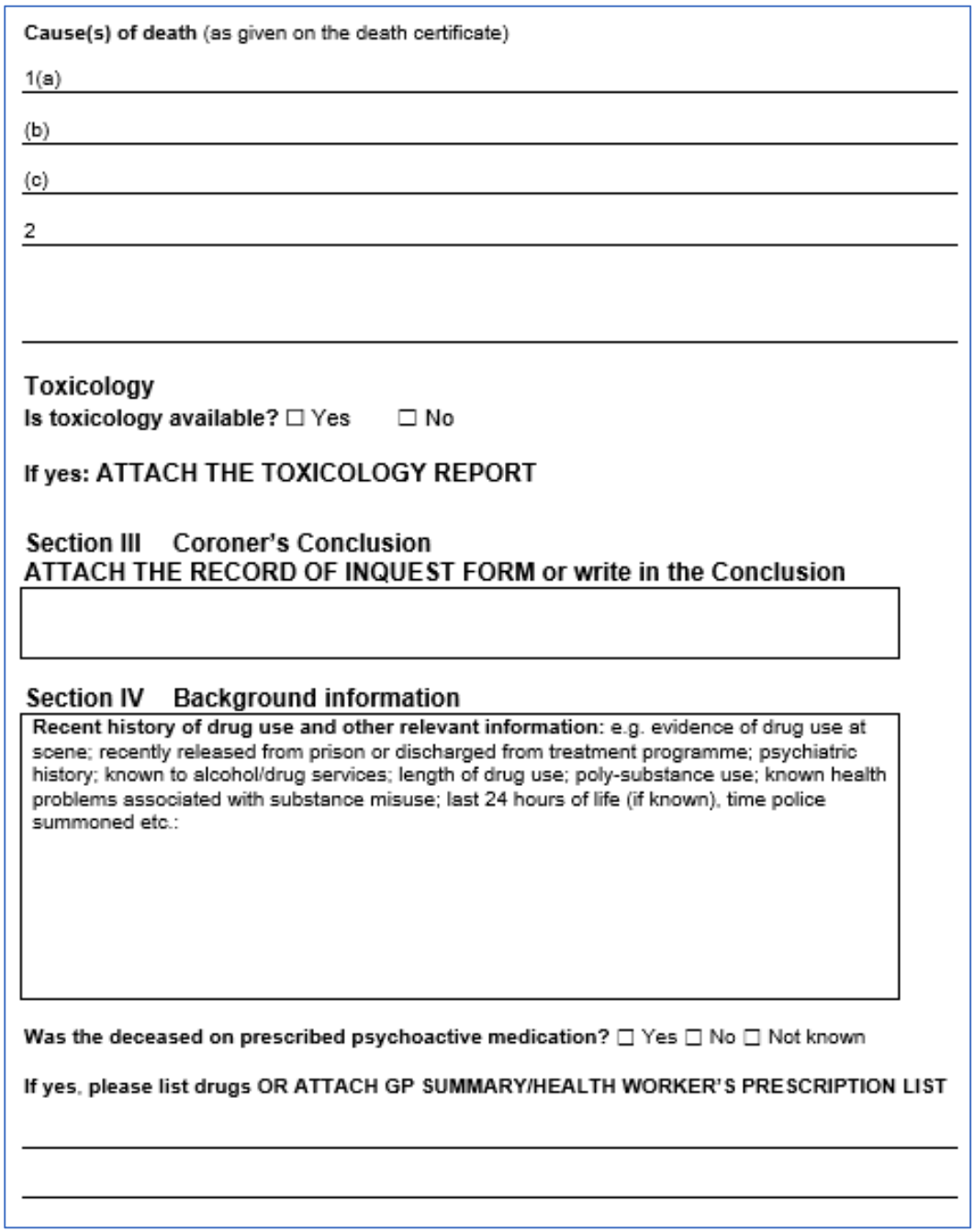
☐ Place of work ☐ Hostel ☐ Treatment Centre ☐ Hospital ☐ Sports facility

☐ Other: Please specify_____

Address/post code of death (if not home address):

Figure 3.5a: Specimen of NPSAD data collection form (2020) - page 1

Reproduced with permission of the National Programme on Substance Abuse Deaths.



Cause(s) of death (as given on the death certificate)

1(a) _____

(b) _____

(c) _____

2 _____

_____

Toxicology

Is toxicology available? ☐ Yes ☐ No

If yes: ATTACH THE TOXICOLOGY REPORT

Section III Coroner's Conclusion

ATTACH THE RECORD OF INQUEST FORM or write in the Conclusion

Section IV Background information

Recent history of drug use and other relevant information: e.g. evidence of drug use at scene; recently released from prison or discharged from treatment programme; psychiatric history; known to alcohol/drug services; length of drug use; poly-substance use; known health problems associated with substance misuse; last 24 hours of life (if known), time police summoned etc.:

Was the deceased on prescribed psychoactive medication? ☐ Yes ☐ No ☐ Not known

If yes, please list drugs OR ATTACH GP SUMMARY/HEALTH WORKER'S PRESCRIPTION LIST

_____

_____

Figure 3.5b: Specimen of NPSAD data collection form (2020) - page 2

Reproduced with permission of the National Programme on Substance Abuse Deaths.

Was the deceased a drug addict or known drug abuser? ☐ Yes ☐ No ☐ Not known

Was the deceased known to inject drugs? ☐ Yes ☐ No ☐ Not known

Did the deceased have any known mental health issues? ☐ Yes ☐ No ☐ Not known
If yes, please specify:

Section V Coroner's details

Coroner's name: Date inquest completed: __/__/__

Jurisdiction: Office:

Signature: Date: ___/___/___

Please send completed form via email to: npsad@sgul.ac.uk

For general enquiries: Tel 0207 848 6088
Email npsad@sgul.ac.uk

Figure 3.5c: Specimen of NPSAD data collection form (2020) - page 3

Reproduced with permission of the National Programme on Substance Abuse Deaths.

NDRDD derives its information from a range of sources with data linkage being conducted: NRS death data; General Acute (SMR01) and Psychiatric (SMR04) inpatient data; and Prescribing Information System data. Following any postmortem investigations on behalf of the Procurator Fiscal, the relevant Local Critical Incident Monitoring Group and Data Collection Co-ordinator decide if the case matches the inclusion criteria for the NDRDD, i.e., the ONS 'drug misuse' definition. If it does, a case record is submitted to Information Services Division (ISD), a division of National Services Scotland, part of NHS Scotland. The data sources are outlined by ISD in the following terms:

"The proforma used for NDRDD data collection was designed to collect data on a wide range of details concerning the individuals' health and social circumstances and circumstances of death. Information on the circumstances of the deceased was collected from a range of sources including the Scottish Prison Service and Scottish Ambulance Service as well as notes from drug treatment services, GPs, hospitals etc. Information was recorded using a secure online database administered by ISD. These data were then anonymised, added to the composite NDRDD dataset and analysed descriptively using SPSS…

In order to provide an alternative perspective on medical and psychiatric co-morbidities, information from ISD's general acute inpatient and day case admissions … and psychiatric inpatient admissions … datasets were linked to the NDRDD cohort. These analyses provide indicators of hospital stays (numbers of stays, time period between discharge and death … and a description of multimorbidity…

In addition, data from ISD's Prescribing Information System was used to supplement the NDRDD dataset, providing further detail about prescribing from 2009 onwards, when patient identifiable Community Health Index numbers were first included… In respect of both linkages, all relevant permissions for use and reporting of data were obtained in accordance with ISD's Information Governance processes."
Barnsdale et al. (2016:6)

Further details can be found in Appendix A2 of Public Health Scotland (2022).

Content and coverage of the main United Kingdom databases on Drug-Related Deaths

This section outlines the origins, purposes, and functions of the five main UK databases that have provided data in recent years, before considering their strengths, limitations, and complementarity. They will be dealt with chronologically in order of their creation. Their outputs will be examined in more detail in Chapter 5.

National Programme on Substance Abuse Deaths (NPSAD)

The Programme has its origins in the Home Office Addicts Index. The Addicts Index appears to have started in the 1920s as a means of keeping track of drug addicts across Great Britain (i.e., excluding Northern Ireland). It gradually developed into a more organised database in the early 1930s maintained by the Drugs Inspectorate within the Home Office. It consisted of a set of cards on which particulars of 'notified addicts' (not 'registered addicts') were kept, e.g., physical appearance, drugs of addiction, drugs used for treatment, prescriber, place of treatment, etc. The cards were indexed in various ways, included names and aliases (to try and prevent addicts getting scripts from different doctors - 'doctor shopping'). Only in 1968 was a statutory requirement introduced for addicts to be formally notified to the Chief Medical Officer at the Home Office, although the Index was still maintained by the Drugs Inspectorate. In the early 1970s the records were transferred to a mainframe computer database which was updated until the Index was closed in April 1997 due to staffing and Information Technology costs (Corkery, 1997; Clancy et al., 1998).

One of the data items recorded, both in the original card index, set up about 1934, and the subsequent electronic database, was the reason as to why an addict had ceased to be notified. One of these reasons was that the individual had died. Information was sought as to the cause of death, and this was also recorded. Various analyses of the deaths were undertaken, on a dedicated dataset extracted from the mainframe database, and included in the published statistics. Some of the information on the deaths of 'notified addicts', 'suspected' addicts and other

drug-related deaths was submitted by Coroners in England and Wales; a separate Addicts Index was maintained in Northern Ireland. When the author, who at that time was responsible for preparing and publishing the Home Office statistical bulletins on drugs, became aware of the proposed closure of the Index, he informed (the late) Professor Hamid Ghodse at St George's Hospital Medical School (https://en.wikipedia.org/wiki/Hamid_Ghodse) of its imminent demise. The reason for doing so was that members of his research team (Research Evaluation and Monitoring Unit, Department of Psychiatry of Addictive Behaviour) used to visit the Home Office Drugs Team, including the author and his predecessor (Miss Joy Mott), to extract information about the deceased addicts which were added to their Dead Addicts Database (DAD). (The DAD contained some 5,628 records compared to the Home Office Dead Addicts Database's 3,995 entries). DAD was used as the basis for a number of papers looking at the mortality of drug addicts (e.g., Oyefeso et al., 1999a, 1999b). The author contributed to this work in his role as an Honorary Research Fellow at St George's.

There was a research need, as well as a desire on the part of key stake-holders (including the author), to see the voluntary flow of information from Coroners continue so that research on the mortality of addicts was not interrupted. Discussions were held between St George's, the Chief Inspector of Drugs (Mr Alan MacFarlane), the Home Office Drugs Team (which included the author), the Home Office Coroner's Unit (headed by Mr Robert Clifford), and the Coroners' Society of England & Wales through its then Honorary Secretary (Mr Michael Burgess, then HM Coroner for both Surrey and the Royal Household) about the way forward. The result was that an announcement was put in the Coroners' Newsletter, issued by the Coroner's Unit, asking Coroners to redirect the information they would normally have sent to the Home Office to the team in the Research Evaluation and Monitoring Unit (REMU).

As a result of a steady flow of information to the REMU at St George's (which now included the author), it was decided to start analysing the data and to collect them on a systematic basis. A data collection form was designed (see Figures 3.5a - 3.5c above) and disseminated to Coroners from the newly formed national programme on Substance Abuse Deaths or *np*-SAD (more recently known simply as NPSAD). This led to an increasing flow of information. In order to thank Coroners for their contribution to NPSAD's research, and to encourage more Coroners to take part, it was decided to share the results of the data analyses with Coroners and other interested stake-holders. The first NPSAD report covering deaths notified during July-December 1997 was released in April 1998 (Ghodse et al., 1998). The most recent published data are for deaths in England 2015 (NPSAD, 2018). However, NPSAD is still continuing to collect data, 27 years after its creation, but its focus in recent years has switched to academic papers on specific drugs or issues (see also Chapter 5).

As defined in the most recent annual report from NPSAD, its principal aim "is to reduce and prevent drug-related deaths in the UK due to the misuse of drugs, both licit and illicit, by collecting, analysing, and disseminating information on the extent and nature of drug-related deaths" (Claridge and Goodair, 2015).

"The Programme's objectives are to:

- Collect and collate drug-related mortality data
- Develop and maintain a computerised surveillance system
- Monitor and examine patterns and trends, e.g. geographic, demographic, substances implicated in death, method of death
- Act as an early warning system for new trends in mortality and drug misuse
- Collaborate with relevant agencies in research on substance-related mortality locally, nationally and internationally
- Inform and facilitate discussion on the prevention of drug-related deaths, whether accidental or intentional
- Provide data for local and national drug abuse policy formulation and programme planning
- Disseminate information on drug-related mortality to the scientific community, clinicians, policy makers and other interested parties"

Claridge and Goodair (2015:30)

As we have seen above, the inclusive NPSAD case definition is wider than what is required for monitoring the national Drug Strategy, i.e., the 'drug misuse' definition, enabling the programme to look at a wider range of scenarios. The lower level of information or 'granularity' means that specific hot spots can be identified, and a closer examination made of the cases in those areas to see what interventions may be appropriate. The coroners' database acts as part of an early warning system, quickly identifying new drugs including licit ones implicated in deaths and new patterns of abuse of existing drugs (Corkery, 2008).

Starting off in 1997 with returns from a handful of Coroners' jurisdictions, the Programme gradually expanded to cover Coroners across England, Wales, Northern Ireland, Guernsey, Jersey, and the Isle of Man. As noted above, NPSAD also managed to get information from the Scottish police up until 2012. As of 1 November 2021, there were in excess of 45,000 case records on the database, of which c. 39,000 were for England (personal communication to author from the NPSAD Director, Dr Caroline Copeland, 4 April 2022). Coverage of coroner's jurisdictions in England was about 90% (personal communication to author from the NPSAD Director, Dr Caroline Copeland, 4 April 2022), compared with 81.5% in 2013 (Claridge and Goodair (2015) and 93% of jurisdictions in England and Wales in 2007 (Ghodse et al., 2008). Coverage in Wales has always quite patchy, both when the author was Programme Manager (2005-10) and subsequently (Claridge and Goodair, 2015), 4/7 of all jurisdictions were reporting in November 2021. The latest academic paper from NPSAD indicates there are over 48,000 deaths recorded in the database (Rock et al., 2023).

The complex nature of the data flows to and from NPSAD were mapped by the author in late 2008 as part of an EMCDDA initiative to compile an inventory of contemporary mechanisms and structures of EU Special Mortality Registries and to describe the available core data (Wirl, 2009). A graphical representation is presented in Figure 3.6; for full details see pp. 171-190 of Annex 3 of the project report.

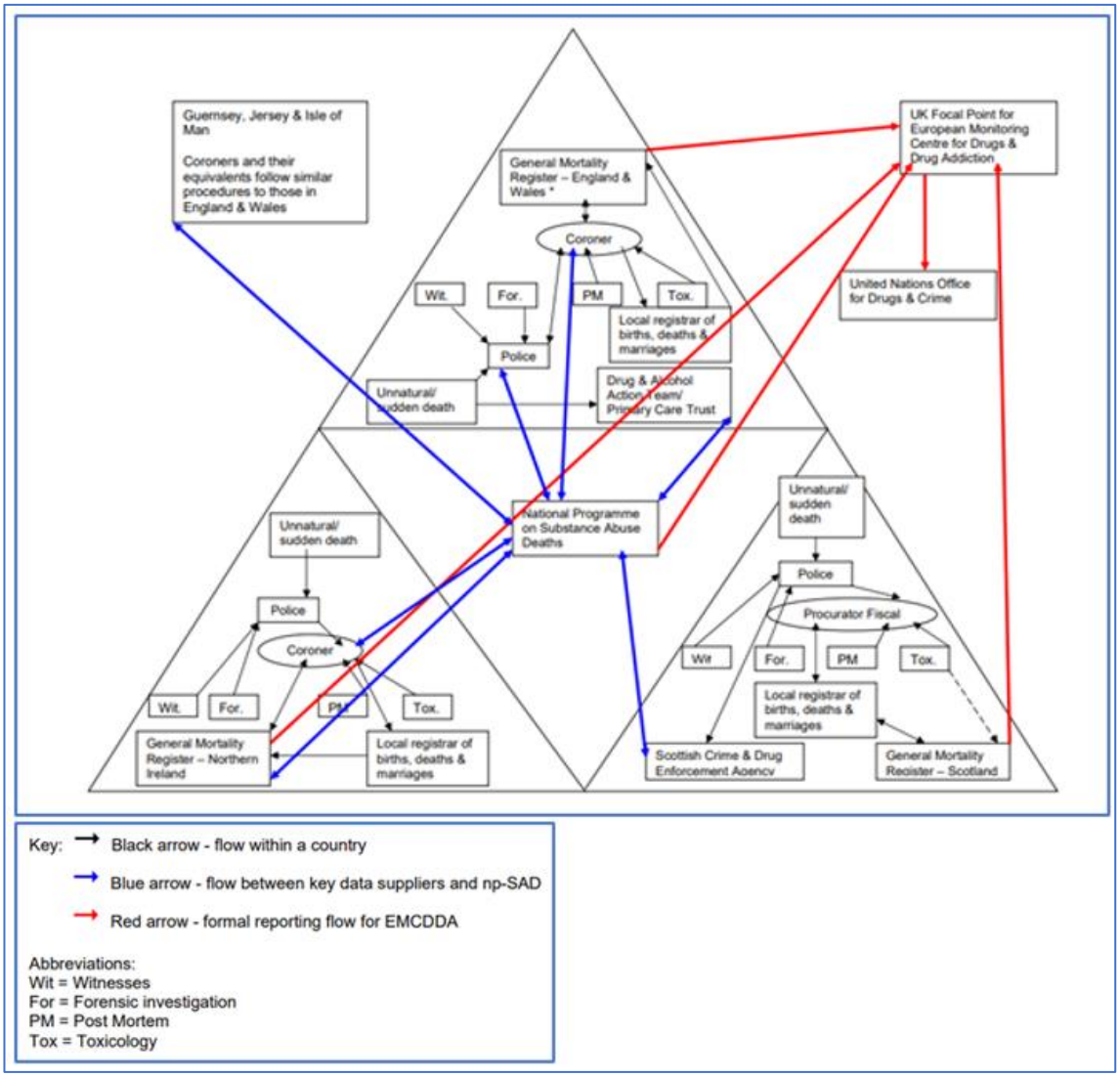


Figure 3.6: Data flow of information regarding drug-related deaths for the United Kingdom Special Mortality Register (NPSAD)

Adapted from Wirl (2009:188-189) but originally created by the author.

Consistency across the last quarter-century has been provided not only in the data collection form remaining stable over time, but also in the database remaining constant in the data it holds (albeit

its design and platforms have changed several times), but also in the continuity of programme members and detailed handovers.

The process of curating information has not changed much. Upon receipt of a form, paper or electronic, a unique case identifier is allocated, and the information entered manually into an SPSS datafile containing both numeric and string (i.e., text) variables. Some new variables are derived from the data entered. Historically, for example, ICD-10 codes (WHO, 1992) were allocated on the basis of the cause(s) of death, verdict and substances implicated. The type of drug-related death, i.e., NPSAD or 'drug misuse' definition is similarly derived using additional information regarding controlled drug status (for further details see the Appendix in Claridge and Goodair, 2015). The datafile is checked for accuracy using various 'cleaning' scripts; this enables any possible errors to be identified and corrected, e.g., misspelling of drug names, place names, coding, etc. Once this stage is completed, the datafile contents are merged with the main database; this currently occurs every four months or so. From there, filters are used in SPSS to extract the cases matching the selection criteria for specific analyses, which are then undertaken.

Due to the nature of the information collected by NPSAD, it is regarded as an observational study; hence, statistical methods typically employed are based on proportions and ratios.

> Where the data include proportions of incidence for particular groups of interest, the ratio of the proportions forms a measure of the relative risk in one group compared with that of another. These scales of measurement are generally known as point estimates. Although point estimates can be calculated they do not represent the 'true' values. Each point estimate is subject to random variation. Confidence intervals (CI) provide an indication of the range in the true values for the population as a whole, which would be expected in future investigations. The methods used for quantitative data relied mainly on complex assumptions of distributional form. It may be the case that the assumptions are not always satisfied. In such cases, methods known as distribution free methods can be applied, also known as non-parametric tests (e.g., Mann-Whitney)
> Ghodse et al. (2008:97-98)

All data held, whether electronic or paper, are stored securely and treated as confidential. Only team members have access to the full information. Any data provided to others for analysis, e.g., student projects, are suitably anonymised. In 2006, the Central Office for Research Ethics Committees (COREC), the predecessor of the National Research Ethics Service (NRES) and now the Health Research Authority, the national body responsible for upholding research ethics in the UK confirmed that approval was not required for NPSAD (Oyefeso et al., 2006). More recently (November 2020) the King's College London Biomedical & Health Sciences, Dentistry, Medicine and Natural & Mathematical Sciences Research Ethics Sub-Committee confirmed that NPSAD does not require ethics review as all subjects are deceased (Kalk et al., 2022).

Office for National Statistics (ONS)

The Central Statistical Office (CSO) and the Office of Population Censuses and Surveys (OPCS) were merged in 1 April 1996 to form the ONS.

Information regarding Mortality Statistics on Injury and Poisoning in England and Wales were published by ONS in their Series DH4 (started in the 1970s) from 2001 up until 2007 (covering deaths occurring in the period 1999 - 2005) when the series was discontinued following a consultation on restructuring ONS mortality statistics. Archived copies are available here: https://webarchive.nationalarchives.gov.uk/ukgwa/20160108040857/http://www.ons.gov.uk/ons/rel/vsob1/mortality-statistics--injury-and-poisoning--england-and-wales--series-dh4--discontinued-/index.html. Prior to this, the annual publications were the responsibility of OPCS.

The statistics contain detailed analyses of all deaths which were attributed to accidents, poisonings and violence, covering both the external cause and the nature of injury. These deaths are analysed by age (typically 10-year age-groups) and sex. Table 2 covers ICD-9 (WHO, 1978) codes: 960-979 (poisoning by drugs, medicaments and biological substances); 980-989 (toxic effects of substances chiefly nonmedicinal as to source) E850-E869 (accidental poisoning); E950 (suicide and self-inflicted poisoning by solid or liquid substances); E952 (suicide and self-inflicted poisoning by other gases and vapours); E962 (assault by poisoning); E980 (poisoning by solid or liquid substances, undetermined whether accidentally or purposely inflicted); E982 (poisoning by other gases, undetermined whether accidentally or purposely inflicted); 304 (drug dependence); and 305 (nondependent abuse of drugs, including deaths involving abuse of alcohol or of tobacco).

Table 18 covers deaths from adverse effects of chemical substances: nature of substance, external cause, etc. for ICD-9 codes 960- 989 (poisonings and toxic effects). Tables 19 and 20 cover suicides: external cause by nature of injury, year of occurrence, numbers, etc., i.e., ICD-9 codes 800-999 including 960-979 (poisoning by drugs, medicaments and biological substances) and 980-989 (toxic effect of substances chiefly nonmedicinal as to source) sub-divided by the external (E) codes: E950; E952; E980-E989; and E950-E959. Tables 21 and 22 provide similar breakdowns for homicides. Table 23 includes breakdowns by inquest verdict of the following ICD-9 codes: E850-E858 (accidental poisoning by drugs, medicaments and biologicals); E860-E866 (accidental poisoning by other solid and liquid substances); E867-E869 (accidental poisoning by gases and vapours); E870-E879 (misadventures during medical care, abnormal reactions, late complications); and E930-E949 (drugs, medicaments and biological substances causing adverse effects in therapeutic use).

The breakdowns in Tables 2 and 18-22 in terms of substances are based on chemical/drug groups rather than individual substances, drugs, chemicals, etc. However, OPCS did publish "a table of deaths due to poisonings which listed the number of deaths from specific drugs or combinations mentioned on the coroner's certificate" in the DH4 series until 1992 (Christophersen et al., 1998:33).

"The data were extracted manually from the registration forms received by ONS. This table only included deaths coded to ICD9 E850–858, E950 and E980 and excluded 304 and 305. It was difficult to extract information from this table since drugs were listed exactly as they were recorded on the coroner's certificate with no attempt to distinguish generic and trade names, single or compound preparations. The table was discontinued in 1993 when the system for collecting and processing mortality data was redeveloped.

Since 1993, data from the registration forms has been stored electronically. In order to quantify the number of deaths due to specific drugs it is now possible to carry out a text search of the cause of death information transcribed from the registration form onto the database. The deaths which contain a mention of the particular drug are then counted manually. This process is complicated by the range of generic, colloquial and brand name terms used by coroners to describe specific drugs and by the presence of compound drugs. Moreover, the registrar is required to transcribe the precise wording from the coroner's certificate, including spelling mistakes which are then entered onto the database. Some allowance is made for this when text searches are carried out but it is not possible to guarantee that every single case has been identified."
Christophersen et al. (1998)

The coding software used by ONS has been updated several times over the last 30 years, the most recent being at the start of 2020 (for further details see section 9 of ONS, 2023).

OPCS/ONS also provided case-level information for England and Wales (until 1994) for the statistics published by the Home Office in their bulletins on the Addicts Index (Corkery, 1997) - see Chapter 5 for further details.

Various outputs from the new drug-related deaths database were published in OPCS/ONS statistical series, particularly *Population Trends* (see https://webarchive.nationalarchives.gov.uk/ukgwa/20090228131447/http://www.statistics.gov.uk/statbase/Product.asp?vlnk=6303 and https://link.springer.com/journal/41499/volumes-and-issues) and *Health Statistics Quarterly* (HSQ) (see https://webarchive.nationalarchives.gov.uk/ukgwa/20090910033127/http://www.statistics.gov.uk/StatBase/Product.asp?vlnk=6725&Pos=&ColRank=1&Rank=422). However, in the last couple of decades the main vehicle for publication has been online via the ONS website (https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsrelatedtodrugpoisoninginenglandandwales/previousReleases). Examinations of these outputs will be found in Chapters 5 and 6.

Whilst theoretically, the ONS - like their counterparts in the rest of the UK - capture all deaths reported in England and Wales, they do not necessarily identify all drug-related deaths (see Chapter 2). As with all deaths, drug-related cause of death data is subject to a range of both routine automated and manual checks, including: compatibility of 'cause' fields against inquest conclusion (verdict) fields; absence/presence of final and original cause of death fields; and the underlying cause of death derived is actually mentioned in either Part I or Part II of the death certificate.

One of the 'vital' or fundamental issues facing ONS, its UK counterparts, and GMRs worldwide in producing statistics on drug-related deaths is that of the level of detail and quality of information regarding the substances causing and/or contributing to death included in the 'cause of death' fields on the MCCD or otherwise provided (if at all). All too often, as demonstrated/seen in Chapter 4, ambiguous wording such as 'multiple drug overdose' is used. This means that inclusive ICD coding (whether version 9 or 10) has had to be applied rather than more specific drug-class or substance-specific codes used, thus reducing the ability to drill down into the data or provide any level of granularity, e.g., looking at specific drug combinations.

National Records of Scotland (NRS)

NRS was created on 1 April 2011 by the merger of two national institutions, the General Register Office for Scotland (GROS) and the National Archives of Scotland (NAS).

Table C2.23 (from 1968 to 1993) and subsequently Table 6.14 (1994 to 1996), Table 6.13 (1997-9), Table 6.12 (2000) in the Registrar General for Scotland's Annual Reports gave breakdowns of poisonings by sex, cause E-codes) and intent; each entry gave the combinations of substances. The 2001 Annual Report introduced the provision of separate tables for each chapter, including deaths, e.g., Table 6.12 in the Vital Events Reference Tables; this practice has continued to the present, the latest relating to 2022 (https://www.nrscotland.gov.uk/statistics-and-data/statistics/statistics-by-theme/vital-events/general-publications/vital-events-reference-tables).

The House of Commons Select Committee on Scottish Affairs looked at drug abuse in the 1993-4 Parliamentary session, and expressed its concern about the quality of information available on this issue (HMSO, 1994). In response, an improved system to collect information on drug-related deaths was designed and introduced in 1994. The main component was a form for forensic pathologists to complete in respect of deaths where decedents were known or suspected to be dependent on drugs or where deaths involved drugs; a paper outlined the definitions used and

contained initial data for 1992-4 (Arrundale and Cole, 1995). This form has changed slightly over time; full details are available in Annex C of the Methodological Annexes (NRS, 2023). See Figure 3.4 for a copy of the version used since 2014.

Definitions changed in 2000 in line with the introduction of the new 'baseline' i.e., 'drug misuse' definition. Short 'occasional' papers were published for the years up to and including 2001, giving basic details of drug-related deaths. Although the name of the publication changed, the format of the report remained consistent. Over time, additional analyses have been added to meet new needs (see below).

GROS followed the example of OPCS and set up a dedicated database for drug-related poisoning deaths in 1994. Since its establishment, the analysis of data from this database has been undertaken/overseen by only four statisticians: Mr Graham Jackson up to 2008, Mr Frank Dixon 2008-2021, Dr Maria Kaye-Bardgett 2021-3, and currently Ms Beth Watson. This means there has been deep and consistent institutional and personal knowledge and understanding of the data received, analysed, and disseminated.

Consistency has also been a feature of the toxicological information generated on drug-related deaths in Scotland since postmortems were carried out in only four academic forensic departments until recent years; they are now conducted in two centres. Forensic Services - Scottish Police Authority do not provide any information direct to NRS; such information probably feeds into the postmortem report that goes to the Procurator Fiscal (personal communication to author from NRS Vital Events Statistician on 27 April 2022). This means that there is a considerable degree of consistency in approach, to pathological investigations, unlike in England and Wales. Advice about the classification of substances reported in the toxicological information received by NRS has been provided on a regular basis by the author to the current and previous statisticians responsible for drug-related deaths - see Annex C pages 7 and 9 of NRS (2023). This provides additional continuity and consistence in interpretation of toxicology.

As with ONS and NISRA, NRS covers all deaths reported within the area for which it is responsible. It too has also had to make changes made in response to UK-wide drug strategy initiatives, e.g., the introduction of the 'drug misuse' baseline definition, modifications to ICD codes (see Chapter 5 for further details and an examination of what the published data show), changes in the range of substances available, e.g., Novel Psychoactive Substances, etc.

Northern Ireland Statistics and Research Agency (NISRA)

NISRA, which also incorporates the General Register Office (GRO), is an executive agency within the Department of Finance (Northern Ireland) and was established on 1 April 1996. It covers all deaths registered within Northern Ireland.

The Registrar General's Annual Reports contained some limited information within the 'cause of death' table, broken down by sex and age-group, on deaths from: drug dependence (ICD-9 code 304); non-dependent abuse of drugs (ICD-9 code 305); poisoning by drugs, medicaments and biological substances (ICD-9 codes 960-979); accidental poisonings by drugs, medicaments and biologicals (E850-E858); drugs, medicaments and biological substances causing adverse effects in therapeutic use (E930-E949); suicide and self-inflicted poisoning by solid or liquid substances (E950); assault by poisoning (E962); poisoning by solid or liquid substances, undetermined whether accidentally or purposely inflicted (E980). Only 960-979 and E850-E858 had breakdowns by type of substance. These breakdowns were provided in Abstract 20 during the period 1979-95 and in Table 6.4 for 1996-2000. With the implementation of ICD-10 in 2001 in Northern Ireland, Table 6.4 started to include the equivalent new codes; this has continued up to the latest published report (for 2022).

Information on substances mentioned in the cause of death field has only been available electronically since the start of 1997; any investigations on pre-1997 data have to be carried out by a manual inspection of death certificates.

"During registration [of deaths] all information is entered on to an electronic system called the Northern Ireland Registration Office System (NIROS), which is managed by NISRA's General Registrar Office (GRO). Statisticians within NISRA's Vital Statistics Unit have access to the data contained within NIROS for analysis on behalf of the Registrar General for Northern Ireland."
NISRA (2020:2)

However, the only published figures that were released into the public domain at this time were those provided by NISRA to the author in his role as the DRD expert for the UK Focal Point on Drugs for inclusion in the annual report to the EMCDDA. The provision of an annual anonymised dataset to the author under a formal arrangement, to enable him to analyse the data and derive the published statistics, continued until the introduction of the General Data Protection Regulation or GDPR in 2017. A similar protocol was agreed for the provision of data covering the period 2014-18 for the EU-MADNESS project (European Commission (Drug Prevention and Information Programme 2014-16; contract no. JUST/2013/DPIP/AG/4823) work-stream on deaths associated with Novel Psychoactive Substances led by the author.

The first annual release of Drug-Related and Drug-Misuse Deaths, Northern Ireland occurred on 26 February 2009, with a time series covering the period 1997-2007 (NISRA, 2009). (The author reviewed the first release for NISRA.) Copies of annual releases are available online for the period 2001 onwards can be found here https://www.nisra.gov.uk/statistics/cause-death/drug-related-deaths. Chapters 5 and 6 include examinations of what the published data show.

Up to the mid-2000s, there were seven separate coroner's jurisdictions in Northern Ireland. These were amalgamated in April 2006 into one centralised Coroners Service for Northern Ireland, headed by a High Court judge supported by four coroners. There is also a single State Pathologist, supported by several pathologists, centred on one main operational unit on the campus of Belfast's Royal Victoria Hospital; they support the work of the coroners. Forensic Science Northern Ireland is also based in a single location. Whilst the Police Service of Northern Ireland is its main customer, the agency provides toxicology services for the State Pathologist. The fact that these all three services are centralised means that there should be consistency of approach within each agency. In addition, they all are responsible to the Northern Ireland Department of Justice.

Whilst all three GMRs in the UK use WHO ICD-10 cause of death coding and internationally agreed rules, there are differences in their implementation. NRS use bespoke software by NRS to apply these rules and produce ICD10 codes. ONS use IRIS Software (http://www.dimdi.de/static/en/klassi/irisinstitute/about-iris/index.htm) to apply coding rules for England, Wales, and Northern Ireland (NISRA, 2020:7). A change was made to the wording of the 'drug misuse' definition used for the 2020 statistics.

"The change involved moving from:
"deaths where the underlying cause is drug poisoning, drug abuse or drug dependence and where any of the substances controlled under the Misuse of Drugs Act (1971) are involved"
to
"deaths where the underlying cause is drug poisoning, drug abuse or drug dependence or where any of the substances controlled under the Misuse of Drugs Act (1971) are involved."
"This allows the direct comparison of NI drug-misuse deaths data with England and Wales."
NISRA (2020:6)

National Drug Related Deaths Database (NDRDD)

Against a background of continual rises in the number of DRDs in Scotland during the early 2000s, a series of national initiatives were taken which, in part, culminated in 2008 with the publication by the Scottish Government of its national strategy for tackling drug misuse "The Road to

Recovery" (Scottish Government, 2008). With support from Alcohol and Drug Partnerships (ADPs) and local DRD monitoring groups, under the auspices of the National Forum on Drug Related Deaths, the development of the Database was led by ISD during 2008-9 "to collect in depth information on the nature and circumstances of individuals who have died a drug related death" (Graham et al., 2010:6). The oversight of data collection and reporting became the responsibility of Partnership for Action on Drugs in Scotland Harms Group in 2016, with ISD remaining responsible for the Database.

As outlined earlier, when an unexpected death occurs a Sudden Death Report is completed and passed by the police to the Procurator Fiscal who may decide to make further investigations. After any autopsy is completed, the Local Critical Incident Monitoring Group and Data Collection Co-ordinator decide if the case is suitable for inclusion in the NDRDD; if so, a record was submitted to ISD for cases occurring before and up to 2013. Thereafter, data co-ordinators in each area have been entering information directly into a secure database managed centrally by ISD.

The routine reporting of DRDs by NRS is complemented by the NDRDD, allowing comparisons to be made. Both agencies employ the 'drug misuse' definition, so the cases covered by NDRDD are a subset of all DRDs collected by NRS. There are some other differences. The main distinction is the range and depth of information collected by NDRDD that are potentially available on individual DRDs, including: socio-demographic information; details of the death; toxicology; substitute prescribing; medical and psychiatric conditions; known substance use; previous overdoses; previous contacts with services. Some of these items draw on other ISD resources which are linked routinely to the database cohort.

The aims of the NDRDD can summarised as follows:

- monitor the number of drug related deaths in Scotland;
- provide data for ADPs and the Scottish Government in progressing the Drugs Misuse strategy and preventing future drug-related deaths;
- assist in identifying or confirming trends;
- identify patterns that can help identify individuals who may be at particular risk to experience a DRD which can lead to the implementation of prevention measures; and
- inform discussion about service provision.

The NDRDD publications cover deaths registered during the period 2009-18, including the most recent (see Public Health Scotland, 2022b). Those that have been issued can be accessed here: https://www.ndc.scot.nhs.uk/National-Datasets/data.asp?SubID=26#:~:text=The%20database%20is%20a%20supplement,be%20used%20to%20draw%20comparisons. The publications contain extensive and detailed analyses of

the various aspects listed two paragraphs above. The revised overall number of records included within the trend analyses in the latest publication (Public Health Scotland, 2022) is in excess of 6,290 for the period 2009-18. Further analyses are also conducted, e.g., on suicides within the cohorts (see, for example, Barnsdale et al., 2018).

It was announced that the Scottish Government would be investing £592,000 "to improve the national drug-related death database" (Constance, 2022). This funding was allocated to Public Health Scotland in order to implement the recommendations from the Drug Death Reporting Short Life Working Group that was held in 2021 (personal communication to author from Lee Barnsdale, Public Health Scotland, on 22 May 2023). The key deliverables from that programme of work are a dataset review and new data collection tool, along with a change back to annual reports published within one year of death (Public Health Scotland, 2022a). An update on these publications was due winter 2023/4, but has not yet appeared (May 2024).

National Postmortem Toxicology Database

Over recent months a UK-wide database to collate postmortem toxicology information has been under development. It is described, thus:

"The National Postmortem Toxicology Database is managed by the Office for Health Improvement and Disparities (OHID) in the Department of Health and Social Care (DHSC). It contains data on psychoactive drugs detected in postmortem toxicology.

Coroners commission toxicological analysis of biological samples collected from the bodies of people who have died, to look for the presence of drugs. This happens where the information may help to establish the cause or circumstances of the person's death.

Laboratories that conduct postmortem toxicology analysis can send the results of individual toxicology analyses to OHID, if psychoactive drugs were found to be present. They can do this where coroners have given them permission to do so. OHID then collects these results into the National Postmortem Toxicology Database and analyses them to monitor and report on drug-related deaths trends."
OHID (2024)

Although the author was aware of this development, through his ACMD and other connections, as are other key stakeholders, e.g., toxicology laboratories, it is unlikely that all stakeholders and the general public are aware of this venture. This document is the only public source which the author can currently identify as even mentioning this project.

Strengths and limitations of Drug-Related Death and associated data

There are a number of strands that have been discussed in several of the preceding sections. They need to be gathered together briefly so that reader can follow the thread without it unravelling.

Making comparisons between the Scottish DRD database maintained by NRS and the NDRDD maintained by ISD allows one to clearly see the relative benefits and limitations of GMRs and SMRs presented in Table 3.1. UK GMRs have coverage of all deaths reported within a country but typically receive limited information from the medical cause of death certificate, with only NRS getting some limited information on toxicology. On the other hand, special mortality registers, such as NPSAD, rely on voluntary submission of information so case and geographical coverage is incomplete; but the level of detail (granularity) provided, including toxicology, is so much greater and more comprehensive.

Some record linkage has been/is performed to great effect in Scotland between the GMR (NRS) and the SMR (NDRDD), thereby enhancing the understanding of DRDs in that country. Some limited record linkage was used by the author when NPSAD programme manager; information from the GMR (NISRA) on individual cases was used to provide the Northern Ireland Coroners Service with a list of names to serve as a basis for obtaining coroner's reports and any toxicology information that it may have had.

'Validation studies' were proposed to ONS by NPSAD several times in the late 1990s, but nothing came of the suggestions. In March 2006, the author undertook a comparison, similar to that outlined in Table 3.1, of the NPSAD and ONS set-ups, and was updated in September 2009 (see Appendix A). This exercise demonstrated how beneficial, for example in terms of audit reporting, can be the use of complementary data; as noted by the EMCDDA (2009).

This led to the author suggesting several times, whilst NPSAD Programme Manager, that linking ONS and NPSAD records or exchanging details of named cases could assist with better case identification, more in-depth understanding at a national level, etc. as was subsequently done in Scotland (see previous paragraph). However, there are legal restrictions which would have to be overcome in terms ONS being able to share information with NPSAD as the latter is not a Government department or Agency; a problem not faced by NRS and NDRDD. [The author understands that it is still on the wish list of the NPSAD Director to link NPSAD data with those of ONS (personal communication, 9 May 2022).]

The limitations of the sources of information on drug deaths and how they are used are the subject of Chapter 4. Attention is now briefly turned to other 'drug indicators'.

Uses of Drug-Related Death data in conjunction with other 'drug indicators'

Data sources for other drug-related information

As we have just noted above, combining datasets or examining links between them can be very beneficial. DRD data need to be seen within the wider fabric/material available on understanding the 'drugs phenomenon'. The final section of this chapter introduces these additional threads which are woven together in Chapters 8 to 12.

Historically (from the 1930s), the only epidemiological sources available to understand the drugs' situation in the UK were the administrative Home Office datasets on notified addicts (treatment and deaths), drug seizures and drug offences (for examples, see Corkery 1997; Corkery, 1999). The first British Crime Survey looking at drug use prevalence was conducted in 1982 when it only asked about cannabis (Mott and Mirrlees-Black, 1995); comparable data have been collected since 1996 across a wider range of substances; it was renamed the Crime Survey for England and Wales in 2012. Crime Surveys have also been conducted at less frequent intervals in Scotland and Northern Ireland. School surveys covering smoking, alcohol and drug use have been conducted at fairly regular intervals across England since 1982 (NHS Digital, 2022), Scotland from 2002 to 2018 on a consistent basis (Scottish Government, 2022), Northern Ireland from 2000 to 2019 (NISRA, 2023), and Wales via the Health Behaviour In School-aged Children (see, for example, Hewitt et al., 2019); this survey is an international one, to which other UK nations contribute. Information on drug use by UK school-aged children is also available in another international study – the European School Survey Project on Alcohol and Other Drugs (ESPAD). The study has been producing reports every few years since 1995, the latest being 2019. However, the UK only participated up until 2011 (ESPAD, 2022).

Purity information has been collected since at least the early 1920s (for example, cocaine seizures are mentioned in the Metropolitan Police Office files (Personal communication to author, 19 April 2024, Geoff Monaghan) and more systematically since at least the late 1960s-early 1970s by the Home Office Central Research Establishment, Drug Intelligence Section. Indeed, purity information on powdered drugs (amphetamine, cocaine, and heroin; latterly 'crack'), dating back to 1984, from the Drugs Intelligence Unit of the then national Forensic Science Service was included in the Home Office statistical bulletins on Drug Misuse and its successor the Drug Seizures and Offenders series. Price data from the National Criminal Intelligence Service

(predecessor of the National Crime Agency) was included in the Home Office Drug Seizures and Offender bulletins for the first time for the 1997 statistics:

> "Under the new drugs strategy one of the performance indicators for aim iv – "to stifle the availability of illegal drugs on our streets" – is to increase the value of illegal drugs seized and/or prevented from entering or being distributed within the U. K. In order to monitor progress an estimate of the value of drugs seized by the police and Customs is required. Therefore, for the first time in this statistical series, average street prices have been applied to main drug types seized in 1997, to calculate values of drugs seized by type."
> Corkery (1999:18)

Other agencies such as DrugScope (https://www.drugwise.org.uk/drugscope-reports/) and the Independent Drug Monitoring Unit (http://www.idmu.co.uk/oldsite/, https://issuu.com/idmu) also conducted surveys of street drug prices. In the early to mid-2000s, the Metropolitan Police Service collected price and purity data resulting from test purchase operations (King, 2004). The fields examined were: type of drug, purchase date, amount purchased (milligrams; mg), price paid (£) and purity (%). A derived quantity, the 'unit price', was defined as the price paid per gram (£/g).

Regional Drug Misuse Databases started to be developed in Great Britain in 1990 (Donmall, 1999); these complemented the treatment data from the Home Office Addicts Index (Hickman et al., 2004). Although the Home Office Addicts Index closed at the end of April 1997 (Corkery, 1997), treatment data were now available from the national drug misuse databases covering the UK; the National Drug Treatment Monitoring System (NDTMS) had replaced the earlier regional ones in England. As outlined above, information on drug-related deaths started being collected in 1997 by NPSAD and subsequently published; alongside this, the three UK GMRs started developing special drug-poisoning deaths databases/datasets and publishing statistics.

The use of death certificate literal or textual 'cause of death' information to investigate and observe patterns in deaths is a well-established technique. Furthermore, it has been internationally deployed in the surveillance and monitoring of drug-related deaths, especially those associated with drug poisoning (e.g., Ossiander, 2014; Trinidad et al., 2016; Hedegaard et al., 2018). The author has used this approach in the UK context (see for example, Corkery, 1997; Schifano et al., 2005; Schifano et al., 2008; Corkery et al., 2022). Chapter 4 examines in detail the use of mortality data for monitoring trends, identifying emerging issues, etc..

Using different datasets on drugs – 'drug indicators'

There are three main groups of indicators suggested for monitoring illegal drug use: drug supply; drug demand; and other qualitative indicators, such as morbidity, mortality, and treatment (Inter-

American Drug Abuse Control Commission, 2017). The epidemiological indicators used in this thesis comprise: DRDs; drug seizures/interdictions/confiscations; price; purity/potency; drug offenders/offences; prevalence; availability; treatment, hospital admissions, and calls to the National Poisons Information Service. These are defined in greater detail in Chapter 8.

The data outlined in the previous sub-section can be beneficially used in conjunction with each other. In this context, the author will be referring to these as 'drug indicators' which facilitate the analyses undertaken in Chapters 8 to 12, where the relationships between them are examined in detail. The starting point for analyses was previous studies undertaken by the author with a range of colleagues over the years, but also involved updating past analyses and undertaking new ones.

Approaches to analyses in this thesis

The methodological approaches taken to produce this thesis (see Chapter 1) differ according to the chapters and sections under consideration. Broadly speaking, they comprise: literature reviews, e.g., Chapters 1 to 5, and 13 and 14. Statistical approaches are primarily used in Chapter 6, with correlations and regressions being used in Chapters 7 to 12.

Chapter overview

The wider context within which drug-related deaths fall is described in terms of how and when any types of death are formally reported to relevant UK agencies, and what facts Coroners, Medical Examiners and Procurators Fiscal seek to establish. The processes for investigating 'drug-related deaths' are outlined; a detailed consideration of how such processes have improved is presented in Chapter 4, together with challenges which still remain in Chapter 14.

The existence of different legal systems within the UK, and different processes and sources of information and how these impact the investigation and recording of such deaths are critically examined. Documentation used in reporting deaths are described, including Medical Certificates of Cause of Death, Coroner's certificates, and the NPSAD data collection form. The content and coverage of the main historic UK databases are detailed and compared.

The chapter concludes with a brief consideration of the strengths and limitations of drug-related and associated data, followed by an introduction to the use of combining drug-death indicators with other 'drug indicators'. This type of approach is demonstrated in detail in Part 4.

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Accessed 27 February 2024

CHAPTER 4 - DEVELOPMENTS IN INVESTIGATING AND RECORDING DRUG-RELATED DEATHS

Mortui vivos docent [The dead teach the living]
Black (2019)

Building on Chapters 2 and 3, this chapter provides a narrative description of changes in a number of key areas associated with the investigation and recording of deaths related to drugs which have contributed to a better understanding of the extent of the phenomenon. These aspects are dealt with in a logical, sequential approach focusing on process rather than presenting a simple chronology of changes. Thus, the main aspects covered are: scene investigation; identification of potential cases; toxicological investigation; autopsy/postmortem examination; understanding mechanisms of death; recording of substances on medical death certificates; International Classification of Diseases (ICD) coding; and counting cases. The basic methodological approach used here is that of the literature review.

One of the key themes in this chapter is harmonisation and standardisation in investigating drug-related deaths. There is great heterogeneity at local, regional, national, and international levels in such contexts, and at all stages of investigations, posing potential challenges for Medical Examiners, Coroners, and Procurators Fiscal.

A useful overview of dealing with the investigation of sudden and unexpected deaths from the police perspective is provided by the flow-chart in Figure 4.1 from the College of Policing (Home Office, 2024).

Scene of death investigation

The *locus* where a death took place or, in the case of a death in hospital, the *locus* where the events leading up to death occurred (including transportation to hospital) can provide vital clues as to whether or not a death may be drug-related. Investigation of such scenes can help provide information on the context of death, whether further investigations(s) and their nature are required, and ultimately facilitate evaluation and determination of the cause(s) and manner of death.

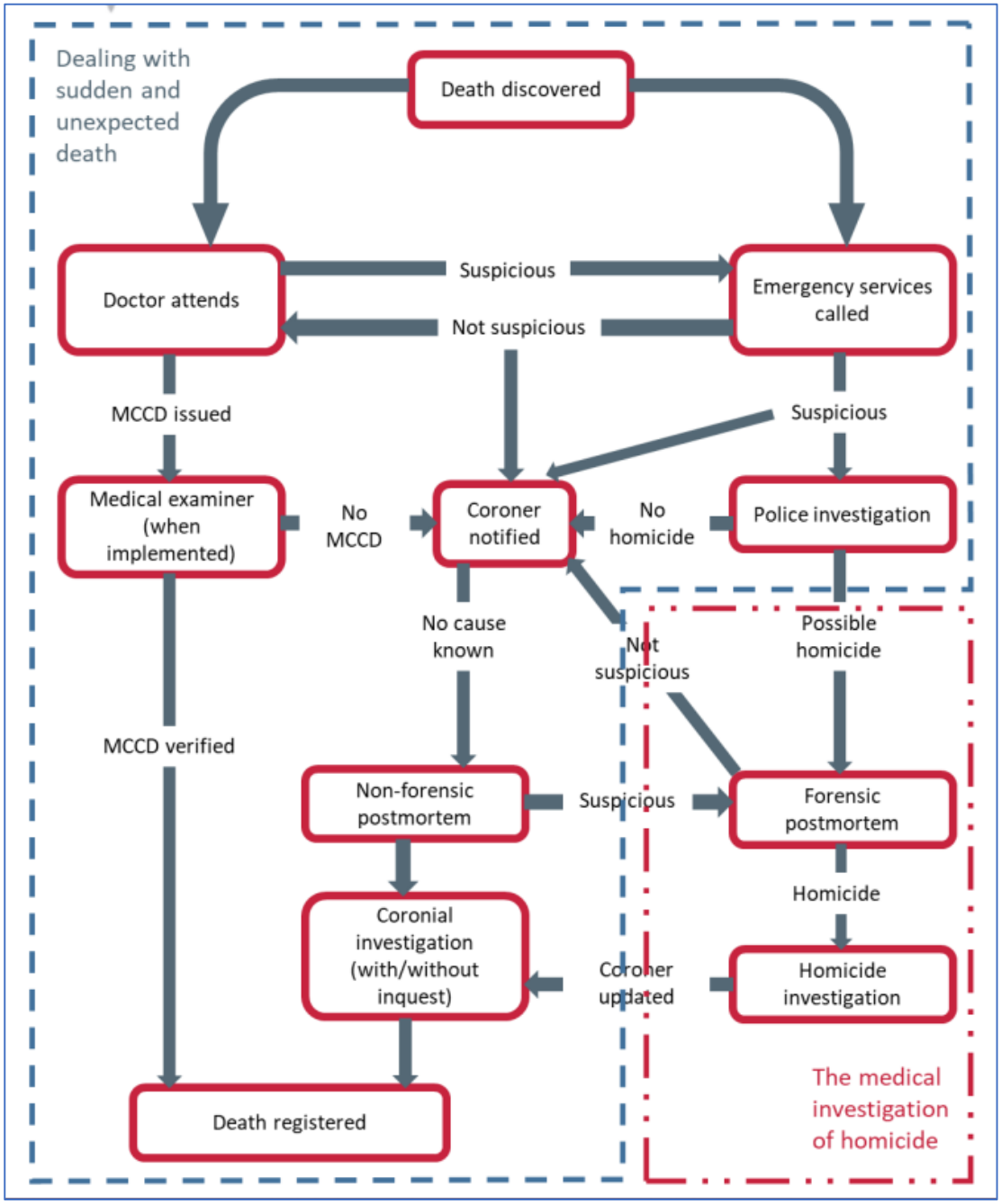

Figure 4.1: Death investigation in England and Wales

Sources: College of Policing (2019a:6); Home Office (2024:4). *© Crown copyright 2024. Reproduced with permission under the terms of the Open Government Licence v3.0.*

When emergency services are called to attend a possible intoxication or overdose, the primary concern is always the patient's safety. However, this may not be the perception that witnesses to an overdose have: "witnesses may be reluctant to call an ambulance for fear that the police will also become involved, and prosecution under some heading ensue" (ACMD, 2000:79). The

ACMD Working Group expressed their views on this point very clearly: “Our view is that a call to a person who has overdosed should be regarded by the ambulance and police services as a *medical emergency* [ACMD emphasis] in the first instance, rather than as a call to the scene of a crime”, and made it one of their recommendations [8.42] - see ACMD (2000: xxviii). This quote is also cited by Monaghan (2012:59) alongside the then existing advice to police: “THINK MURDER until the investigation proves otherwise. Initial Attendance [at the scene of a suspicious death] encompasses basic crime scene and evidence preservation as a precursor to launching the investigation”.

In a situation where speed is of the essence, it can be imagined that some clues may be overlooked and/or vital witnesses missed. Indeed, Monaghan – a retired police drug detective - makes the point: “In the absence of police to safeguard the scene, the risk of contamination by family members, friends, onlookers or even paramedics is increased” Monaghan (2012:60). “The above excerpts indicate the inherent difficulties police services face in their efforts to adopt and implement ‘harm reduction’ policies and practices” (Monaghan (2012:59).

In order to mitigate such scenarios, it is appropriate that relevant guidance and training be provided to those responsible for attending the scene of death or place of substance administration. A range of stake-holders could be involved: Emergency Services, including First Responders; Paramedics; Ambulance; Police; Fire and Rescue; Coastguard, Mountain Rescue, Royal National Life Institution (RNLI), etc.; Coroners’ Officers; Forensic Investigators; Medical Examiners, Pathologists; and Coroners or Procurator Fiscals.

International standards even include forensic investigation. For example, ISO (International Organization for Standardization) 17020 covers all aspects of incident scene investigations: including, but not limited to: assessment, search, identification of the decedent(s), body recovery, and recording (e.g., photography). This and other ISOs are listed in the United Kingdom’s (UK) Forensic Science Regulator’s Codes of Practice and Conduct (Forensic Science Regulator, 2021a). The need for such an approach to their work was recognised by the Coroners’ Officers and Staff Association (COASA):

> “It was clear [in 2011] that we should operate to a consistent and minimum standard and it was therefore agreed to set up a national training programme to achieve a measure of standardisation across the country.”
> COASA (2022)

A draft code of practice and explanatory memorandum have now been published by the Forensic Science Regulator (2023a and 2023b).

Training and guidance

The author has endeavoured to put together an overview of training and guidance put together for relevant UK stake-holders. This involved examination of institutional websites and requests, including Freedom of Information ones, to them. Several online Zoom/Microsoft Teams sessions were also conducted.

The College of Policing (https://www.college.police.uk/), a Home Office 'arm's length body' established in 2012, sets standards and curricula for English and Welsh police forces, but it is up to each Chief Constable to decide how to provide teaching/learning. The College can only rarely mandate on learning problems, e.g., firearms. Although it has not issued any guidance specifically on managing investigations of drug-related deaths, some of its online resources/reports involved reviews of drug-related cases that were missed, including as a result of 'cognitive bias' (personal communication to author from Duncan Brown, Senior Policy Advisor, College of Policing, on 14 June 2022). For example, a study into decision-making at the initial scene of unexpected deaths noted:

"Drugs and/or alcohol were factors in 13 of the 33 cases, 6 of which were either homicide or suspicious deaths. One force visited by the HOFPU [Home Office Forensic Pathology Unit] during the research period had identified (during their own in-force research) that alcohol and drugs were a feature of some death scenes which had influenced officers to make isolated decisions that the cause of death was not suspicious. Officers appeared to presume that death was because of alcohol consumption leading to injury through falling or some other cause due to intoxication. The presence of alcohol/drugs needs to form part of a broader assessment."
Home Office Forensic Pathology Unit (2015:13)

"One senior police officer stated that in their experience what tends to happen at a scene is that the first attending officer makes up their mind as to whether the death is suspicious or not, sometimes believing the first account they are given. A 'cognitive bias' … is then potentially adopted by the investigator with regard to any new evidence which comes forward and also when briefing senior officers and the coroner."
Home Office Forensic Pathology Unit (2015:14)

The College's practice advice on investigating suspected homicides covers such aspects as: initial response and actions to be taken before postmortem; victim identification; postmortem examination report, results, interpretation; release of the body; retention and disposal of materials (College of Policing, 2019b). These principles are equally applicable to suspected drug-related deaths. The College's aide-memoire (Figure 4.2) for first actions at the scene of a sudden and unexpected death illustrates some of the key aspects to be considered by the police (College of Policing, 2016; Home Office, 2024).

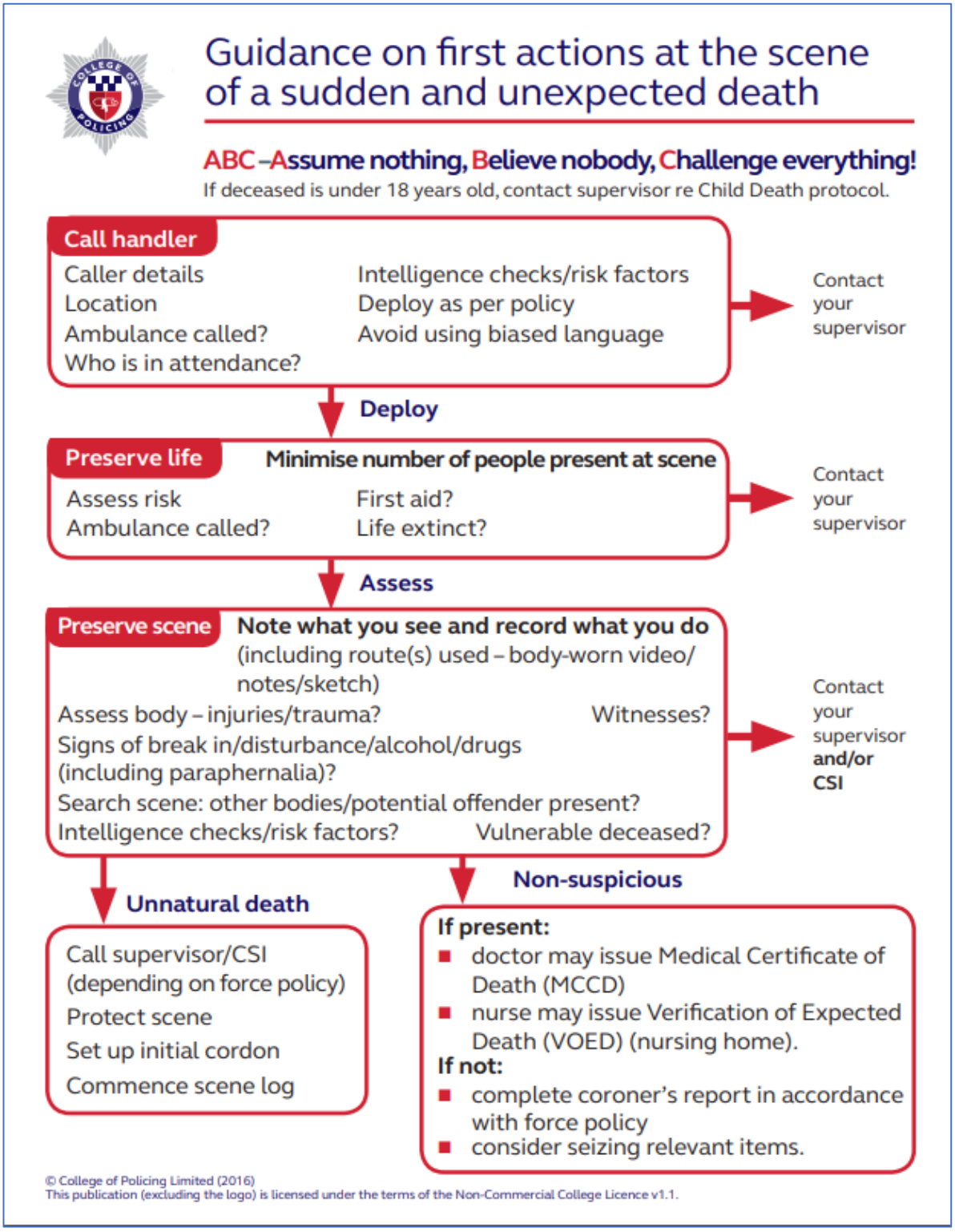

Figure 4.2: Aide-memoire for first police actions at scene of sudden or unexpected death
Sources: College of Policing (2016:7); Home Office (2024:7).

As noted earlier, it is for individual police forces to provide detailed guidance and procedures for their officers. The website (https://www.npcc.police.uk/) of the National Police Chiefs' Council (NPCC), which replaced the Association of Chief Police Officers (ACPO), has nothing specific about scene investigation or drug incidents. Indeed, enquiries made of them ended in a referral to the College of Policing (personal communication to the author from the NPCC's Business Support section, 27 July 2022). Procedures provided by Hampshire Constabulary (which also covers the Isle of Wight) also contains references to the role(s) of the local ambulance service and HM Coroners (Hampshire Constabulary, 2019). However, it only mentions drugs in passing. Other forces have very detailed guidance, e.g., Merseyside Police (2023).

The Metropolitan Police Service's "Homicide investigation policy", sourced from its Intranet site, covers the following basic principles in cases of (potential) homicides: preserve life; preserve scene(s); secure evidence; identify the victim; and identify the suspect(s) (Response on 6 August 2022 to the author's FOI request FOI-5005-22-0100-000 – see Metropolitan Police Service (2022)). The closest reference to drugs is a mention of chemical and biological material.

The Police Service of Northern Ireland (PSNI) has a similar Service Instruction providing guidance on investigating deaths as an agent of HM Coroner (PSNI, 2016). By contrast with Hampshire Constabulary, the PSNI guidance contains an eight-page section specifically on "The Investigation of Suspected Drug Related Deaths" including: Procedure on attending a Suspicious Drug Related Death; First Officer at the Scene; Scene Preservation; Police required to attend the Scene; Removal of Remains; Investigations; Attendance at Post Mortem; etc.

The responsibility for investigating most sudden or suspicious deaths usually falls to the police in England and Wales. As Coroners' Officers rarely go out to scenes of such events, they do not receive any training in that respect. As noted in the preceding paragraphs, such scenes are typically managed by the police and, as such, any evidence is preserved and stored by the police, usually until the inquest has been completed; Coroners' offices do not have the storage facilities for retention of evidence (personal communication to author from the Coroners' Officers and Staff Association, 25 July 2022). In some Coroner's jurisdictions force areas, Coroner's officers may be "required to attend sudden deaths when necessary to assist in ensuring all evidence is secured and to work with the investigative team" (Lumesse Limited, 2020).

In respect of other emergency service national training and guidance there is little or nothing regarding (potential) drug incidents/deaths. In terms of fire services, there is National Operational Guidance on compromised investigations and scene preservation, but there is no specific mention of drugs (NFCC, 2022).

The National Ambulance Resilience Unit's (NARU) remit is only "hazardous area paramedic response" (personal communication to author from Communications Manager, NARU, 26 July 2022). Even the London Ambulance Service does not appear to have any internal information on these aspects, and "there are no specific guidelines in general use within the Trust regarding scene preservation" (personal communication to author from London Ambulance Service NHS Trust, on 14 June 2022). The Association of Ambulance Chief Executives (https://aace.org.uk/) has not published anything on drugs/drug users. It would appear that nothing has been published yet by NHS England.

Ambulance team leaders who attend at crime scenes have to prepare reports, otherwise there would not appear to be any national guidance from the College of Paramedics or local guidance from Ambulance Trusts (personal communication to author, Julia Williams, Professor of Paramedic Science at the University of Hertfordshire, 26 August 2022).

Medico-legal death investigations

Medico-legal death investigations where drugs are suspected to have been involved are inextricably linked to other forensic disciplines, namely pathology and toxicology. In England and Wales, the Forensic Science Regulator "ensures that the provision of forensic science services across the Criminal Justice System complies with a high standard of scientific quality" (Forensic Science Regulator, 2021b). The Regulator reports to the Home Secretary and provides guidance, standards, and regulation of services including forensic pathology and toxicology. As yet, there is no specific guidance for investigating crimes where a suspected drug-related death has occurred.

Financing of pathological and toxicological investigations

Perhaps, one of the main determinants of what investigations are conducted and for what purpose(s) is the financial constraints within which the instructing investigators (e.g., Coroners, Procurators Fiscal, etc.) must work.

Coroners in England and Wales are funded by local authorities. Although there would appear to be no national figures available such costs, the author estimates an annual cost of about £80 million for the two countries in 2020-21 (based on extrapolations from data for a part of a Welsh coroner's jurisdiction (Flintshire County Council, 2021). The Ministry of Justice does not collate information on such expenditure (personal communication to author from the Death Management, Miscarriages of Justice, Inquiries & Coroners section, Ministry of Justice, on 21 September 2022).

Responsibility for the Coroners' Service for Northern Ireland comes within the remit of the Northern Ireland Courts and Tribunals Service [NICTS], which is an Executive Agency of the Department of Justice in Northern Ireland. As such, it is mainly supported by "funds approved by the [Northern Ireland] Assembly through the annual Supply process, with additional non-supply funding from the Northern Ireland Consolidated Fund in respect of the costs relating to Judicial Salaries [including Coroners]. As a business area of NICTS, the Coroners Service is allocated a budget from these funds" (personal communication to author from the Coroners' Service for Northern Ireland, on 24 August 2022). Unfortunately, a breakdown of expenditure for the Coroners' Service is unavailable in the NICTS Annual Report and Accounts (https://www.justice-ni.gov.uk/publications/nicts-annual-report-and-accounts).

Central funding is received by the COPFS in Scotland so that it can conduct its joint functions: (a) prosecution of crime and (b) investigating sudden, suspicious, unexpected, and unexplained deaths; occasionally these roles may overlap. There is no specific breakdown available by different death categories (personal communication to author from the Principal Procurator Fiscal Depute, Scottish Fatalities Investigation Unit, on 25 August 2022). The cost of court proceedings, including Fatal Accident Inquiries (FAIs), is not recorded on an individual or annual basis (personal communication to author from The Freedom of Information Officer, Scottish Courts and Tribunals Service HQ, on 20 September 2022).

Forensic pathology

The Home Office Pathology Unit maintains a register of approved pathologists who investigate homicides and suspicious deaths, as well as monitoring the standards set by the Forensic Regulator. The latter, in conjunction with the Home Office, Department of Justice, and The Royal College of Pathologists, publishes a code of practice and performance standards for forensic pathology in England, Wales and Northern Ireland, see, for example, Home Office, The Forensic Science Regulator, Department of Justice and The Royal College of Pathologists (2021). This document, originally issued in 2012, includes sections on: scene of discovery of the body; the autopsy; the pathologist's autopsy report; attendance at court, etc. Whilst there is obvious reference to toxicology, there is no guidance on what drugs should be searched for or how toxicology should be recorded and reported.

Annual audits of the work of UK-based forensic pathologists are undertaken by the Regulator's Forensic Pathology Specialist Group.

"The 2012 exercise focussed on two different types of post mortem examination. The first of these was a death due to use of an illicit substance. The second was one in which the forensic pathologist had to take over a case already started by a non-forensic specialist. Anecdotally such cases are often considered to give rise to difficulties in ascertaining the course of events leading to the death. … Each participating pathologist was asked to submit two specific case reports for audit. One was to be the first case involving illicit substance use examined after 1st August 2011."
Forensic Science Regulator – Forensic Pathology Specialist Group (2015:3)

The audit looked at 43 'drugs death' cases. Some of the points made were:

"Descriptions of the external appearance of the body were acceptable in every case. The use of headings to separate and record marks of note – for instance, old scars and tattoos – was considered helpful. 29 Twenty three (53%) case reports contained good descriptions of the injuries. Others were brief but nonetheless sufficient for cases in which the deceased had collapsed from drug use. However, the descriptions were considered too brief in 3 cases (7%). …
Descriptions of the internal examination were acceptable although in 2 cases (5%) these were considered somewhat brief. …
Urine volume had not been recorded in 6 (14%) cases, although this is required by the Code of Practice in cases in which urine is taken for analysis. …
Vitreous fluid may be less affected by post mortem changes than blood, and analysis of this should be considered in appropriate cases. It may be that practitioners should be reminded of this …
Forensic Science Regulator – Forensic Pathology Specialist Group (2015:6)

Substance use was recorded as a cause of death in 45 cases, including 2 from the 'second PM' category. More than one drug was implicated in most cases (75%). Other substances, albeit in lower concentrations were also detected in many of the other cases. Information regarding lethal dosages of substances was only recorded in 9/45 cases. 'Prompts for discussion' included: "Would mention of the specific drugs involved be better than 'mixed drug toxicity'?" and "Would such an approach enable more accurate statistics to be collected?". These aspects remain an issue today (2024).

Forensic toxicology

An EMCDDA study found that there was great variation in postmortem toxicology practices in drug-related death cases in Europe (Heinemann and Iwersen-Bergmann, 2019). The UK Forensic Science Regulator's (2021a) Codes of Practice and Conduct refer to a specific ISO standard for both drug analysis and toxicology:

"Drug analysis to evidential standards (ISO 17025)
Presumptive drug testing (for example under Evidential Drug Identification Testing (EDIT) guidance or HOC 15/2012 [14]) is currently permissible outside of the ISO 17025 standards framework. For evidential purposes, all drugs for which the forensic unit routinely tests (in relation to the Misuse of Drugs Act 1971 and/or Psychoactive Substances Act 2016) shall be within its scope of accreditation (either by being named in the scope or as a result of flexible scope) and new drugs, as they become more common, shall be brought within the scope in a timely fashion. The forensic unit shall have a

procedure setting out how it analyses drugs that are new or rarely tested for and are not in scope of accreditation, covering how the laboratory assures the quality of such analyses."
Forensic Science Regulator's (2021a:11)

"Toxicology (ISO 17025)
Presumptive toxicology testing (using Home Office type approved equipment) is permissible outside of the ISO 17025 standards framework. For evidential purposes, all compounds for which the laboratory routinely tests as part of a toxicology service shall be within its scope of accreditation (either by being named in the scope or as a result of flexible scope … and new compounds, as they become more common, will be brought within the scope in a timely fashion. The laboratory must have a procedure setting out how it analyses compounds that are new or rarely tested for and are not in scope of accreditation, covering how the laboratory assures the quality of such analyses. Analysis in relation to section 5a of Road Traffic Act 1988 is subject to specific requirements set out in FSR-C-133. Provided the accreditation takes into account ILACG19:08/2014 Modules in a Forensic Science Process and therefore has Forensic Testing/Analysis clearly indicated in the scope of accreditation, ISO 15189 is a suitable alternative to ISO 17025. Due regard should be given to the laboratory guidance issued by the UK and Ireland Association of Forensic Toxicologists …"
Forensic Science Regulator's (2021a: 9-10)

To coincide with the coming into force of the Psychoactive Substances Act 2016, a Home Office circular was released outlining the background to the legislation and the changes that it made to dealing with Novel Psychoactive Substances (Home Office, 2016a). This was accompanied by a joint release by the Home Office Drugs and Alcohol Unit and the Centre for Applied Science and Technology of a forensic strategy (Home Office, 2016b). This document sets out a number of elements, including: demonstrating "psychoactivity" for the purposes of the Act; guidance from the Advisory Council on the Misuse of Drugs; fundamental science of the *in-vitro* test; Home Office programme of *in-vitro testing*; processing a seizure of suspected psychoactive substances; and evidential considerations.

In light of the continuing emergence of numerous Novel Psychoactive Substances, the American National Standards Institute (ASNI) and Academy Standards Board (ASB) have developed a new standard outlining the scope and sensitivity of what should be analysed (ANSI and ASB, 2021; LeBeau et al., 2022). It includes a table listing "Required Minimum Analytical Scope and Sensitivity for Testing of Blood in Suspected Toxicological Cause of Death Determination", and a second table giving "Required Minimum Analytical Scope and Sensitivity for Testing of Blood in Cases with a Known Anatomical Cause of Death". The first table covers a total of 82 substances, and the second table lists 18.

An overview of the process of developing US forensic toxicology standards, together with their associated best practices, guidelines, and standards, has also been published (Jones and Stypa, 2023). The document includes information on (a) a "standard for report content in forensic toxicology" and (b) "analytical scope and sensitivity of forensic toxicological testing of blood in

Medicolegal death investigations".

Argo et al. (2022) have produced a 'diagnostic algorithm' to provide investigators, such as coroners, with guidance on "all the elements to investigate drug-related deaths and cooperate with toxicologists", drawing on their experience of case-working in Italy. More recently, an overview has been published of "systematic toxicological analysis strategies and their coverage of substances in forensic toxicology" (Rygaard et al., 2023). It is suggested that forensic providers should employ analytical methods of sufficient quality to detect and identify as many potentially toxicologically relevant molecules as possible. Even this approach, it is recognised, will not necessarily identify every last substance in all scenarios or situations.

At the time of writing (May 2024), no Home Office circulars have been issued since, at least, 2003, in relation to this issue. The challenge of producing and maintaining up-to-date comprehensive lists of Novel Psychoactive Substances (NPS) and metabolites of existing substances for which to screen is of concern to advisory bodies, such as the UK's Advisory Council on the Misuse of Drugs (ACMD) (ACMD, 2022) as well as professional bodies, such as the LTG (formerly the London Toxicology Group) [based on the author's membership of relevant ACMD committees and working groups, and of the LTG].

"Recommendation 4. In light of the continuing emergence of NPS and particularly synthetic opioid NPS, a working group should be established to consider and provide recommendations on a UK-wide minimum standard set of post-mortem toxicology tests for apparent drug-related deaths, to include testing for relevant novel psychoactive substances to improve consistency of analysis and detection. The best practice recommendations agreed would include standards for reporting."
ACMD (2022:24)

The Government's response to this suggestion was:

"The government agrees with the principle of this recommendation. However, given that coroners are independent judicial office holders and independent in the discharge of their statutory functions, it would not be appropriate for the government to seek to establish minimum standards for post-mortem toxicology tests. However, we would encourage coroners to consider this recommendation carefully and we will continue to raise this with relevant officials, including those in devolved governments."
Home Office (2023:3)

Forensic toxicology is important for a number of reasons. The main principle should be to provide accurate death certification. This, in turn, should lead to more accurate mortality data which can then feed into local, regional, national, and international monitoring of drug-related deaths and mortality. At the same time, forensic toxicology can inform pathological evaluations, determination of manner and cause of death, which will enable those officials responsible for investigating death

to determine/reach their conclusions (e.g., Coroners, Medical Examiners, and Procurators Fiscal) and also assist prosecuting authorities (e.g., Crown Prosecution Service, Procurators Fiscal) decide if any criminal investigations or proceedings are appropriate and feasible. Above all, such investigations can help provide some level of closure for the decedent's family and friends.

Specifying what toxicology to order

There are several constraints which have to be borne in mind when pathologists, Medical Examiners, and even Coroners are considering what types of toxicological investigations should be undertaken and for what substances testing should occur.

An initial consideration is whether, based on the circumstances and *locus* of death, toxicology is even needed to determine the cause(s) and manner of death. For example, if a decedent had been undergoing in-patient treatment for a condition with a known cause, even if triggered by administration of a drug or poison, and died in hospital, the cause of death is likely to be known and no further purpose would be served by toxicological investigation. In this scenario, the manner of death would also be known.

Although a decedent's cause of death or the mechanism(s) leading to extinction of life may be known, the manner in which a person met their death may be unknown or not understood. In other situations, there may be no apparent cause of death, based on autopsy results. In other situations, the circumstances and *locus* of death may be suspicious. Therefore, toxicological investigation may be deemed necessary.

What substances are looked for by forensic toxicological providers also depends on a number of factors. What is known about an individual's past drug use (whether prescribed, over-the-counter, illegal, diverted, natural product, novel psychoactive), witness accounts, evidence found at the scene of death (or events leading to death), how much time has elapsed between administration/consumption of substances and samples being taken should inform what is sought.

The specific substances that investigators ask forensic service providers to search for are also informed by the resources and capabilities of individual laboratories. This depends, in turn, on: the range (scope) of substances; quantitative vs. qualitative assays; the degree of sensitivity required; availability and cost of reference samples (especially for NPS); type(s) of biological specimens available from the decedent; the experience/expertise of those undertaking the toxicology, etc.. Looking for obscure or ultra-recently created molecules (or indeed unknown/unidentified ones) is very expensive. Nevertheless, a balance has to be struck between

being thorough/comprehensive and identifying (potential) causative agents.

Information to be contained in toxicology reports

As far the author can establish, there are no UK guides on what should be included in a standard drug screen. Similarly, in the USA there are no federal or state guides/standards for lists of drugs to screen for. Even international professional organisations for forensic providers/ toxicologists (such as the Society of Forensic Toxicologists (SOFT), the Société Française de Toxicologie Analytique (SFTA), The International Association of Forensic Toxicologists (TIAFT), The UK & Ireland Association of Forensic Toxicologists (UKIAFT)), let alone the LTG lack such guidance. However, these bodies are actively debating the need for such guidance.

Obviously, details of the agency requesting toxicological tests and their relevant reference numbers should be included, along with details of the decedent(s), and samples/specimens (including drug paraphernalia), as well as any specific substances to be screened for.

Ideally, the substances screened for (and relevant methods) should be clearly presented. Negative as well as positive findings should be included. Positive findings should report: specimen type (and site/source/location and whether ante-mortem or post-mortem); parent drug(s) and metabolite(s); level(s); unit(s) of measurement; instrument(s); indication of sensitivity and confidence levels. Any limitations should be stated not only for the results but also their interpretation.

Interpretation of results, such as blood concentrations, should include guidance as to how the level(s) measured equate to: 'normal' or clinical therapeutic, 'recreational', post-mortem therapeutic, toxic, and fatal/lethal levels. These equivalences also are likely to be qualified by reference to: clinical studies, combinations of other substances; drug-drug interaction; drug half-life; tolerance vs. naïvety of the decedent; other factors influencing metabolism, e.g., ethnicity, gender, age; drug stability (time, type of container, storage, etc.); length of time between death and sample collection (postmortem interval); route and frequency of drug administration.

It would be good practice to indicate in toxicology reports which metabolites of index molecules have been screened for and/or found, and to which parent drug(s) they may relate; a single metabolite may be a derivative of more than one parent drug or indeed act as a parent drug in its own right, giving rise to yet more metabolites. For example, diclazepam (a 'designer benzo') can produce delorazepam (an active metabolite and a pharmaceutical drug) and lormetazepam (an active metabolite and a pharmaceutical drug); these, in turn, can both yield lorazepam (an active

pharmaceutical drug). Furthermore, both a parent drug and a metabolite may be prescribed for slightly different conditions, e.g., amitriptyline and its metabolite nortriptyline. Both of these are tricyclic antidepressants but have different half-lives, oral bioavailability, and mechanism of action (Hyttel et al., 1980).

Most of the thousands of UK postmortem toxicology reports read by the author, during the course of working on NPSAD and other research activities, have included information on drug interactions and also drug-drug interactions. This is good practice and helps pathologists correctly interpret and understand the implications of the toxicology results. However, such matters become problematic when toxicologists and pathologists are faced with newly emerging NPS or previously unencountered natural substances/derivatives. For these substances and molecules, little or no information is available on such aspects as binding affinity, metabolism, potency, addiction potential, pharmacological activity, etc. as, typically, there have been no pre-clinical, *in vitro*, *in vivo* or, indeed, *in silico* studies undertaken (Catalani et al., 2021; Catalani et al., 2023; Corkery et al., 2020; Orsolini et al., 2019).

Usually days, if not weeks, elapse before clinicians in Accident & Emergency/ Emergency Departments receive the results of ante- and post-mortem toxicology investigations (as opposed to immediate drug screening tests covering a very limit range of commonly-encountered drugs), especially for NPS. Although this may be useful for epidemiological research, it is often too late to inform treatment or care plans. However, in-field or on-site toxicological investigation using hand-held Raman spectroscopy could be used to inform such clinicians in a much quicker, real-time, time-frame (just a couple of minutes - UNODC (2017)) as has been demonstrated by both academic research (Guirguis, 2017; Guirguis et al., 2017) and in real-life settings, such as drug-treatment services (Guirguis et al., 2020), and has the potential to be used in other settings such as prisons, road-side, border control, Accident & Emergency/Emergency Departments (Bakeev and Thomas, 2014). If available, such information could assist in directing toxicologists working on behalf of pathologists, Coroners, and Procurators Fiscal towards specific substances to look for using lab-based confirmatory techniques (UNODC, 2017).

Approaches to investigating suspected drug-related deaths

Several different approaches can be used to investigate deaths suspected of being connected with drugs. Invasive techniques include dissection and internal examination of bodies (pathology), histology and toxicology - commonly called postmortems or autopsies.

However, there are also less (minimally) invasive and non-invasive techniques available. These can include an external examination on its own or in combination with the use of technologies such as, endoscopy, X-rays, ultrasound scans, magnetic resonance imaging (MRI) scans, computed tomography, etc.. Their appropriateness will depend on: the suspected manner of death; suspected cause of death; known medical history of the deceased; family wishes; cultural and/or religious observances; health and safety concerns (e.g., contagious/infectious diseases, deadly poisons); and available resources (equipment and qualified personnel).

In Scotland, for example, whilst a medico-legal autopsy is conducted in about 70% of deaths reported to Procurators Fiscal, there is provision for what is known as a “View and Grant” autopsy. In agreement and consultation with the relevant Procurator Fiscal, a pathologist may determine that the information from police investigations and the decedent’s medical records (if any) will enable the cause of death to be decided without recourse to dissection. All that is required is careful external examination by an experienced forensic pathologist of the body; incisions necessary to take samples for toxicological investigation are allowed under this approach. “View and Grant” investigations are conducted in about 15% of cases submitted by Procurators Fiscal for autopsy, typically in: road traffic collisions (with no pending criminal cases); unexplained but witnessed deaths (cardiac arrest during sport or exercise); or suicides by suspension (Parks and Maskell, 2022).

The above options will be considered by a Coroner, Procurator Fiscal, Medical Examiner, or pathologist in the UK context. This evaluation is usually undertaken with regards to single incidents involving the death of an individual or a small number of decedents.

On occasion, however, it may be necessary to undertake a wider review of events, into which the investigation of individual deaths may feed. Whilst this may still involve oversight by a judicial official (typically a judge), the review will employ other public health approaches, such as epidemiology, e.g., retrospective case-finding.

A similar, but prospective, method was undertaken in the initial stages of understanding outbreaks of infection with *Clostridium novyi* type A bacteria amongst injecting drug users (mostly heroin users) in Scotland, England, and Dublin during 2000 (Jones et al., 2002; McGuigan et al., 2002). A total of 108 cases, including 43 deaths, were identified.

The author attended a scientific meeting held on15-16 October 2001 in Glasgow, the location of the main outbreak, which drew together all the available information about these outbreaks. Specialists from a range of disciplines (epidemiology, law enforcement, microbiology, pathology,

and pharmacy) gave presentations about their contributions to both the investigation and management of these outbreaks, which had necessitated the activation of national and international alert systems. Although not a speaker at the meeting, the author (in his Home Office capacity) had helped by providing intelligence about heroin supply routes. Chemical and statistical (principal component analysis) investigation of the heroin involved in giving rise to the infections

"indicated that it was derived from opium produced in Afghanistan. It is likely that a single contaminated batch was distributed simultaneously via a dealer network serving the three affected areas. Documentary evidence of the methods used to convert the opium to heroin showed ample opportunity for bacterial contamination."
Ahmed and Gruer (2001)

The meeting drew together conclusions about what lessons had been learned from these *Clostridium novyi* outbreaks, discussed what could be done to prevent or minimise outbreaks in the future by this and other bacteria, and made five recommendations aimed at stake-holders.

Another approach to examining clusters of deaths in a geographical area is that of the 'psychological autopsy'. This term was coined in the late 1950s and originally "conceptualized as a thorough retrospective analysis of the decedent's state of mind and intention at the time of death. It focused on the psychological aspects of the death" (Botello et al., 2013).

Normally, this approach is used to try and understand the mental state of a deceased individual by constructing a psychological profile of the decedent; thereby to determine the cause, nature, and intention of the death, and whether it was the result of an accident, homicide, natural causes, or suicide. A range of sources, both oral and documentary, which can provide relevant information is needed to build up as complete a picture as possible.

Historically, this approach was used to investigate and understand intentional and suspected suicides, including those involving drugs, so as to inform suicide prevention interventions and treatment of those at risk of suicide (Botello et al., 2013). However, according to some commentators, "the same method has not been described scientifically as a method for the corresponding research in fatal accidental drug overdoses in substance use disorders, and with few exceptions […], it has not been mentioned in the context of such overdose deaths" (Hakansson and Gerle, 2018).

One of the two exceptions cited by these authors (Hakansson and Gerle, 2018), is a study conducted by NPSAD researchers, including the author, which compared suicide verdicts with accidental deaths in UK substance-related fatalities during 2001-2007 (Vento et al., 2011). This examined 2,108 suicides, providing information on decedents' socio-economic characteristics,

medical and psychiatric history, prescribed medications, and post-mortem toxicology. The sole source of information for these deaths were records kept by Coroners (and Procurators Fiscal). There were no contacts with decedents' relatives or friends, witnesses, etc.

NPSAD also adopted this approach, i.e., examination of documentary information provided by coroners in a series of 16 surveillance reports commissioned by stake-holders, usually local Drug and Alcohol Action Teams, across England during the period 2003-2007. The author was involved in all of these investigations, including data collection, analysis and writing-up of the completed (unpublished) reports. Here the focus was on what was going on within a specific geographical area, taking into account the types of data items mentioned in the previous paragraph. (The author's Principal Supervisor was also part of the team responsible for these reports.)

Other agencies have conducted and still do conduct their own local or regional inquiries (see, for example, Clifton and Sparkes, 2011; Whitehead, 2019; Zador et al., 2005). Local or confidential inquiries are also conducted into specific types of drug-related deaths. Deaths involving specific drugs have been investigated, for example: methadone (Scott et al., 1999; Seymour et al., 2003); dihydrocodeine (Seymour et al., 2001); and tramadol (Randall and Crane 2014). Groups at risk of overdose have also been investigated, for example, those in police custody (e.g., Best et al., 2004), or those released from prison (e.g., Farrell and Marsden, 2008; White et al., 2015). (The identification of 'at-risk' populations is examined in Chapter 7.)

National guidance and data collection forms based on the NPSAD methods and data collection form (see Figure 3.5) have been published. For example, the Welsh Assembly Government first published guidance in 2005 (Welsh Assembly Government, 2005) which was updated a decade or so later to assist Overdose Review Panels (Welsh Government, 2014). In England, the National Treatment Agency for Substance Misuse (NTA) published guidance on setting up local review processes (National Treatment Agency for Substance Misuse, 2011). They had previously published a research briefing reporting the outcome of a psychological autopsy investigation into fatal, non-deliberate, opiate-related overdoses (Oliver et al., 2007).

The creation of local and regional databases, the setting-up of overdose review panels and related activities, such as confidential inquiries can and have led to appropriate recommendations and initiatives being proposed to mitigate further occurrences. The findings from such developments can be fed into local prevention initiatives, informing service provision and treatment. These can also filter upwards and inform regional (country) and national (UK) policy-making, political strategies, advice on clinical issues, legislative and other control measures. Indeed, ultimately, they have and continue to feed into the deliberations of international bodies such as the European

Union, United Nations, and World Health Organization. (These aspects are further explored in Chapter 13.)

Under the provisions of paragraph 7 of Schedule 5 of the Coroners and Justice Act 2009, Coroners in England and Wales have a duty, when they believe that action should be taken to prevent future deaths of a specific nature, to send reports to an agency, government department, local authority, organisation, or person. The procedures applying to Prevention of Future Death Reports and responses to them are set out by Regulations 28 and 29 of the Coroners (Investigations) Regulations 2013. A database of these "Regulation 28" Prevention of Future Death Reports is available and can be searched here: https://www.judiciary.uk/?s=&pfd_report_type=&post_type=pfd&order=relevance. Procurators Fiscal in Scotland may include in their determination of a Fatal Accident Inquiry (FAI) advice to prevent future similar deaths or injuries. A searchable online database of FAI determinations is available at https://www.scotcourts.gov.uk/search-judgments/fatal-accident-inquiries. These types of reports may, therefore, feed into changes in the practice of healthcare (and other) professionals, treatment regimens, and drug controls/regulations at local, regional, national and UK levels.

In the USA, the Centers for Disease Control and Prevention (CDC) have a programme (Overdose Data to Action) which supports 47 states and the District of Columbia to submit detailed information from a range of sources (such as, death certificates, coroner/medical examiner reports, toxicological investigations) to the State Unintentional Drug Overdose Reporting System (SUDORS - https://www.cdc.gov/drugoverdose/fatal/sudors.html). A contribution to this by the agencies conducting medico-legal investigations helps to inform policies and provisions in respect of monitoring and surveillance of drug overdoses, prevention, and responses.

Such information, as in the UK, can assist further in several ways: describe trends in overdose deaths and typical scenarios; identify new substances or molecules; identify new forms and routes of administration. For example, evidence from death scenes and toxicological investigations was employed to understand the involvement in opioid-related overdose deaths of heroin, morphine, pharmaceutical and illicitly-produced fentanyl (O'Donnell et al., 2022).

Identification of potential drug-related deaths

A range of factors, many outlined above, can influence how and whether a death is identified as potentially drug-related, even such straightforward cases as acute fatal intoxications, let alone those with a less direct connection with drugs. Instead, a few brief comments will suffice to illustrate that it is vital to correctly identify potential drug-related deaths, otherwise they cannot be accurately recorded on death certificates, correctly coded using ICD codes, be reported in statistics, and inform policy and practice around monitoring and surveillance, treatment, and prevention.

A fundamental element that underpins the thoroughness of the entire process from a body being found to it becoming a statistic (but hopefully more than that) is 'cognitive bias'. This term describes the way in which the human brain applies a systematic thought process, informed by personal preferences and experiences, to simplify vast amounts of information so that it can be rapidly analysed, and priorities formulated. Sometimes, logical tenets are not adhered to or selectively dismissed. The issue of cognitive bias has increasingly emerged as a problem in forensic science and criminal investigations (Nakhaeizadeh et al., 2015; Cooper and Meterko, 2019). This can be illustrated by reference to a death by hanging, and determining whether it was a suicidal hanging or an accidental hanging associated with autoerotic activity (Zou et al., 2020), or even 'staged'.

Poor communication between and competency of those handling death investigations can lead not only to cause of death not being understood and making links to other possible deaths, but also to how those deaths are recorded in official statistics. An example*, par excellence*, of this is the way(s) in which the victims of Stephen Port were treated. It was only through the pressure of next-of-kin and friends that the police finally made a connection between these deaths, and that fact that there was a "lack of professional curiosity" about their cases according to the Coroner, Judge Sarah Munro KC, (Hope, 2022). Port had administered GHB/GBL (gamma-hydroxybutyric acid/gamma-butyrolactone) and other substances to his victims before killing them. The original Coroners' open verdicts were set aside by the coroner's jury in Judge Munro's inquest who found that they were unlawfully killed. On 21 January 2022, Judge Munro sent Regulation 28 reports to the Metropolitan Police Service (MPS), National Police Chiefs' Council, College of Policing, and the Department for Digital, Culture, Media & Sport (Courts and Tribunals Judiciary, 2022). The responses from these agencies are also available.

This, in turn, has led to the Independent Office for Police Conduct announcing it would take a fresh look into how the MPS investigated the cases (Mayor of London, 2022); it has yet to report

(May 2024). In addition, Her Majesty's Inspectorate of Constabulary and Fire & Rescue Service (HMICFRS) conducted an inspection within the MPS and published its report in May 2023 (HMICFRS, 2023a).

"Inspectors concluded that the Met's flawed handling of the Port investigations could broadly be explained by the following issues:
poor training and supervision for inexperienced police officers responding to unexpected deaths;
unacceptable record keeping, confusing case management systems and poor handling of property and exhibits;
confusing policy and guidance; and
inadequate intelligence and crime analysis processes, which make it difficult for officers to link deaths.

HMICFRS has made 20 recommendations for the Met, which include increasing the use of intelligence by officers responding to deaths and improving family liaison in unexpected death cases."
HMICFRS (2023b)

The Metropolitan Police Service and the NPCC announced that they would be reforming the national approach to investigating unexplained deaths (Parnaby, 2022). It was reported that four new classifications of death would be introduced by July 2022: (a) Expected deaths where there is a medical diagnosis; (b) Unexpected death investigated and not suspicious where evidence shows no third party involvement; (c) Unexpected death under investigation where further investigation is required; and (d) Homicide where it is likely there was third party involvement (BBC News London, 2022; Courts and Tribunals Judiciary, 2022). The Metropolitan Police Service said they would "embed these changes across the whole organisation by 30th June 2022." In response to a Freedom of Information Act request by the author, the following information was provided about these new categories:

"Investigating death is one of the most important jobs that the police do and how we go about it leaves a lasting impression on families and communities. The MPS Death Investigation policy provides guidance for all police officers and members of police staff when responding to and attending deaths across London. This policy changed in the summer of calendar year 2022 following the East London inquests that took place in 2021. The policy made changes to the language used, by moving away from use of the term 'unexplained death' to the following four categories:

- Expected death
- Unexpected death - investigated and non-suspicious
- Unexpected death - under investigation
- Homicide

The policy also introduced:

- Changes to the initial response at the scene
- Clarification of ownership of death investigations
- New recording and review periods for all officers, including Detective Inspectors and Detective Chief Inspectors whilst

death investigations are ongoing

The policy places an emphasis on professional curiosity and the THRIVE+ (threat, harm, risk, investigation, vulnerability, engagement + Prevention and Intervention) framework, to ensure that each death is investigated as suspicious until it can be determined otherwise. The policy also, as referred to above, introduced a new review process for death investigations which aligns to the investigation of other serious crimes, placing an emphasis on substantive supervisors and substantive detectives taking key roles. This ensures that investigations are given the appropriate level of supervision and that officers making difficult decisions are equipped to do so."
Information Rights Unit, Metropolitan Police (2023)

To date (May 2024), the author is unaware of any guidance being issued on these new categories. A reply to an FOI submitted by the author to the NPCC on 3 June 2023 (chased 28 February 2024) is awaited. A follow-up email to the Metropolitan Police Service on 28 February 2024 resulted in the previous information being repeated.

Deliberately or subconsciously ignoring or overlooking circumstantial evidence can affect what is written on death certificates (Dror et al., 2021). Every stage of the process can be subject to bias, from initial scene investigation, identifying witnesses and getting their testimony, and looking for drug paraphernalia through to understanding the context and setting, as well as pathology and toxicology, and recording of substances on death certificates.

To correctly understand what has happened to a decedent, as well as how, when, and why; and to identify, categorise and classify, and report the death, objectivity must be paramount. There may well be other shortcomings that have to be dealt with, in addition to what might have been labelled as 'cognitive bias' (Oliver et al., 2015). Investigational objectivity can be influenced by availability of data/information, and approaches to case identification and classification.

An illustration of the practical effects of these factors can be provided by reference to a study commissioned from the author by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). The EMCDDA wanted to get a better understanding of the emerging cocaine-related deaths epidemic in Europe (Corkery, 2012). The sources most often used by General Mortality Registers or GMRs (such as ONS) to identify cocaine-related deaths were "mostly cause of death (i.e. the underlying and/or contributory cause of death, stated by the medical doctor on the death certificate and used to code the main cause of death in the mortality registries) and post mortem (PM) toxicology results", whereas Special Mortality Registers (such as NPSAD) used "a wider range of factors, the most important being toxicology, post mortem (PM, i.e. autopsy) and evidence as well as cause of death" (Corkery, 2012:3).

We have already noted that not all NPS, including their metabolites are universally screened for. This is also the case for 'traditional' stimulants such as cocaine.

"Whilst not all cocaine metabolites are screened for in all countries, the common ones are typically identified. The products of combustion can be used as a means of distinguishing smoked cocaine/crack from other modes of intake. However, toxicologists are not usually looking for such products. Information on the use of crack immediately prior to death usually comes from police examination of the death scene and/or witness statements. But such information would not appear to be either systematically recorded or collated; thus the role of crack in cocaine deaths is probably under-reported."
Corkery (2012:22)

This was certainly the author's experience when NPSAD Programme Manager; even with access to witness and police investigators' statements, it was exceedingly rare that it was possible to determine that 'crack' cocaine, as opposed to snorting cocaine, had been used by the decedent in the period up to death and that its characteristic forensic toxicological markers had been looked for. Such information, e.g., the type of cocaine implicated in a death, is very rarely included in the 'cause of death' field on death certificates.

Recording of information on Medical Certificates of Cause of Death

The accuracy and completeness of what information is captured in the 'cause of death' field on medical certificates of cause of death (MCCD) (which are submitted to national GMRs to enable official national vital registration statistics to be compiled) and death certificates (issued for arranging burials and cremations, as well as for genealogical and other purposes) determines how useful they can be for different purposes. (See Chapter 3 for more information on the death registration process.) Accuracy and completeness are particularly important in epidemiological research, for example understanding: the involvement of particular substances in deaths; the mechanisms, nature and cause(s) of death; and the characteristics of decedents. The contribution of particular categories of substances to drug poisoning deaths is underestimated on data solely derived from death certificates; however, simple adjustments can be applied to generate more accurate estimates (Drake and Ruhm, 2023).

The World Health Assembly (WHA) recommends the use of the "International form of medical certificate of cause of death", which was last revised in 2016 (WHO, 2022b); guidance on its completion is provided by the World Health Organization (WHO) (WHO, 2022b). The MCCD form provides space for those completing it, in Section 1 to: "Report disease or condition directly leading to death on line a"; "Report chain of events in due to order (if applicable)"; "State the underlying cause on the lowest used line". In Section 2, the information requested is "Other significant conditions contributing to death (time intervals can be included in brackets after the

condition". The international MCCD form has provisions for 4 lines (a to d) in Section 1. This approach is used in Scotland (see Chapter 3) and Northern Ireland, whereas for England and Wales the guidance only lists three lines (ONS, 2022a). (The author has even seen a fifth line used occasionally.)

If properly completed the MCCD will provide "a description of the order, type and association of events that have resulted in the death" (WHO, 2022b). However, proper completion is dependent on the competence and knowledge of the individuals completing such forms, how frequently they do so, as well as initial and 'refresher' training they may receive (if any).

The WHO provides a range of training and tool-kits for those completing MCCDs (WHO, 2022b). At the UK level, ONS provides guidance for doctors completing MCCDs in England and Wales (ONS, 2022b). Guidance for Scotland was issued in a joint letter from the Chief Medical Officer (CMO) for Scotland and NRS (2018). In Northern Ireland guidance has been provided by the Department of Health (Northern Ireland Department of Health, 2022).

So far as the author can ascertain, no training is provided in UK medical schools at undergraduate level on completed MCCDs concerning drug-related deaths (Academy of Medical Royal Colleges and Royal College of Psychiatrists, 2012; Carroll et al., 2014; Notley et al., 2014; Crome and Goodair, 2021; personal communication from Christine Goodair, Population Health Research Institute, St George's, University of London, 11 May 2022).

Whilst there is Continuous Professional Development (CPD) training for confirmation and verification of death, e.g., for nurses, there appears to be limited provision for doctors to refresh their learning about completing MCCDs. The Royal College of General Practitioners does not offer CPD on this topic. Whilst the Royal College of Pathologists does not provide CPD on this topic, it does refer members to the guidance issued by the ONS (2022b). The Medical Defence Union (MDU) offers an online self-taught refresher course about completing death certificates and referral of deaths to the Coroner (MDU, 2022). NHS Education for Scotland has a resource which can be used as a 'refresher' on its Support around Death website (NHS Education for Scotland, 2022). The Faculty of Forensic & Legal Medicine of the Royal College of Physicians has offered a one-hour webinar on completing a MCCD hosted by a former President of the Faculty (The Faculty of Forensic & Legal Medicine of the Royal College of Physicians, 2020).

As noted earlier, very often the names of specific substances (whether poisons or drugs) are often omitted from MCCDs and, therefore, from published statistics on drug-related poisoning deaths. This shortcoming has been often noted, internationally as well as within the UK, by General and

Special Mortality Registers alike as well as by other commentators over the past four recent decades or more (e.g., Millar, 1978; Ashworth, 1991; Wysowski et al., 1993; Lahti and Penttilä, 2001; Gossop et al., 2002; Zoorob, 2019). Clearly, such omissions have consequences for epidemiological research on mortality, especially of drug (mis)users. Even in recent times, ONS still feel the need to note the following limitation with regard to the 2022 statistics:

"The Office for National Statistics (ONS) does not have access to post-mortem reports or toxicology results, so the accuracy of figures depends on the information provided by the coroner on the death certificate; because of incomplete information, figures for drug misuse and for specific substances are underestimates."
ONS (2023)

In the USA, the National Vital Statistics System (NVSS) has published a reference guide for completing death certificates in drug toxicity cases (NVSS, 2019). This also includes injunctions such as:

- Include the name(s) of the specific drug(s) that have been determined to have caused the drug toxicity death,.. if the specific drug(s) are known.
- Avoid using vague phrases such as "drug overdose," "multiple drug toxicity," or "polypharmacy" without including the specific drug(s) involved. While these phrases identify the death as having some aspect of drug involvement, the detailed information on the specific drug(s) is still needed.
- If information is only available about the drug class (e.g., opiate) and not the specific drug (e.g., hydrocodone), list the drug class. … However, if information on the specific drug is known (e.g., from the scene investigation), naming the specific drug is preferable.
- Use generic drug names rather than brand or trade names.
- Name the parent drug rather than a metabolite (breakdown product) of the parent drug. The parent drug is of primary interest for public health surveillance and prevention

NVSS (2019:2)

The shortcomings noted in this sub-section are inter-connected with other aspects that have already been mentioned in this chapter, e.g., under-reporting of drug-related deaths generally (Fugelstad et al., 2020), under-reporting of deaths associated with particular (classes of) drugs (Buchanich et al., 2018), and misunderstanding the full ranges of cause(s) of death in at-risk populations (Gossop et al., 2002; Slavova et al., 2017).

Amongst others, Slavova et al. (2017) mention the need for postmortem and autopsy reports to be linked up with MCCDs so as to address some of these shortcomings. Whilst we have already briefly mentioned the importance of toxicological reports being more complete than hitherto, there is also a need for improvements to autopsy reporting.

The Royal College of Pathologists issues autopsy guidelines on a range of types of death (https://www.rcpath.org/profession/guidelines/autopsy-guidelines-series.html). They published guidance for when drugs or poisoning might be involved in a death (RCP, 2018). These are very detailed, with one-quarter being devoted solely to toxicology, including: when to take toxicology specimens; what samples should be taken; scenarios for toxicology analysis; extent of toxicology screens; the role of the toxicologist and referral laboratory; what information to provide the toxicology laboratory; and interpretation of results. This guidance was due for review in December 2023.

Although the Council of Europe Committee of Ministers (1999) made a recommendation to harmonise medico-legal autopsy rules, this recommendation does not appear to have been taken note of in the UK, despite the author mentioning its existence at opportune times and on relevant occasions. Perhaps more notice will be taken of a recent position paper on a code of practice for medical autopsies from the European Society of Pathology (Alfsen et al., 2022), although it makes no mention of drugs.

A comparison of US deaths investigated with and without autopsy shows that 11-13% of drug deaths were found to have alternative cause of death (Andrew and Duval, 2017). It is important that pathologist and toxicologist liaise closely so that all aspects of a death are considered; in this way a coroner or medical examiner has as complete a picture as possible. "The "autopsy of the circumstances" is probably the most important aspect of being a medical examiner charged with the responsibility to determine cause and manner of death" (Dr Joseph Davis, cited in Gill, 2022:48). This holistic approach is also recommended by a position paper (Davis et al., 2020).

Such collaboration will enable not only pathologists and toxicologists, but also Coroners/Medical Examiners understand better the interactions of, very often, multiple substances (see Chapter 6) and how they affect the body, and mechanisms of death. As there is a lack of standard criteria for clinically deciding which of the several diagnoses is the actual cause of death, it is not possible to obtain precise figures on deaths caused by specific substances using data collected at death registration.

> “General [Mortality Register] … estimates of the number of deaths due to specific drugs are therefore based on the number of deaths where the underlying cause of death was drug-related and where the drug is mentioned on the coroner’s certificate, regardless of whether it was the primary cause of death. The published figures should therefore be regarded as an estimate of the number of deaths associated with particular substances rather than the exact number directly due to these substances.”
> Corkery (2008)

This aspect is discussed in Chapter 6, but it is important to remind the reader that:

There are concerns that inaccurate reports on death certificates often result in error in death classification. [As noted above, these]" may be due to:

- Insufficient recognition of the impact of changes in the modality and precision of diagnostic technology
- Lack of, or insufficient, guidelines or training for doctors in preparing death certificates
- Low frequency or absence of post-mortem confirmation of cause of death
- Where toxicological screening is conducted, the protocols vary across coroner's jurisdictions within the same country."

Corkery (2008)

These factors can affect how information from MCCDs is transformed into statistical data. In Scotland, the results of research undertaken by the Death Certification Review Service (DCRS), which "was setup in 2015 to review the cause of death in approximately 12% of randomly selected deaths that were not reported to the Procurator Fiscal [found that in] … 2020 around 20% of randomly selected cases were considered "not in order" and required changes (this may be the correction of an administrative error (such as a spelling mistake) or a clinical error (such as an incorrect cause of death or a cause of death that is too vague)" (Parks and Maskell, 2022).

The coding of suicides in England and Wales by ONS is likely to be impacted by a Supreme Court ruling on 13 November 2020 in the case of *Maughan, R (on the application of)v Her Majesty's Senior Coroner for Oxfordshire* [2020] UKSC 46, where it upheld that for inquests dealing with cases of suicide and unlawful killing the criminal standard of "beyond reasonable doubt" should not be applied, but rather the civil standard of the "balance of probabilities". The effect of lowering the standard of proof will be to mitigate the number of suicides under-reported by applying the criminal standard (Fouzder, 2020). However, following the earlier decision in the High Court on 26 July 2018 involving these parties which led to the original change in the standard of proof, ONS found little overall change in proportions of deaths classified as suicide/intentional (ONS, 2020). The ruling in the 2018 case also applied to Coroners' conclusions in Northern Ireland (NISRA, 2023).

International Classification of Diseases coding

The basic tool for codifying deaths over the decades has been the International Classification of Diseases (ICD). The ninth (ICD-9) and tenth (ICD-10) revisions are the ones which have been used across the UK during the period covered by this thesis. ICD-9 (WHO, 1978) was introduced internationally in 1979, and came into use in the UK in that same year. ICD-10 (WHO, 1992) was introduced internationally in 1993, but not implemented until 2000 in Scotland and a year later (2001) in the rest of the UK. The statistics presented and discussed in the following chapters are

based on ICD-9 and ICD-10 coding.

Most of the statistical information about death comes from death certificates in which deaths are coded, by international agreement, according to an underlying cause, using ICD codes (Corkery, 2008). The author has previously written (Corkery, 2008) that "An underlying cause of death has been described as the condition that initiated the series of unwholesome events that led directly or indirectly to death or the circumstances of the accident that produced the fatal injury (National Center for Health Statistics, 1983)." However, other approaches are used, for example when looking at the involvement in death of specific (classes of) drugs the relevant information may be found in another line of section 1 or indeed in section 2 of the MCCD.

The ICD taxonomy has provided the basis for major attempts to standardise statistics on drug-related deaths (Corkery, 2008), in order to try and quantify trends in drug-related deaths (DRDs) both internationally and nationally. However, as indicated above, there are limitations in simply using the 'underlying cause of death' as the basis for counting DRDs. Flanagan and Rooney (2002) outline the approach taken by ONS in respect of DRDs in England and Wales to coding DRDs using ICD-9; these principles still apply with the use of ICD-10. They outline how ONS tried to mitigate and overcome such issues. One strategy, starting with 1993 data, was to code all diseases, injuries, and external causes (including poisons) in addition to the underlying and secondary causes mentioned on the death certificate.

They also describe the setting up, again starting with 1993 data, of a special drug deaths database:

"ONS takes an annual 'drug and poisoning' extract from the national mortality database. This includes all deaths with an underlying cause of death of drug dependence, drug abuse, accidental, suicidal, homicidal, or 'undetermined intent' poisoning (coroner's 'open' verdict) with any drug or medicine. The extract includes age, sex, date of death, underlying and multiple cause ICD codes, cause of death text, any text from the coroner's description of how the 'accident' occurred, and coroner's verdict. Each individual drug mentioned is derived from the text, using standard names …"
Flanagan and Rooney (2002).

Similar databases were set up for Scotland and Northern Ireland, although the latter was not computerised until 1997 data were processed.

Such developments vastly improved the quality and reliability of statistical information on drug-related deaths which was published for Great Britain and subsequently the UK by the Home Office (Corkery, 1997). These databases subsequently paved the way for replacing statistics based on the Home Office Addicts Index with data from the UK's GMRs to international bodies including

the United Nations Office on Drugs and Crime (UNODC) and EMCDDA. Such data and related information/commentary were supplied by the author in his role as an official in the Home Office Drug Statistics Section, and subsequently in his role as the UK Focal Point expert on drug-related mortality for the EMCDDA (2000-15). In his/this latter role, the author was a contributor and participant in the EMCDDA's revisions of its own DRD definition (see, for example, EMCDDA 2002:2). The latest revision was in 2009 (EMCDDA, 2009). The author provided guidance to the UK's GMRs in implementing these definitions, and changes to them. The WHO revised the way in which the underlying cause of death was coded; these had to be implemented in the UK, for example, this was done in 2011 in Scotland (NRS, 2023a), leading to some discontinuities in analyses, including those for 'drug misuse' deaths.

Given the vast range of codes that could be employed to classify deaths happening to individuals using drugs, the Australian National Drug and Alcohol Research Centre recently revised its 2009 guidance to help facilitate the process and to encourage more consistence across research studies (Santo et al., 2022). One way of improving consistency is the use of technology.

Several softwares are available which enable the automated coding of 'cause of death' information. This approach has been used in the UK for some decades. However, there is a continued need to have input from human 'medical coders', e.g., to deal with misspellings, transpositions, and transcription errors. This is particularly important when it comes to chemical names (both traditional drugs such as benzodiazepine and heroin, but especially NPS molecules) and medical terms. Coders are also used to enter information from Coroners' inquests (see for example, NISRA, 2021).

Other experts (including the author) are called upon by the GMRs to provide input on what the correct name of an NPS molecule may be or the current legal status of a molecule. Such information is fundamental to providing statistics on 'drug misuse' deaths in the UK; these are a sub-set of drug-related poisoning deaths. The ICD taxonomy does not distinguish between illicit and prescribed drugs (Corkery, 2008). This is important where breakdowns for specific classes of drugs, such as benzodiazepines, need to distinguish between 'prescribed/prescription' drugs and 'street' or so-called 'designer' drugs (NRS, 2023b).

Other developments to help ICD coding of drug-related deaths [could] include the use of natural language processing and machine learning, as has been trialled for medical examiners reports in the USA (Harris et al., 2020; Goodman-Meza et al., 2022). This principle has been applied to death certificates relating to drug overdoses in Kentucky under research conditions as part of a PhD (Ward, 2021; Ward et al., 2019). These approaches could also help speed up the provision

of epidemiological information. Such developments appear to be part of the way forward (see also Chapter 14).

The World Health Assembly formally adopted ICD-11 in May 2019 and Member States committed themselves to commence using this revision for mortality and morbidity reporting in 2022 (WHO, 2022a). It is understood that, as of October 2021, the new ICD Revision is undergoing trials, that it will take a couple of years to sort out 'teething' problems, and to roll it out (possibly from 2025). One proposed suggestion is to give all drugs a T code (i.e., 'overdose') rather than just overdoses *per se* (Margaret Warner, NVSS, "Fatal Drug Overdose Surveillance using death certificate data", lecture on CFSRE module "Investigation and Certification of Drug Toxicity Deaths in Today's Complex Drug Environment", 29 October 2021). As presently understood by the author, the situation in the UK is that ICD-11 will not be implemented across ONS outputs (including DRDs) before 2025 (personal communication to author from Jon Darke, Data & Analysis for Social Care and Health, ONS, on 14 November 2022) and that NISRA will follow ONS' lead (personal communication to author from Elaine Longden, Assistant Statistician, NISRA, on 10 November 2022). The same time-frame is also likely to apply in Scotland as the IRIS software which most countries used will need to be adapted to run on this new ICD version (personal communication to author from Maria Kaye-Bardgett, NRS, on 15 November 2022).

One of the main benefits that ICD-11 will provide is "the ability to link and specify consequences (i.e., harm or injury) arising from a healthcare-related activity" (Southern et al., 2021). In terms of drugs, the following scenarios may occur:

> "For example, when a medication causes an adverse event in a healthcare context, the new 3-part model permits the specification of precisely how harm occurred (i.e., an overdose of drug vs. drug interaction vs. incorrect drug vs. allergic reaction, etc.)… Recognizing that there are some instances where a healthcare-related adverse event has a clear high-level cause (e.g. "drug causing an event"), but an uncertain or unspecified mode/mechanism (i.e. overdose? Underdose? Interaction?), ICD-11 also provides an option to code *other specified and unspecified mode/mechanism* for each of the four categories of substances, procedures, devices, or other causes of healthcare-related harm."
> Southern et al. (2021).

Additional drugs have been specified in this revision, but it is still going to be a problem coding NPS. Even long-established NPS such as mephedrone do not have a specific code, it would have to be treated as a generic form psychostimulant; similarly for synthetic cannabinoids, only natural ones have been allocated unique codes. Such shortcomings were foreseen (by the author and others) and these concerns were fed into the general discussions conducted by the WHO as part of its consultations.

Counting drug-related deaths

As we have seen, in this and the preceding chapters, ascribing certain deaths to drugs, e.g., Road Traffic Collisions, falls from height, drownings; HIV/AIDS, hepatitis and other blood-borne diseases; consequences of injecting/sharing equipment (*clostridium novyi*, etc), or homicides committed whilst under the influence of drugs, can be very difficult compared with acute (or even) chronic toxicity or poisoning. This, in turn, means that knowing the true extent and nature of drug-related deaths is fraught with difficulties. Further difficulties arise, albeit in rare instances, where a decedent's body is so very badly decomposed that the cause of death is regarded as "unascertained" and coded to ICD-10 code R99. A recent study indicates (Hiam et al., 2023) that the number of deaths has increased over time in England and Wales. In recent years, so-called 'deaths of despair' (that is deaths related to drug and alcohol use, or suicide) have increased amongst those in middle-age (Walsh et al.,2021; Augarde et al., 2022); these may be contributing to the increasing number of men found decomposed at home.

On the other hand, we have seen that toxicology, when reported and recorded correctly/fully, provides a crucial element of granularity that allows for a far deeper understanding of the role of specific molecules and/or combinations of substances and their role(s) in causing and/or contributing to death. Such details can throw light of some of the categories of death listed in the previous paragraph. That said, it is worth repeating a previous observation made by the author:

"The only studies that take a comprehensive look at the causes of death among drug dependent individuals or addicts are cohort mortality studies. However, in the UK context, such studies have been few and far between and small-scale since the closure of the Home Office Addicts Index in 1997.This means it is difficult to gauge the impact of the long-term consequences of drug use such as hepatitis and, to a lesser extent, HIV/AIDS."
Corkery (2008)

The remaining chapters of this thesis will, therefore, focus on the more direct types of drug-related deaths. Some of these will, without doubt, relate to individuals who have used drugs over a long period of time, or who have become dependent on drugs. Equally, some deaths will have occurred on the first use/administration of a substance. Finally, deaths occur as a result of deliberate self-harm (suicides) or homicide.

Chapter overview

In this chapter, the focus has been on the processes whereby deaths related to drugs are investigated. This starts with scene of incident preservation and recording, through to investigation, in the UK context, by the police on behalf of a Coroner or Procurator Fiscal, and indeed Medical

Examiners. These are then complemented by the use of autopsy and toxicology. The key role of toxicology in drug screening, identification, recording, and reporting has been highlighted. Without accurate and complete information on toxicology being passed to 'vital statisticians' and their teams responsible for official mortality statistics, our understanding of the number and nature of drug-related deaths will remain partial and incomplete.

The next three chapters (Chapters 5-7) attempt to make sense of what is known about such matters in the UK context over the past three decades.

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CHAPTER 5 – IMPROVED REPORTING, PUBLISHING AND DISSEMINATION OF DRUG-RELATED DEATH STATISTICS

"Wide dissemination of accurate drug death surveillance information in an easily accessible … format promotes societal awareness of the drug death epidemic, but also provides information to public health, law enforcement, regulatory, and other community-based organizations that can benefit from the most up-to-date knowledge."
Williams et al. (2017)

Developing some of the themes commented on in the previous three chapters (Chapters 2 to 4), this chapter provides a narrative description - using relevant literature, personal knowledge and information from key informants - of changes in what has been reported and published in respect of drug-related deaths (DRDs), and to a lesser extent on drug-related mortality. Since the United Kingdom (UK) has and has had international obligations on reporting such statistics to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) and the United Nations Office on Drugs and Crime (UNODC) these aspects will also be covered. The main focus here still remains on what has happened in the UK, and how that fed and feeds into the wider context. The approach here is more of a chronological one compared to preceding chapters.

A number of key themes from earlier chapters re-emerge here, especially harmonisation and standardisation - both at national and international levels – as well as continuity. The main aspects covered in this chapter are: parallel sources of information; reporting of statistics to international agencies; General Mortality Register (GMR) reporting of and on drug-related deaths in the UK; UK Special Mortality Register (SMR) reporting on DRDs; other publications about UK DRDs in the UK; international dissemination of UK DRD statistics and information; emerging improvements and recent challenges.

Background - two parallel sources of information

The two key sources of information on drug-related deaths and drug-related mortality have been introduced and briefly described in Chapters 3 and 4. At the start of the period covered by this thesis, there were three GMRs, all of which remain: the Office for Population Censuses and Surveys (OPCS), which merged on 1 April 1996 with the Central Statistical Office to form the Office for National Statistics (ONS); the General Register Office for Scotland (GROS) merged with the National Archives of Scotland on 1 April 2011 to form the National Records of Scotland (NRS); and the General Register Office (Northern Ireland) is part of the Northern Ireland Statistics

and Research Agency (NISRA) which was established on 1 April 1996. The information they published is described in Chapter 3.

The Home Office Addicts Index was set up in the early 1930s and started providing basic information and statistics on addicts to the League of Nations (forerunner of the United Nations) in 1934. Initially, the statistics only covered drug seizures and offences, but after a few years information on deaths of notified addicts were included. Subsequently, the number of deaths of addicts notified to the Home Office were included in the annual statistical bulletins; this was a means of accounting for their removal from the Addicts Index. This continued up to and including the 1989 bulletin which included information on deaths up until 1988. There was a brief hiatus of a couple of years before information on deaths was again included in the statistical bulletins.

The 1991 bulletin started to provide breakdowns of deaths by age, sex and year of death from 1979 to 1989; some information was presented on those deceased individuals whose addiction was therapeutic in origin. Further tables gave breakdowns by: cause of death; drugs involved in overdose deaths; time between first and latest notification and death; deaths with an underlying cause of death described as drug-dependence or non-dependent abuse of drugs, by type of drug, sex, and year of death; a similar table gave a breakdown by age-group. Information from the OPCS and GROS on deaths from poisoning by solid and liquid substances: accidental, suicidal and undetermined whether accidentally taken or purposely inflicted, broken down by age-group and sex for the year reported on (e.g., 1989) was also included; and information on the number of deaths of reported AIDS cases, including an indication as to whether these were of injecting drug users, was presented. These breakdowns continued to be included in the statistical bulletins until they were discontinued with the closure of the Addicts Index in April 1997; the final statistics relating to 1996 (Corkery, 1997). The final statistical bulletin, compiled by the author, was the first publication of any sort to contain statistics on drug-related deaths for the whole of the UK.

With the closure of the Addicts Index, one of the most important and accurate sources of information on deaths of addicts could have dried up - Coroners' reports. However, discussions were initiated between the Home Office Drug Statistics Section (including the author), the Home Office Coroners' Unit, the then Honorary Secretary of the Coroners Society (Mr Michael Burgess, then Her Majesty's Coroner for Surrey and the Royal Household), and the late Professor Hamid Ghodse and his research unit at St George's Hospital Medical School. With input from Professor Virginia Berridge, Mr Alan MacFarlane (the then Chief Inspector of the Home Office Drugs Branch), it was agreed that a request be included in the Coroners' Newsletter to invite Coroners in England and Wales to redirect their reports on deaths of suspected drug addicts from the Home

Office to St George's. This led to a number of Coroners taking up this invitation, with the number increasing in subsequent years.

In order to thank Coroners for their support and to encourage others to participate it was decided to provide feedback on the information provided, and six-monthly surveillance reports were launched in 1998, to be followed by annual reports. The research team (including the author) subsequently branded itself as the National Programme on Substance Abuse Deaths (NPSAD) (see also Chapter 3). Statistical reports and peer-reviewed journal articles from NPSAD are still being released more than 25 years after its establishment. The author and his Principal Supervisor (FS), both former members of NPSAD, continue to collaborate on research on drug-related deaths and related matters.

NPSAD is the longest-established Special Mortality Register (SMR) in the UK researching drug-related deaths. The other SMR is the Scottish Drug-Related Deaths Database (SDRDD); this database and its outputs are described in Chapter 3.

GMRs and SMRs complement each other. Although there are legal constraints about sharing information, there has been some liaison between ONS and NPSAD. There is a much easier and formal relationship between NRS and SDRDD. Sharing of information facilitates improved understanding of the phenomenon of drug-related deaths. Statistics from both GMRs and SMRs are useful for triangulating statistics and looking at trends. Technically, the original Home Office Study registered in 1978 with OPCS and GROS to look at deaths of drug addicts could be resurrected to create the largest-ever cohort study of mortality of drug addicts.

Reporting to the UNODC and EMCDDA

The Addicts Index Mortality Research project (see previous paragraph) enabled basic characteristics to be captured regarding deaths of addicts notified to the Home Office. The information collected was based on the National Health Service Central Register, and included: name of the addict, age, gender, place, and date of death.

"A simplified coding system was used whereby the cause of death was assigned to one of eight codes and up to two notifiable drugs involved in the death were coded. … The causes of death used, in descending order of priority, were
suicide
homicide
overdose (includes any mention of drugs with intoxication, poisoning, inhalation of stomach contents, asphyxia, respiratory failure)
AIDS/HIV

drug addiction/suspected drug-related (any other mention of drugs or inhalation of stomach contents)
accident
natural causes
unknown …
Only the 14 notifiable drugs (see Note 1.1) were separately identified in the codes. Where more than two controlled drugs were mentioned the priority order was as follows:
Diamorphine (heroin)
Methadone
Dipipanone
Cocaine
Morphine
Pethidine
Dextromoramide
Levorphanol
Hydrocodone
Oxycodone
Phenazocine
Piritramide
Hydromorphone
Opium or unspecified opiates"
Corkery (1997: 54-55)

Not all of this information was presented in the annual statistical bulletins (see above for details).

However, information on the numbers of deaths of notified addicts was provided by the author, in his Home Office role, via the UK Focal Point to the EMCDDA when the agency was established in 1997 (see, for example, ISDD, 1997). This information served to provide an early insight into drug-related mortality for the drug-related deaths and mortality indicator which was being developed at a European level. However, the data from the Addicts Index were limited as they were only available for deaths of addicts occurring from 1985 up to and including 1996 (ISDD, 1999).

With the evolving development of an EMCDDA definition of Drug-Related Deaths (DRDs), which was more comprehensive and broader in terms of capturing DRDs related to anyone irrespective of their addiction or dependence status, it became necessary to start drawing on GMR data to meet this new requirement. The UK Focal Point Report for 1999 used data from the GMRs for the first time, reporting deaths up to the end of 1997 (ISDD, 1999).

Similarly, acting in his Home Office role, the author (and his predecessors, such as Miss Joy Mott) provided information on the numbers of deaths of notified addicts to the UNODC using the Annual Request Questionnaire, thereby continuing a process which had started with reporting such

deaths to the League of Nations in the 1930s. However, with the closure of the Addicts Index, data from the UK GMRs gradually replaced those derived from the Addicts Index. The author continued to collate the statistics for the UNODC up to and including 2010, first in his Home Office role, and then as the UK Focal Point expert on DRDs for the EMCDDA.

One of the major developments in data submission to the EMCDDA was the development of what became Standard Tables 5 and 6. These tables enabled the collation of information using the agency's DRD standard as well as national definitions of DRDs, across the eventual 28 European Union Member States plus Norway and Turkey. The Standard Tables ask for numbers of death broken by gender (male and female) and age-groups, as well as information on 'toxicology', i.e., substances recorded on death certificates rather than mentioned in postmortem toxicology reports, with an emphasis on opioids and alcohol (central nervous system depressants). Standard Table 5 provides information on the current year of reporting, whereas Standard Table 6 provides trend information. There are alternative forms for GMR and SMR returns, which are based on slightly different criteria for data extraction using International Classification of Diseases (ICD) codes.

Standard Tables 5 and 6 provided the main framework for analyses in the UK Focal Point annual reports to the EMCDDA. However, the author developed reporting of GMR data using the three national DRD definitions which were eventually used: the EMCDDA DRD Standard; the ONS 'wide' definition., i.e., deaths due to drug poisoning; and the UK 'drug strategy' or Drug Misuse definition – see Chapter 2 for details of these definitions. This enabled comparisons to be made between the numbers captured by the different definitions and simultaneously trends over time, as well as providing an opportunity to see the contribution to the UK total made by the individual GMRs (see Chapter 6 for more details).

Rates of deaths per 100,000 population were introduced into the Focal Point annual reports by the author from 2002 up to and including 2012; these showed major differences between Scotland and the rest of the UK (see Chapter 6 for a further discussion).

Information on the main drugs recorded on death certificates as being implicated in deaths were included from the early Focal Point reports onwards, although their range was gradually extended to capture drug classes that were emerging as causing concern, initially benzodiazepines and later on Novel Psychoactive Substances (NPS). Requests by the author to the GMRs for such information subsequently led to these drug classes being included in the GMRs' published statistics.

The author also included in his commentary in the Focal Point annual reports summary information on statistics and other findings from the two UK SMRs (NPSAD and NDRDD). Whilst the Volatile Substance Abuse (VSA) Mortality Project was running, the author also reported on trends and findings from that programme; the author and his Principal Supervisor were involved in the production and publication of the final two reports in the series (Ghodse et al., 2012). However, it should be noted that, strictly speaking, VSA deaths did not come within any of the definitions used by the GMRs; but there was significant international interest in such statistics as there was and still is little published on such events.

Submissions to both international agencies (EMCDDA and UNODC) included information on HIV/AIDS deaths. As noted above, initially the information contained in the Home Office statistical bulletins only enumerated deaths due to HIV/AIDS acquired through injecting drug use. A further category was subsequently added to make the statistics more comprehensive – deaths where the infection had been acquired by men having sex with men (MSM). There is a possible overlap between MSM and People who injection drugs (PWID). The final Focal Point annual report to reference such information was that for 2015 (Crawford et al., 2016), whereas the previous report contained more detailed analysis by the author of this thesis (Burton et al., 2014), the final year he acted as the Focal Point expert before that work was taken in-house by Public Health England (PHE) causing a break in continuity of approach. Another development introduced by the author was the reporting of descriptive statistics on age; he developed a method for providing information on mean age, range and standard deviation based on the age-groups requested by the EMCDDA.

After PHE took over responsibility for the DRD indicator, they started doing their own analyses on data extracts provided by ONS relating to England (Crawford et al., 2016). The following year, the Focal Point reported that they had reverted back to submitting UK data based on the year of occurrence of deaths (Crawford et al., 2017), rather than year of registration which had been the basis of submission, by the author and his predecessors, from 1985 for Scotland and Northern Ireland. For England and Wales, deaths registered in a year were submitted from 1985 to 1992, but this was changed to year of occurrence from 1993. Such changes meant that trend data had to be re-extracted on several occasions over a period of 15 years or so. There were no changes in the information presented in the annual report for 2017. There was no report for 2018; the final UK Focal Point (UKFP) annual report being for 2019 (UKFP, 2021). In the author's opinion, this was a very 'stripped-down', basic summary. It was only undertaken to comply with the EMCDDA reporting requirements following the UK's exit from the European Union (EU) ('Brexit'); although this is not stated on the UK Government's website.

General Mortality Register reporting of and on Drug-Related Deaths in the United Kingdom

Apart from the UK Focal Point annual report which contained a chapter or section on Drug-Related Deaths (DRDs), the main vehicles within the UK for reporting GMR deaths were statistical bulletins and ad hoc reports published by the individual GMRs. Contributions were also made by GMR staff to peer-reviewed journals.

England and Wales

Statistics on deaths from poisoning published in *Mortality Statistics Injury and poisoning, England and Wales (Series DH4)* were discontinued in 2005 (see Chapter 3), to be replaced in 2011 by *Injury and poisoning mortality in England and Wales* (ONS, 2011). Some updates were also provided in *Health Statistics Quarterly* (see Table 5.1).

Information on drug-related mortality started to be released in *Population Trends* by OPCS in 1998 (Christophersen et al., 1998) and its sister publication *Health Statistics Quarterly* from 2000 (Atcha and Majeed, 2000). Production of the latter publication ceased in Spring 2012; reports have been archived on https://data.gov.uk and can be found here: https://www.data.gov.uk/dataset/900f703f-a893-4b5a-a0c8-17d49b2fb5cf/health-statistics-quarterly. Issues of particular interest in this series are given in Table 5.1.

The topics covered in *Health Statistics Quarterly* include: methodological issues, such as the impact of moving from ICD-9 to ICD-10 and Coroners' narrative verdicts; looking at geographical differences in specific types of death; seasonality of drug-related deaths; consideration of deaths involving specific drug classes; the impact on death certification and statistics of unique events such as homicides committed by Dr Harold Shipman; as well as annual updates on drug-poisoning related deaths.

Table 5.1: Reports of relevance to drug-related deaths in *Health Statistics Quarterly*

Issue No.	Date:	Report title	Pages
1	Spring 1999	Death certification and the epidemiologist	21-33
3	Autumn 1999	1997 Mortality statistics: injury and poisoning (England and Wales)	35-37
5	Spring 2000	ONS drug-related deaths database: first results for England and Wales, 1993–97	57-60
7	Autumn 2000	Paracetamol related deaths in England and Wales, 1993–97	5-9
7	Autumn 2000	Deaths related to drug poisoning: results for England and Wales, 1994–98	83-86
7	Autumn 2000	Mortality statistics1998: injury and poisoning	95-100
8	Winter 2000	Implementation of ICD-10 for mortality data in England and Wales from January 2001	41-50
9	Spring 2001	Deaths related to drug poisoning: England and Wales, 1995–99	70-72
11	Autumn 2001	Geographical variations in deaths related to drug misuse in England and Wales, 1993–99	25-35
11	Autumn 2001	Mortality statistics1999: injury and poisoning	86-90
13	Spring 2002	The implementation of ICD-10 for cause of death coding – some preliminary results from the bridge coding study	31-41
13	Spring 2002	Deaths related to drug poisoning: results for England and Wales, 1993 to 2000	76-82
14	Summer 2002	Results of the ICD-10 bridge coding study, England and Wales, 1999	75-83
15	Autumn 2002	Mortality statistics 2000: injury and poisoning	79-82
17	Spring 2003	Deaths related to drug poisoning: results for England and Wales, 1997–2001	65-71
19	Autumn 2003	The impact of Harold Shipman's unlawful killings on mortality statistics by cause in England and Wales	5-9
19	Autumn 2003	The effect of the introduction of ICD-10 on trends in mortality from injury and poisoning in England and Wales	10-20
21	Spring 2004	Deaths related to drug poisoning: England and Wales, 1998–2002	59-66
23	Autumn 2004	Fatal toxicity of antidepressants in England and Wales, 1993–2002	18-24
23	Autumn 2004	Mortality statistics 2002: injury and poisoning	89-94
25	Spring 2005	Deaths related to drug poisoning: England and Wales, 1999–2003	52-59
26	Summer 2005	Death certification: issues from a pilot of the Shipman Inquiry's interim proposals	23-26
27	Autumn 2005	Geographical variations in fatal poisoning due to antidepressant drugs in England and Wales, 1993–2003	6-12
27	Autumn 2005	Mortality from suicide and drug-related poisoning by day of the week in England and Wales, 1993–2002	13-16
27	Autumn 2005	Mortality statistics 2003: injury and poisoning	68-73
29	Spring 2006	Deaths related to drug poisoning: England and Wales, 2000–2004	69-76
31	Autumn 2006	Trends in deaths related to drug misuse in England and Wales, 1993–2004	23-27
31	Autumn 2006	Mortality statistics 2004: injury and poisoning	98-103
33	Spring 2007	Deaths related to drug poisoning: England and Wales, 1993–2005	82-88
35	Autumn 2007	Mortality statistics 2005: injury and poisoning	72-77
36	Winter 2007	Mortality statistics 2005: injury and poisoning	66-72
39	Autumn 2008	Geographical variations in deaths related to drug misuse in England and Wales, 1993–2006	14-21
39	Autumn 2008	Deaths related to drug poisoning in England and Wales, 2003–07	82-88
43	Autumn 2009	Deaths related to drug poisoning in England and Wales, 2008	48-55
49	Spring 2011	Narrative verdicts and their impact on mortality statistics in England and Wales	81-100

Population Trends issues 91 (Spring 1998) to 145 (Autumn 2011) are also archived at https://www.data.gov.uk/dataset/b26340c6-9db3-4a26-93cd-46256c0bc2f7/population-trends. Issues of particular interest in this series are given in Table 5.2.

Table 5.2: Reports of relevance to drug-related deaths in *Population Trends*

Issue No.	Date:	Report title	Pages
17	Autumn 1979	Fatal adverse effects of medicines and surgery	17-22
67	Spring 1992	Death certification from the point of view of the epidemiologist	22-28
69	Autumn 1992	Trends in suicide deaths in England and Wales	10-16
71	Spring 1993	Suicide deaths in England and Wales: trends in factors associated with suicide deaths	34-42
73	Autumn 1993	Automatic coding of causes of death	36-38
75	Spring 1994	Homicides in England and Wales	26-29
76	Summer 1994	Deaths associated with the use of alcohol, drugs, and volatile substances	7-16
80	Summer 1995	Suicide deaths in England and Wales, 1982–92: the contribution of occupation and geography	16-25
86	Winter 1996	Mortality trends by cause of death in England and Wales 1980–94: the impact of introducing automated cause coding and related changes in 1993	29-35
88	Summer 1997	The time taken to register a death	48-55
92	Summer 1998	Trends in suicide in England and Wales, 1982-96	29-41
93	Autumn 1998	Drug-related mortality: methods and trends	29-37

Whilst the main focus of this statistical series is on demography, there are also articles with relevance to this thesis, albeit fewer in number than *Health Statistics Quarterly*. Topics covered include: methodological issues, such as the impact of introducing automated coding for causes of death, and time taken to register a death, and death certification from the epidemiologist's perspective; suicides and associated factors; homicides; fatal adverse effects of medicines; and, finally and most relevant, methods and trends in drug-related mortality, and deaths associated with the use of psychoactive substances (alcohol, drugs, and volatiles).

ONS started publishing statistical bulletins on deaths related to drug poisoning in England and Wales in 2010, the first one covering 2009 figures (ONS, 2010). Earlier reports, up to and including 2014, are available on the ONS website on The National Archives website here: https://webarchive.nationalarchives.gov.uk/ukgwa/20160105160709/http://www.ons.gov.uk/ons/index.html. Reports on deaths from 2011 to date (trend data back to 1993) can be found here: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/deathsrelatedtodrugpoisoninginenglandandwales/previousReleases.

Currently (2024), the main ONS bulletin provides a commentary on: deaths from drug poisoning in England and Wales; drug misuse deaths in the two countries; drug poisoning deaths from selected substances. Comments are also provided on delays in death registrations, and possible reasons for increases in the number of drug-related deaths. Technical information is also presented. The bulletin is accompanied by four supporting datasets in Excel (xlsx) format, and are described by ONS (2022) as follows:

"Deaths related to drug poisoning by date of occurrence, England and Wales
Annual number of deaths occurring related to drug poisoning in England and Wales. Data presented by cause of death, sex, age, substance(s) involved in the death, and country and region.

Deaths related to drug poisoning by local authority, England and Wales
Annual number of deaths registered related to drug poisoning, by local authority, England and Wales.

Deaths related to drug poisoning by selected substances, England and Wales
Annual number of deaths registered related to drug poisoning in England and Wales by sex, region and whether selected substances were mentioned anywhere on the death certificate, with or without other drugs or alcohol, and involvement in suicides.

Deaths related to drug poisoning, England and Wales
Annual number of deaths registered related to drug poisoning and median registration delays, in England and Wales. Data presented by cause of death, sex, age, substance(s) involved in the death, country and region, and areas of deprivation."
ONS (2022)

Occasional reports are also made available online by ONS, e.g., ONS (2018b, 2019). In addition, 'user data requests' (e.g., Freedom of Information Requests, including those made by the author) are also published online, e.g., ONS (2018a). As mentioned above, 'user data requests' made to UK GMRs by the author, in his Focal Point role, for breakdowns of deaths involving newly emerging classes of substances causing concern, have led to new substances or classes of substances (e.g., GHB/GBL, mephedrone, etc.) being included in the published statistics (see https://www.ons.gov.uk/search?q=drug+deaths). The author has also advised (and continues to do so) the Secretariat of the UK's Advisory Council on the Misuse of Drugs about data requests to the GMRs; for example, on dissociative drugs, nitrous oxide, alkyl nitrites, etc. He has also made 'user data requests' to obtain statistics for academic papers, e.g., alprazolam (ONS, 2018a).

There have been many individual statisticians involved with producing the drug-related death statistics for ONS over the past three decades, most of whom were personally known by the author through his Home Office and UK Focal Point roles. Although some 16 or so individuals have been given as contact points during this period, there has also been some degree of continuity in personnel with oversight of the production of the annual statistics, so institutional memories have presumably remained intact.

Scotland

The first regular statistical report/bulletin on drug-related deaths in Scotland dealt with figures for 1997 (Jackson and Cole, 1998). However, several papers outlining the improved system developed in 1994 (Arrundale and Cole, 1995) in response to concerns expressed by the House of Commons Select Committee on Scottish Affairs about the quality of information available on deaths arising from drug abuse, also presented data for 1992-4 and, subsequently, 1995 and 1996. The first report by Jackson and Cole (1998) and all subsequent ones up to and including 2020 can be found on the archived website of the National Records of Scotland (https://www.nrscotland.gov.uk/statistics-and-data/statistics/statistics-by-theme/vital-events/deaths/drug-related-deaths-in-scotland/archive).

The range and levels of analyses presented, together with supporting datasets, have evolved and increased over the past 25 years or so. There has been continuity of approach and the institutional memory of those responsible for producing these statistics has been uniquely preserved. The author only had to deal with five individual statisticians during the whole of the period covered by this thesis. The present incumbent has inherited a very well-documented repository of data and knowledge; this augurs well for the future.

The current (2024) outputs from NRS can be found here: https://www.nrscotland.gov.uk/statistics-and-data/statistics/statistics-by-theme/vital-events/deaths/drug-related-deaths-in-scotland.
Outputs available include: a press release with a brief summary and links to the outputs; a statistical report covering breakdowns of, principally, drug misuse deaths by variables such as sex, age, deprivation, Scottish areas, cause of death, substances implicated, as well as comparisons with other countries in the UK and Europe; Excel datasets for (a) the figures and tables in the statistical report, (b) additional data for the period 2000 to date; additional analyses including “some more detail on the numbers of deaths for which certain drugs were reported, death rates for problem drug users, and further analyses of the figures for NHS Board areas”; as well as methodological annexes. Within the last category, Annex A refers to some of the author’s earlier research (Corkery, 2008). NPS are covered by Annex E. Some trend data provided go back to 1996, others start in 2000. Trend data are also available using the ‘wider ONS’ definition, i.e., deaths from drug poisoning.

Northern Ireland

NISRA started publishing their annual reports and accompanying tables on drug-related deaths in 2009, with a time series going back to 1997. The period covered by the currently accessible reports and accompanying Excel tables starts in 2001; each publication covers registrations in the most recent and the preceding 10 years. Figures in these releases cover fatalities "where the underlying cause of death indicated drug poisoning, abuse or dependence or a controlled drug was involved" (NISRA, 2024a). These tables can be accessed here: https://www.nisra.gov.uk/statistics/cause-death/drug-related-deaths. Technical information on how cases are defined, data collected, etc. are also provided (NISRA, 2022). Some socio-demographic analyses are also published, along with some user-requested data.

Currently, the information contained in the annual statistical release comprises: a press release; the statistical bulletin; and tables in Excel (xlsx) and ods (open document spreadsheet) formats. The statistical bulletin (NISRA, 2024b) presents: a summary of key points; an Introduction; a commentary looking at sex and age, drug types, underlying cause of death, alcohol mentions, number of implicated drugs, geographical areas, and deprivation levels; an annex contains definitions and lists of the accompanying tables. The number and contents of tables have evolved over time, especially as interest as grown in particular substances (e.g., fentanyl) or drug classes (e.g., synthetic cathinones and other NPS). In response to user feedback, NISRA have also included high-level geographical breakdowns for drug-misuse deaths.

As with Scotland, the author has had to deal with only half a dozen or so individuals within NISRA (which comes under the Department of Finance and Personnel in Northern Ireland) in his various Home Office, St George's, UK Focal Point, and University of Hertfordshire roles over the past couple of decades. Some individuals have been contacts for a decade or more, thereby ensuring continuity of approach and safe-guarding of the Agency's institutional/collective memory.

United Kingdom Special Mortality Registers reporting on Drug-Related Deaths

NPSAD

Background information has already been presented in this chapter on the origins and establishment of NPSAD, and also on its case definition (Chapter 3). The Programme published the first of its 6-monthly surveillance reports in Spring 1998; this issue reported on deaths reported during the period July - December 1997 (Ghodse et al., 1998). After several years it became apparent that there was a need to also produce an annual report analysing deaths by year of

occurrence as this approach was considered much more useful in epidemiological terms. The first annual report appeared in 2000; it covered deaths occurring in the 1999 calendar year, but also included the latest 6-monthly surveillance report (Ghodse et al., 2000). Initially, geographical coverage was limited to coroners in England and Wales, but by 2001 the author had persuaded the statistician in the GROS to contribute to the annual report (Ghodse et al., 2002). The following year saw coverage expand to include coroners in Northern Ireland, the Isle of Man, Guernsey, Jersey, as well as Procurators Fiscal in Scotland (Ghodse et al., 2003). Thus, the first UK-wide publication on drug-related deaths since the Home Office Addicts Index statistical bulletin for 1996 (Corkery, 1997) became available. The annual report for 2005 included data from Scottish police forces for the first time (Ghodse et al., 2006); this arrangement continued for several years through a formal Memorandum of Understanding with the Scottish Crime & Drug Enforcement Agency (SCDEA), co-drafted by the author as the NPSAD Programme Manager.

During the period 2003-7, NPSAD undertook 17 surveillance reports (including psychological autopsies) which were commissioned by local authorities, Drug (and Alcohol) Action Teams, and National Health Service Trusts; the author did most of the analyses and drafting of these reports. On behalf of NPSAD, the author led on a special report commissioned by the Department of Health in 2006 looking at drug-related deaths in England and Wales during the period 1999-2004.

The Programme had funding from the Department of Health in the period 2005-10 to cover its running costs, including the employment a research assistant and a Programme Manager (the author). This period probably corresponds with the Programme's highest level of visibility and geographical coverage. Subsequently, Scottish coverage disappeared following the re-organisation of police in that country. Compliance from Coroners in Wales became somewhat lower, although cases are still being reported to NPSAD. A lack of consistent funding has led to a decline in the resources available to the Programme, and thus its outputs. The last annual report covered deaths occurring in 2012 (Corkery et al., 2014). The focus of effort has shifted back to England in terms of geographical coverage. This is enhanced by close collaboration by the present Programme Director (Dr Caroline Copeland, based at King's College, London) with Public Health England. The latest data released by NPSAD were for deaths in England in 2015. Unfortunately, they are currently unavailable online, although the NPSAD Director is seeking to redress this deficit (personal communication to author from Dr Caroline Copeland, 8 March 2024).

Although formal links by the author and his Principal Supervisor, in the form of honorary positions, ceased in 2015, there was strong collaboration within a European Commission funded research project (EU-MADNESS – see https://www.facebook.com/EUmadnessproject/, https://twitter.com/eu_madness). Furthermore, collaboration continues between the author and

the NPSAD Programme Director on joint peer-reviewed journal articles (e.g., Corkery et al., 2019; Corkery et al., 2021), and providing input to ACMD Working Group reports, e.g., Nitrous Oxide (ACMD, 2023a), Diphenidine (ACMD, 2023b), and alkyl nitrites ('poppers') (ACMD, 2024) - these will provide the basis for future publications led by the author (see Chapter 7).

Such activities continue a long tradition of using NPSAD data (along with other sources of information) to research original and innovative aspects of drug-related deaths and associated mortality, born out of the use of Coroners' data for investigating and understanding deaths of notified addicts. The author has been involved in such research since 1999 (e.g., Oyefeso et al., 1999a; Oyefeso et al., 1999b). Examples of using drug-related death statistics with other drug indicators to tell the story of specific drugs include: buprenorphine (Schifano et al., 2005); ecstasy-type drugs (Schifano et al., 2006); and cocaine/crack (Schifano et al., 2008). These relationships are the focus of Chapters 8 to 12.

National Drug Related Deaths Database (Scotland)

The NDRDD's background has been described in Chapter 3. The latest report covers 2017 and 2018 (Public Health Scotland, 2022); further reports are due to be published. As well as the report and a summary being available online and in pdf format, tables are also provided in Excel (xlsx) format. The report introduces the database and the methodology used. The commentary covers: demographics; substance use history; medical and psychiatric history and significant life events; contact with services; circumstances of death; toxicology; and prescribing. A number of appendices present additional technical information, contact points, etc. The latest data release presents 65 tables across the themes outlined above. Currently (2024), trend data cover the period 2009-2018.

Developments since the first report about the database, include a doubling of the number of tables presented (n = 32). Although the range of themes covered has remained constant, newer issues have been introduced, such as NPS (e.g., etizolam), misuse of gabapentinoids. The report covering 2017 and 2018 deaths also takes a look at deaths by suicide.

As far as the author can establish, the database has been used as a resource for only a couple of peer-reviewed journal articles, i.e., McAuley et al. (2015) and Tweed et al. (2022). By comparison, the NPSAD database has been and is being extensively used for such publications.

Other publications about drug-related deaths in the United Kingdom

This section briefly mentions some additional sources of information on drug-related deaths in the UK. Its coverage is broad but is neither an exhaustive description nor a bibliography.

Several additional official resources have historically provided or continue to provide some information on drug-related deaths or drug-related mortality.

Northern Ireland Addicts Index

The Northern Ireland Drug Addicts Index was set up under the Dangerous Drugs (Notification of Addicts) Regulations (Northern Ireland) 1968 and was superseded by the Misuse of Drugs (Notification of and Supply to Addicts) (Northern Ireland) Regulations 1973. It was run on similar lines to the Home Office Addicts Index (Corkery, 1997) but was a separate entity and closed much later (see below). Annual statistics included information on those individuals added to, or removed from, the [Northern Ireland] Addicts Index; the latter category included by reason of death.

The total number of individuals notified to the Index never exceeded 315 (peak in 2010), and the number of removals by reason of death ranged from 0 to 8 per year. However, these figures represent an annual proportion of deaths ranging from 0% up to 20% during the period 1992 to 2012 (NISRA and DHSSPS, 2006; NISRA and DHSSPS, 2013). Annual statistics for the period 2005-12 can be found archived here: https://www.health-ni.gov.uk/publications/statistics-northern-ireland-drug-addicts-index-2005-2012.

In August 2015, the Advisory Council on the Misuse of Drugs wrote to the then Minister for Health, Social Services and Public Safety in Northern Ireland recommending that “the obligations placed on doctors under the [1973 Regulations] to report cases of addiction should be removed in order to bring the Northern Ireland regulations in line with the rest of the UK” (ACMD, (2015).

Scotland

Information on Fatal Accident Inquiries held in Scotland has already been outlined in Chapter 3. The reader’s attention is drawn here to the fact the case determinations, including some drug-related cases can be found here: https://www.scotcourts.gov.uk/search-judgments/fatal-accident-inquiries. These can provide useful, and sometimes unique (e.g., Corkery and Schifano, 2022), insights into such incidents.

Earlier, in connection with NPSAD reports, reference was made to data collated by the SCDEA. A more recent development (September 2021) has been the quarterly release of "management information from Police Scotland on suspected drug deaths, to provide as timely an indication of current trends in drug deaths in Scotland as is possible (reports are available here: https://www.gov.scot/collections/suspected-drug-deaths-in-scotland/). Statistics from the National Records of Scotland (NRS) are also presented for wider context", with the latest figures covering the fourth quarter of 2023 (Scottish Government, 2024).

There have also been national confidential inquiries in Scotland into specific drugs such as methadone (see, for example, Scott et al., 1999; Seymour et al., 2003), or specific regional geographic areas (see, for example, Neufeind et al., 2012; Tayside Drug Death Review Group, 2020).

England and Wales

Coroners in England and Wales have a duty, under the provisions of paragraph 7 to Schedule 5 of the Coroners and Justice Act 2009, to send reports to a person, organisation, local authority, government department or agency, where they believe that action should be taken to prevent future deaths. Such reports, and responses to them, are submitted to the Chief Coroner who then publishes them in compliance with Regulations 28 and 29 of the Coroners (Investigations) Regulations 2013 (https://www.legislation.gov.uk/uksi/2013/1629/part/7/made). Most of these reports are in the public domain (see here: https://www.judiciary.uk/?s=&pfd_report_type=&post_type=pfd&order=relevance). Many reports relate to drug-related deaths, including both prescription drugs and 'recreational' substances. The author has drawn on such reports in preparing contributions to ACMD reports and advice.

In addition to the local surveillance reports undertaken by NPSAD (see above), local confidential inquiries or reviews have been conducted in Wales, using the current guidance issued by the Welsh Government (2014) and earlier advice (based on the author's NPSAD data extraction form).

International dissemination of United Kingdom Drug-Related Death statistics and information

Data and information on drug-related deaths and mortality of drug users in the UK have been provided for inclusion in international publications and statistics for over eight decades.

As mentioned earlier, information on the deaths of addicts notified to the Home Office were included in annual reports from the League of Nations and its successor the United Nations (based on the Annual Request Questionnaire (ARQ)), as well as in the early years of the EMCDDA. Statistics from the UK's GMRs were also submitted once robust statistical databases and related statistical publications had been developed, eventually replacing information from the Home Office statistical bulletins (e.g., Corkery, 1997). Currently, the GMR data, submitted via the ARQ, were incorporated into the commentary which appears in volume 2 of the UNODC's *World Drug Repor*t (UNODC, 2022). However, the most recent detailed breakdowns appeared in the *2020 World Drug Report Annex* (UNODC, 2020). This presents the "number of drug-related deaths, mortality rates per million persons aged 15-64 years and ranking of drugs as primary cause of death (2018 or latest year available)". All statistics published by the UNODC in this format tend to be several years out of date, due to the nature of the collation and publishing processes; the UK figures relate to 2017. More recent statistics are unavailable.

Turning to Europe, an outline is presented earlier in this chapter about the provision of UK data to the EMCDDA, starting with data from the Home Office Addicts Index, which were then replaced by GMR data up until the end of January 2020 when the UK left the EU (Brexit).

Over the course of the UK's membership of the EMCDDA, its data on DRDs constituted the largest single contribution of any Member State in terms of numbers. This often led to the UK being incorrectly nicknamed the 'drug capital of Europe'. This was due to misunderstandings, and probably also deliberate dissemination of misinformation, about: differences in data sources and their inherent variety in purpose(s) for collection; definitions; quality and accuracy of case identification, recording and classification; etc.

Underpinning the process of data collation and submission by the UK Focal Point experts to the EMCDDA was the unseen work involving such activities as: development and refinement of the DRD standards (e.g., EMCDDA, 2010); mapping of data flows from SMRs (Gesundheit Österreich GmbH, 2009); a pilot study (field trial) in 2005-6 to explore the feasibility of collating information on what the EMCDDA termed 'toxicology'(i.e., drugs implicated in the cause of cause), which led ultimately to a full-blown examination of toxicology practices across EU Member States

(EMCDDA, 2019); as well as focused studies commissioned to look at specific technical, including epidemiological, aspects of DRDs and associated mortality (e.g., Corkery, 2012). The latter types of studies often emerged from workshops held during the 'expert' meetings at the EMCDDA in Lisbon, during which reports from individual countries were presented on the situation relating to DRDs (see, for example, https://www.emcdda.europa.eu/drugs-library/annual-expert-meeting-drug-related-deaths-drd-and-drug-related-infectious-diseases-drid-%E2%80%93-preliminary-summary-and-highlights-meeting). The author was involved in all of these activities during 2000-14.

Data presented about DRDs in the annual EMCDDA statistical bulletins are, therefore, just the visible tip of a much larger iceberg of underlying but fundamental supporting activities. The UK contribution to the visible EU iceberg tip is demonstrated below. Figure 5.1 illustrates how, in 2018, as they did in previous years, the UK (with one-third) and Germany accounted for half of all deaths by overdose reported to the EMCDDA. This diagram needs to be understood in the context of both under-reporting in some countries and the magnitude of populations at risk of such deaths in the UK and Germany (EMCDDA, 2020). Figure 5.2 shows that the overall UK drug-induced mortality rate was amongst the highest in Europe in 2015-16, although it obscures the differences within the UK (see Chapter 6).

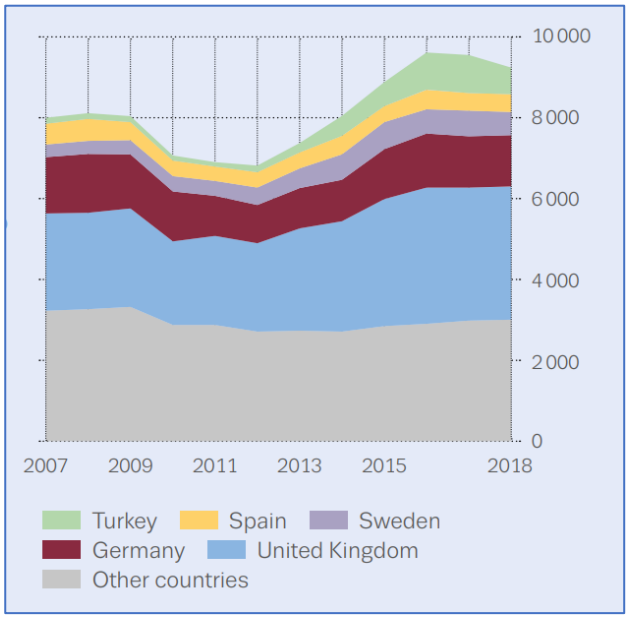

Figure 5.1: Trends in overdose deaths, European Union, Norway and Turkey, 2007-2018

Source: European Drug Report 2020: Trends and Developments (https://www.emcdda.europa.eu/system/files/publications/13236/TDAT20001ENN_web.pdf)

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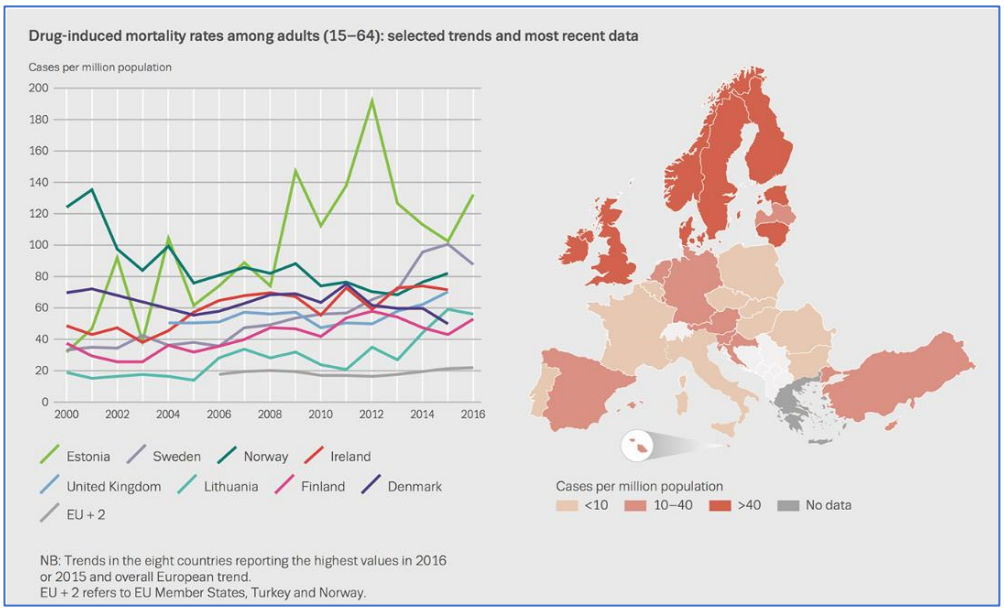

Figure 5.2: European drug-induced mortality rates among adults (15-64): selected trends and most recent data, 2015-16

Source: EMCDDA Statistical bulletin 2018 graphic (https://www.emcdda.europa.eu/data/stats2018/drd_en)

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Emerging improvements and recent challenges

Graphical representations of illicit drug use and associated overdoses are now beginning to appear “visualized by maps” (Raffa et al., 2022a, 2022b; Ritchie and Moser, 2022). This helps to facilitate a global perspective for the general reader, and to understand how data presented in Global Burden of Disease publications (e.g., GBD 2019 Diseases and Injuries Collaborators, 2020) relate to different parts of the world.

In some parts of the world, access to anonymised datasets is being piloted, albeit with restricted access, to facilitate *ad hoc* independent analyses. For example, in the United States of America (USA) the National Vital Statistics System (NVSS) provides data on fatal injury that can be analysed and visualised here https://www.cdc.gov/injury/wisqars/index.html using the WISQARS tool. Similarly, the WONDER online databases (https://wonder.cdc.gov/) employ an *ad hoc* query system for the analysis of public health data, including cause of death. Both of these facilities are offered by the Centers for Disease Control and Prevention (CDC) which has also developed the SUDORS (State Unintentional Drug Overdose Reporting System) dashboard

which has not only cause of death data but also comprehensive postmortem toxicology information (https://www.cdc.gov/drugoverdose/fatal/sudors.html). This dashboard also facilitates data visualisation. Coronial and Medical Examiner databases have also been developed along similar lines (Williams et al., 2017). Statistics Canada has also developed a data visualisation dashboard for provisional deaths (https://www150.statcan.gc.ca/n1/en/catalogue/71-607-X2021028).

In the UK context, we have noted earlier in this chapter the existence of the FAI and Regulation 28 report datasets that can be searched. Sharing of information is also demonstrated through data linkage between the GMR (NRS) and SMR (NDRDD) in Scotland, along with other agencies in that country. The ONS drug poisonings datasets include a pivot table that can be interrogated to facilitate more bespoke searches looking at substance mentioned alone or not, gender of deceased, and area of usual residence registered in each year since 1993. So, there is some gradual progress towards more accessible data and statistics in the UK.

Development in data linkage in the UK has been well-demonstrated by the NDRDD in Scotland (see above). The author is aware that local data exchange has been going on in various parts of the UK, including Hampshire where relevant stakeholders have access to a central database of suspected drug-related deaths and are able to share information 'in real time'.

The Report Illicit Drug Reactions (RIDR) website was piloted in March 2017 on a one-year basis but ran until February 2020, when it was closed due to a low volume of reports. The aim of the exercise was to enable healthcare professionals coming into contact with patients experiencing harm associated with use of illicit drugs, particularly NPS, to report drug reactions, thereby to "better collect data on harms from illicit drug use, to support provision of clinical guidance to professionals" (MHRA, 2017). However, health professionals in England and Wales can still use the national Public Health England (PHE) drugs alert via the dedicated Drug.Alerts@phe.gov.uk inbox. An initiative, similar to these channels of information sharing, was launched north of the (English) border in October 2022. The Rapid Action Drug Alerts and Response (RADAR) is Scotland's drugs early warning system. It assesses and validates information that can: (a) "allow for the rapid and targeted deployment of interventions" and (b) "prevent and reduce the risk of drug-related harm" (Public Health Scotland, 2023).

The timely communication of these types of information to relevant stakeholders, after due diligence as to assessment and validation, can speed up consideration and implementation of initiatives to prevent potential further poisonings, overdoses and even deaths. This is equally true of the publication of single case-reports involving NPS; these cases should be written up and

published as soon as possible; often there is a lack of information on their pharmacological, toxicological and potentially lethal properties.

The timely release of information on deaths can help alert stakeholders to emerging concerns. Reference has been made earlier in this chapter to the release in Scotland of police estimates of suspected DRDs (Scottish Government, 2024). This provides an earlier insight into potential emerging issues than having to await the collation and publication of the NRS annual statistics. However, formal investigations must be conducted by the relevant agencies. Similarly, as outlined in Chapter 3, due process is also followed by Coroners in the rest of the UK.

Unfortunately, the Covid-19 pandemic is likely to have adversely impacted the investigation of drug-related deaths across the UK. The author understands from UK colleagues in the toxicological field that the pandemic has led to delays in getting NPS reference samples. Coroners and police are likely to have had reduced staff resources to deploy with respect to death investigations. There is currently (May 2024) little information published either by UK GMRs or in academic papers about this aspect. An internet-based study of the circumstances of 66 national civil registration services during the 'lock-down' period March-November 2020 found that services continued to be maintained by only a minority of countries (AbouZahr et al., 2021). Birth and death registrations fell in most countries surveyed due to both operational and legal restrictions. England and Wales were placed in the "Civil registration considered essential but limited to certain vital events" category (AbouZahr et al., 2021). Deaths and still-births could be registered by telephone, birth and registration services based in hospitals were suspended whilst Covid-19 restrictions were in place; priority was given to registration of still-births and deaths over births and other vital events (United Kingdom, 2020b).

Coroners in England and Wales reported a four-week increase in the estimated average time taken to process an inquest from 27 weeks in 2020 to 31 weeks in 2021; "this is likely due to a backlog of cases caused by the Covid-19 pandemic" (Ministry of Justice, 2022). Such backlogs were acknowledged by the Chief Coroner in July 2022 (Chief Coroner, 2022). Changes made to civil registration by the Coronavirus Act 2020 (United Kingdom, 2020a) noted by ONS in December 2020 included this aspect:

- "The time taken for deaths to be registered (registration delay) in 2020 decreased compared with the previous year during the first wave of the coronavirus (COVID-19) pandemic; this was because of a combination of factors including a more efficient 'virtual' death registration processes and a reduction in coroner-certified deaths which typically take longer to register.
- The proportion of deaths certified by a doctor increased and the proportion certified by a coroner decreased during the first wave of the coronavirus pandemic.

- Longer delays in coroner-certified deaths are expected, as during the height of the pandemic, the majority of coroner's inquests were halted; this will especially affect deaths due to suicide and violence.

ONS (2020)

The impact of the pandemic on drug marketing and use patterns (Arillotta et al., 2021; Di Trana et al., 2020) and on treatment and provision of medication (Chiappini et al., 2020) and thus on overdoses and deaths is an area that merits investigation. An examination of routine care toxicological screening performed on patients hospitalised in Grenoble University Hospital in France, indicated an increased occurrence of positive results for psychoactive substances during periods of lockdown (Spinelli et al., 2022). There are indications from Finland of changes in the number of post-mortem findings for amphetamine (in particular), buprenorphine, and cannabis increasing directly after implementation of the national government's lockdown restrictions (Mariottini et al., 2021). Changes in the availability of MDMA (ecstasy) following lock-down in the UK led to increased use of synthetic cathinones (Pascoe et al., 2022).

Differences in the volume of autopsies have been detected in the UK during the Covid-19 pandemic. Some medico-legal centres conducting postmortem investigations showed a near-complete closure of their coronial autopsy service (Roberts and Traill, 2021). A study of nine coronial jurisdictions in England found there was a nominally significant ($p = 0.0477$) increase in the proportion of drug and alcohol-related deaths between 2018 and 2020, although no detailed breakdown between these is presented in the paper (Pell et al., 2023). Yates and Jaynes (2021) noted a more than double increase in alcohol-related deaths examined by their medico-legal centre in central southern England during the first nine months of the Covid-19 pandemic.

It is inevitable that such delays will have a consequent knock-on effect for epidemiological investigations since these should be based on occurrence on death rather than when reported or registered. This should be borne in mind when looking at long-term trends (see Chapter 6). Such delays can also affect the provision of up to date advice for policy formulation, changes to legislation, clinical guidance, etc. (see Chapter 13).

Chapter overview

Collaboration is a key theme that links the features examined within this chapter, namely, data collection, analyses, sharing, and dissemination. There has been an increase in the number and range of agencies collecting, analysing, and publishing data and statistics on drug-related deaths across the UK. Some exercises were 'one-off' activities, whereas others have evolved and established themselves as 'go-to' places to obtain timely, accurate and detailed information. These

resources and their major outputs have been described. Emerging improvements and recent challenges (e.g., Covid-19) have been discussed.

The next chapter (Chapter 6) looks at changes over time in the types and nature of drugs involved in drug-related deaths; the characteristics of those dying are examined in Chapter 7.

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PART 3 – EPIDEMIOLOGY OF UNITED KINGDOM DRUG-RELATED DEATHS

This Part consists of two chapters (6 and 7) that provide detailed epidemiological descriptions, analyses and evaluations of drug-related deaths (DRDs) in the United Kingdom (UK). These chapters are empirically based (as are those in Part 4) in contrast with the narrative approaches in Part 2 describing the relevant data sources and processes.

Chapter 6, through a series of in-depth secondary analyses of data (published and supplementary unpublished material provided for the purposes of the author's doctoral research programme) from the UK's General Mortality Registers, explores the evolution of UK DRDs at a macro level, both at sub-national and UK levels. The principal aspects include: the demographic and other characteristics of those dying of drug-related poisoning; the spatial (*locus*) and geographical characteristics of deaths; changes over time; the nature of the drugs involved in deaths; and characteristics of deaths associated with drug poisoning.

Chapter 7 employs findings from Special Mortality Registers (SMRs), e.g., the National Programme on Substance Abuse Deaths (NPSAD) to provide low level (micro) explorations of the more detailed data on a wider range of information and how they can assist in identifying those groups 'at risk' of a drug-related death. The key aspects examined include: demographic; social; economic, health (physical and mental); and substances. This is demonstrated, in part, by reference to relevant studies, using NPSAD and other resources, undertaken by the author and colleagues in the past and for the purposes of this doctoral research programme.

CHAPTER 6 - IN-DEPTH SECONDARY ANALYSES EXPLORING THE EVOLUTION OF DEMOGRAPHIC, SPATIAL, TEMPORAL, AND TOXICOLOGICAL ASPECTS OF DRUG-RELATED DEATHS IN THE UNITED KINGDOM

"Drug-related mortality provides a definitive index of the severity of drug abuse and dependence from both clinical and public health perspectives. It provides information about the natural history of addiction, and the emergence of and increase in drug abuse-related problems."
Corkery (2008)

"Behind every statistic there is a grieving family and a life lost."
Constance (2023)

Previous chapters (3, 4 and 5) have provided information on the sources available in the context of the United Kingdom (UK) to provide not only an overview of drug-related deaths (DRDs) but also insights into their nature and extent. This chapter (6) and several of the following chapters (especially 7 to 12) describe and illustrate some of these aspects. The main facets examined in this chapter include: those relating to the demographic and other characteristics of those dying of drug-related poisoning; the spatial (*locus*) and geographical characteristics of deaths; changes over time; the nature of the drugs involved in deaths; and characteristics of deaths associated with drug poisoning. Due to space and word constraints, this chapter provides a comprehensive but not exhaustive overview of the evolution of such deaths in the UK over the past three decades or so.

The primary sources that facilitate an examination of long-term trends are the UK General Mortality Registers (GMRs) maintained by: the Office for National Statistics (ONS) covering England and Wales; the National Records of Scotland (NRS); and the Northern Ireland Statistics and Research Agency (NISRA). The reader will recall that the data provided by these sources are effectively limited to those on the Medical Certificate of Cause of Death (see Chapter 3 for more details). This means that there are a limited number of variables or parameters that can be reported on, i.e., year (of registration) of death, gender, age, cause/mechanism of death, substances mentioned in the cause of death, underlying cause of death, and intentionality, country and area where the death was registered. The more 'in-depth' or 'deep dive' types of investigation, such as those in Chapter 7, necessarily involve the wider range of information available to Special Mortality Registers, such as the National Programme on Substance Abuse Deaths (NPSAD).

The following accounts are all secondary analyses of existing published data, ***supplemented by specific additional data provided to the author for the purposes of his programme of research***. Although data are being pooled from several sources, this does not mean that the analyses presented here can be regarded as meta-analyses. For the latter, one would also have to:

"use well recognised, systematic methods to account for differences in sample size, variability (heterogeneity) in study approach and findings (treatment effects) and test how sensitive their results are to their own systematic review protocol (study selection and statistical analysis)."
Shorten and Shorten (2013)

To illustrate particular aspects, it will be necessary to draw on data using the different definitions outlined in Chapter 2. However, wherever possible, the wide ONS definition is preferred.

Trends in numbers of United Kingdom Drug-Related Deaths

This section provides an overall context for the more detailed examination that follows by presenting graphically information on the number of UK DRDs over the past three decades or so. Figure 6.1 includes information on deaths on deaths of addicts notified to the Home Office, and to the Northern Ireland Addicts Index in order to provide an indication of trends prior to and into the period covered by this thesis.

"The [Home Office Addicts Index] … is important historically as one of the earliest and longest running reporting systems of 'addicts' … It is important, also, that these long-term trends are not lost, as they provide an invaluable picture of the spread of opiate use and the treatment response in the UK."
Hickman et al. (2004)

Such epidemiological considerations also apply to DRDs and other drug indicators (Chapters 8 to 12).

Figure 6.1 shows a gradual increase in the number of deaths of addicts in Great Britain notified to the Home Office from 18 in 1983 to a peak of 570 in 1993, followed by a fall to 148 in 1996 (Corkery, 2002). The decline between 1993 and 1996 may be due, in part, to delays in deaths being notified by service providers and/or coroners. It would not be sensible to try and predict how deaths of notified addicts were subsequent to 1996; any such study would involve the resurrection of the mortality cohort study set up by the Home Office in 1978, and last used (by the author) to prepare the final statistical bulletin containing such data (Corkery, 1997). To improve an understanding of previous trends, the author has included information from the final Home Office Statistical Bulletin on notified addicts (Corkery, 1997). Table 16 in that publication provides figures for UK (Great Britain from 1988-1990) deaths where the underlying cause of

death was (a) drug dependence or non-dependent abuse of drugs and (b) deaths from poisoning where a controlled drug was mentioned. These statistics, therefore, capture a narrower range of deaths than the ONS (drug poisoning) definition. Nevertheless, these show a continuing rise in deaths across the period 1988-1995, with numbers in the final years being at a similar level to those for the Drug Strategy and EMCDDA definitions starting two or three years later.

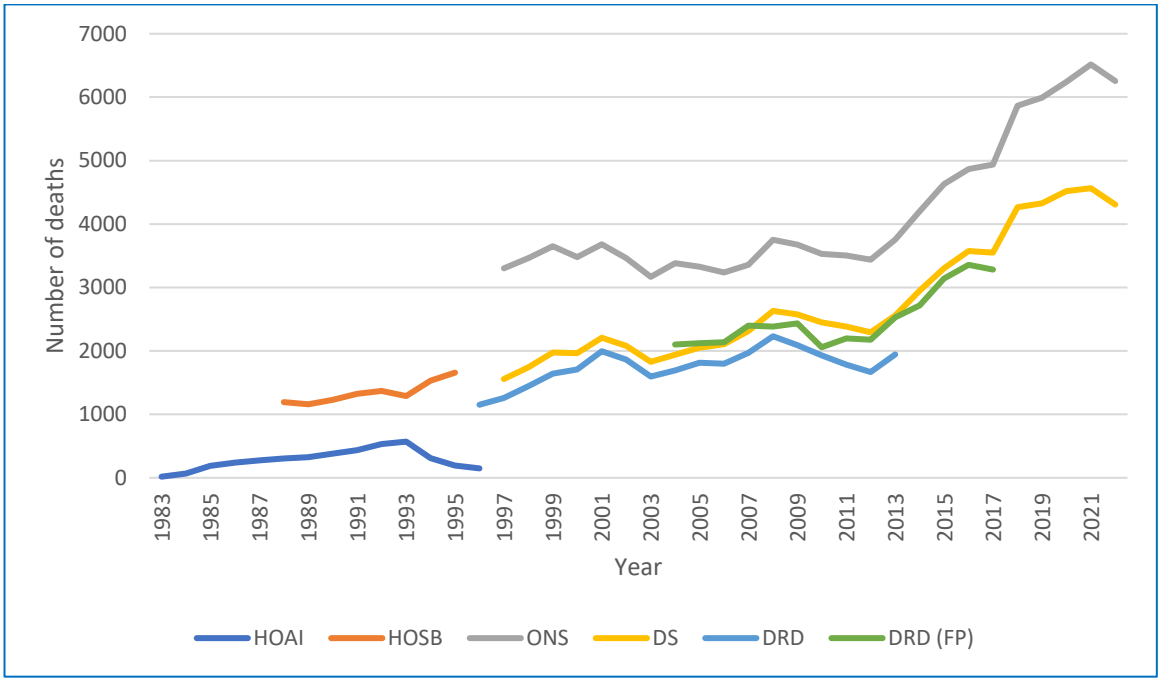

Figure 6.1: Numbers of drug-related deaths using different definitions, United Kingdom, 1993-2022

Notes: HOAI = Home Office Addicts Index; HOSB = Home Office Statistical Bulletin; ONS = Office for National Statistics (drug poisonings; DS = Drug Strategy; DRD = Drug-Related Deaths; DRD (FP) = Drug-Related Deaths (Focal Point).
Sources: Corkery (1997); Corkery (2002); returns to the European Monitoring Centre for Drugs and Drug Addiction.

Whilst there is continuity in the definitions used by the GMRs across the period reported on in this chapter, there were some modifications made in the interpretation of the DRD (i.e., European Monitoring Centre for Drug and Drug Addiction - EMCDDA) definition by the UK Focal Point when they took over this work from the author in his EMCDDA expert role and conducted in-house preparation of the returns to the EMCDDA (Crawford et al., 2017:84-85). This led to higher numbers than the previous ones submitted by the author.

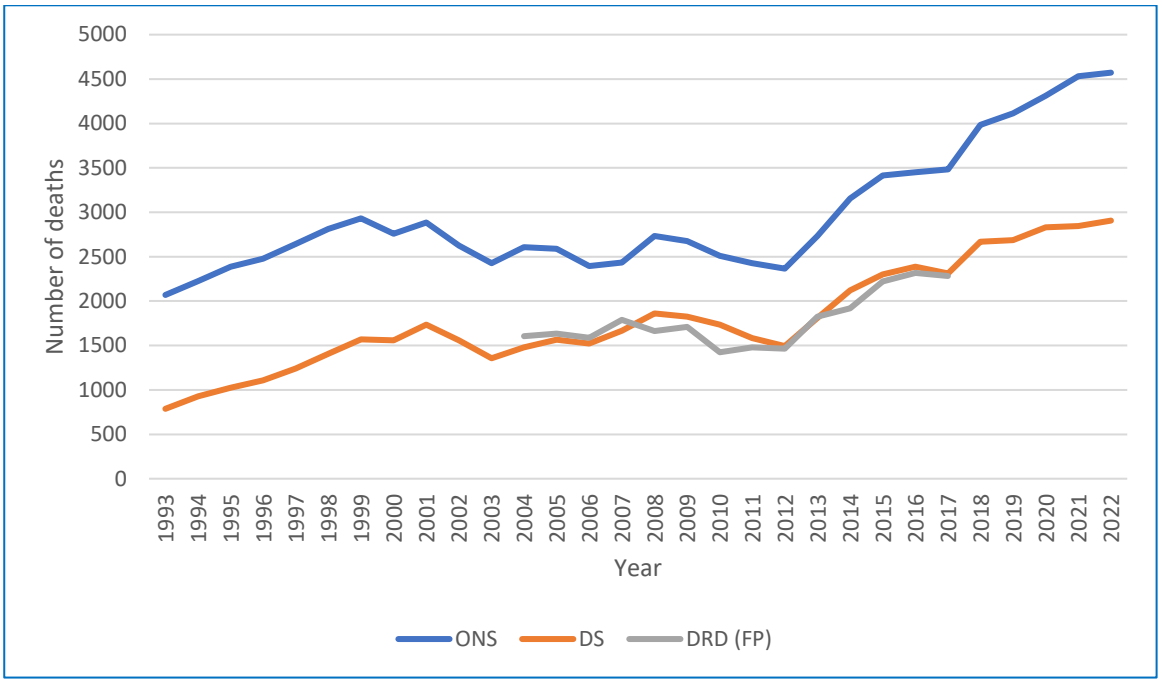

Figure 6.2: Numbers of drug-related deaths using different definitions, England, 1993-2022

Notes: ONS = Office for National Statistics (drug poisonings; DS = Drug Strategy; DRD (FP) = Drug-Related Deaths (Focal Point).

Sources: Returns to the European Monitoring Centre for Drugs and Drug Addiction; ONS (2023)

The following analyses relate to deaths registered in a calendar year. It can be seen that, both at the UK level and at the level of the constituent countries of the UK (see Figures 6.2 to 6.5), the 'ONS' definition leads to a higher number of deaths being registered, compared to the UK Drug Strategy and the EMCDDA DRD definitions, respectively. At the UK level, the direction of movement in the evolution of deaths is mirrored across the time-period 1996/7 onwards. There is considerable fluctuation from year to year between 1996/7 and about 2012. From 2013 onwards, the numbers of deaths have increased rapidly nearly every year. In the last few years there seems to have been a widening of the gap between the ONS and Drug Strategy definitions, possibly due to an increasing contribution being made to the ONS figures by Novel Psychoactive Substances (NPS), especially in Scotland (NRS, 2023). This is because NPS are not captured by the Drug Strategy definition.

Similar observations can be made of the numbers presented in Figure 6.2 for England, which accounts for the majority of deaths in the UK related to drug use, but not necessarily in a proportionate way - as will be seen later. Deaths rose steadily year on year from 1993 to 1999, followed by a period of oscillation lasting until 2012. In the following decade or so, the number of deaths rose again but at an increased rate. The movements in the ONS definition deaths are

echoed by those using the other two definitions, which are in close alignment. Again, there appears to be widening in the gap between ONS and the other definitions in recent years.

The picture for Wales shows an overall upward trend over the past three decades, but with many more peaks and troughs, especially evident from 2018 (Figure 6.3). Otherwise, similar comments about the relationships between the three definitions remain valid for Wales.

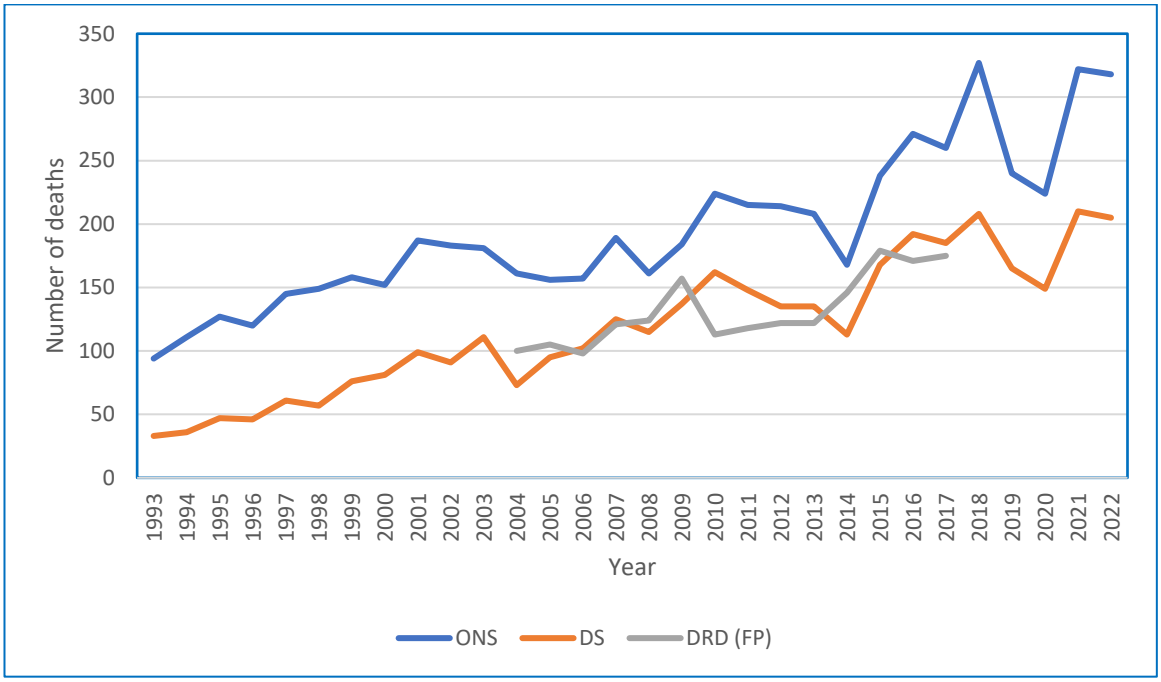

Figure 6.3: Numbers of drug-related deaths using different definitions, Wales, 1993-2022

Notes: ONS = Office for National Statistics (drug poisonings; DS = Drug Strategy; DRD (FP) = Drug-Related Deaths (Focal Point).

Sources: Returns to the European Monitoring Centre for Drugs and Drug Addiction; ONS (2023).

The trends in Scotland show the smoothest transitions year on year of the four constituent parts of the UK (Figure 6.4). There is a fairly stable rate of increase between 1993 and 2013, but the rate then accelerates at a much quicker pace. A peak seems to have occurred in 2020 with a slight levelling off in 2021, and large fall in 2022 (NRS, 2023). However, the decline in those years may be, in part, the effect of the Covid-19 pandemic; this aspect will be considered later in this chapter. Most of the historic increase is probably associated with an increasing proportion of deaths in Scotland involving NPS, especially 'designer' benzodiazepines (Corkery et al., 2020). For most of the period examined here, the Drug Strategy and EMCDDA definitions produced very similar numbers of deaths. However, these move away from each other from 2013 onwards; this may also be an artefact of the increasing contribution made by 'designer' benzodiazepines as many of these remain outside the European definition.

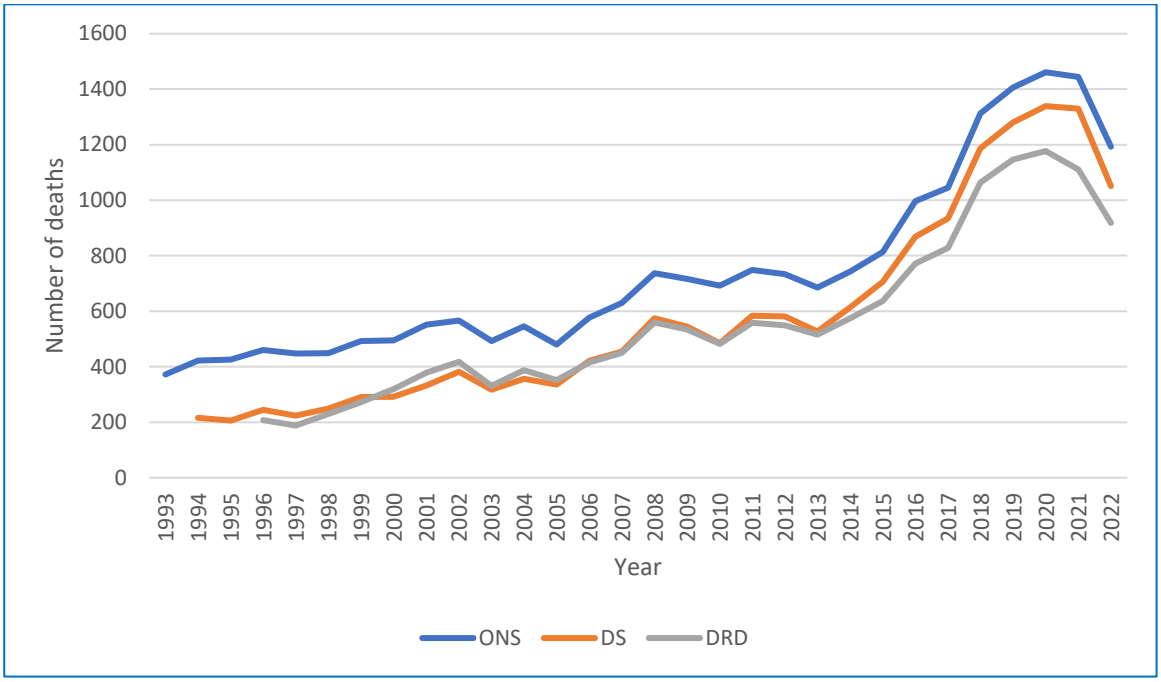

Figure 6.4: Numbers of drug-related deaths using different definitions, Scotland, 1993-2022

Notes: ONS = Office for National Statistics (drug poisonings; DS = Drug Strategy; DRD = Drug-Related Deaths.

Sources: Returns to the European Monitoring Centre for Drugs and Drug Addiction; NRS (2023).

Northern Ireland has also experienced an overall increase in the number of deaths related to drugs over the past three decades (Figure 6.5). The direction of movement is mirrored across all three definitions, although it is difficult say what has happened in terms of the EMCDDA definition since 2016. As with Scotland, Northern Ireland may have experienced a peak in the number of deaths in 2020, but figures for another few years will demonstrate if these are permanent changes or just a year-on-year blip. However, there appears to have been a significant drop in 2022 (NISRA, 2024). It is important to remember that the numbers of deaths in Northern Ireland are low in number compared to the absolute numbers in the other parts of the UK.

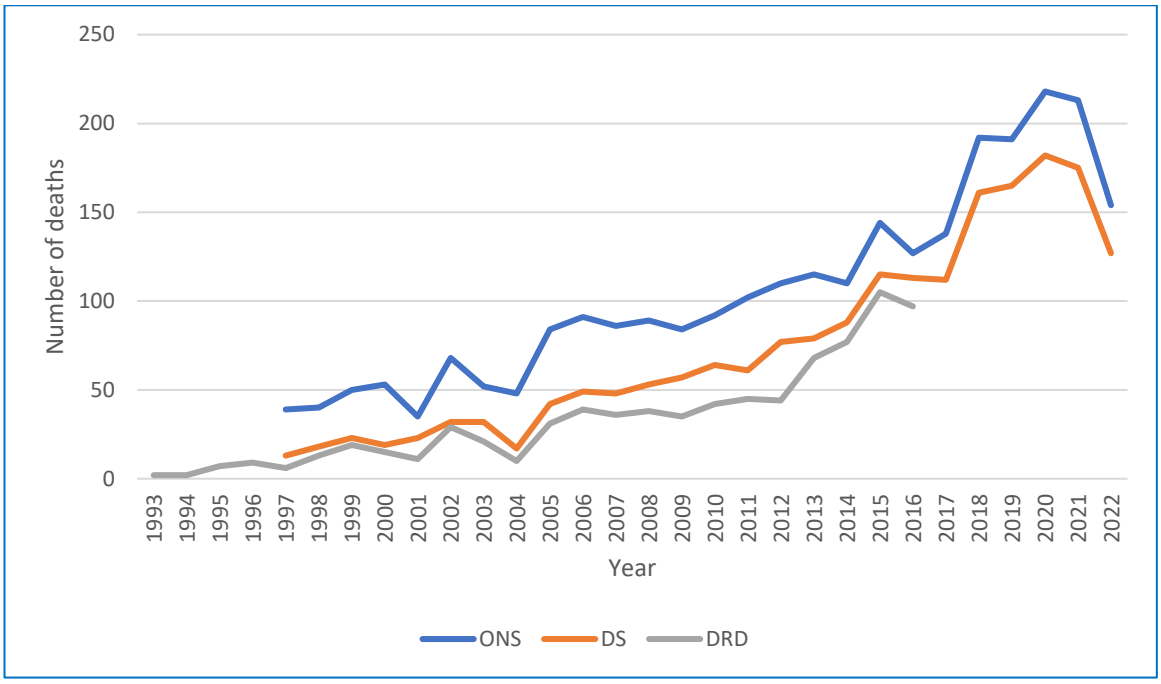

Figure 6.5: Numbers of drug-related deaths using different definitions, Northern Ireland, 1993-2022

Notes: ONS = Office for National Statistics (drug poisonings; DS = Drug Strategy; DRD = Drug-Related Deaths.

Sources: Returns to the European Monitoring Centre for Drugs and Drug Addiction; NISRA (2024)

Contribution to overall drug death totals by constituent parts of the United Kingdom

The relative contributions made by the different parts of the UK to the overall total of deaths associated with drugs are presented using the ONS definition in Figure 6.6 and the Drug Strategy definition in Figure 6.7. The respective proportions are summarised in Table 6.1 for the period 1997-2022. Obviously, the overall cumulative patterns exhibited in Figures 6.6 and 6.7 map directly on to those presented in Figures 6.1 to 6.5.

Given that England is the most populous country within the UK, it is to be expected that it makes the largest contribution to the overall totals, no matter which definition is used. It is followed, in descending order, by Scotland, Wales and Northern Ireland. However, the numbers of deaths in both of the latter two countries have not been too far apart since 2018, irrespective of the definition used, despite the difference in population sizes.

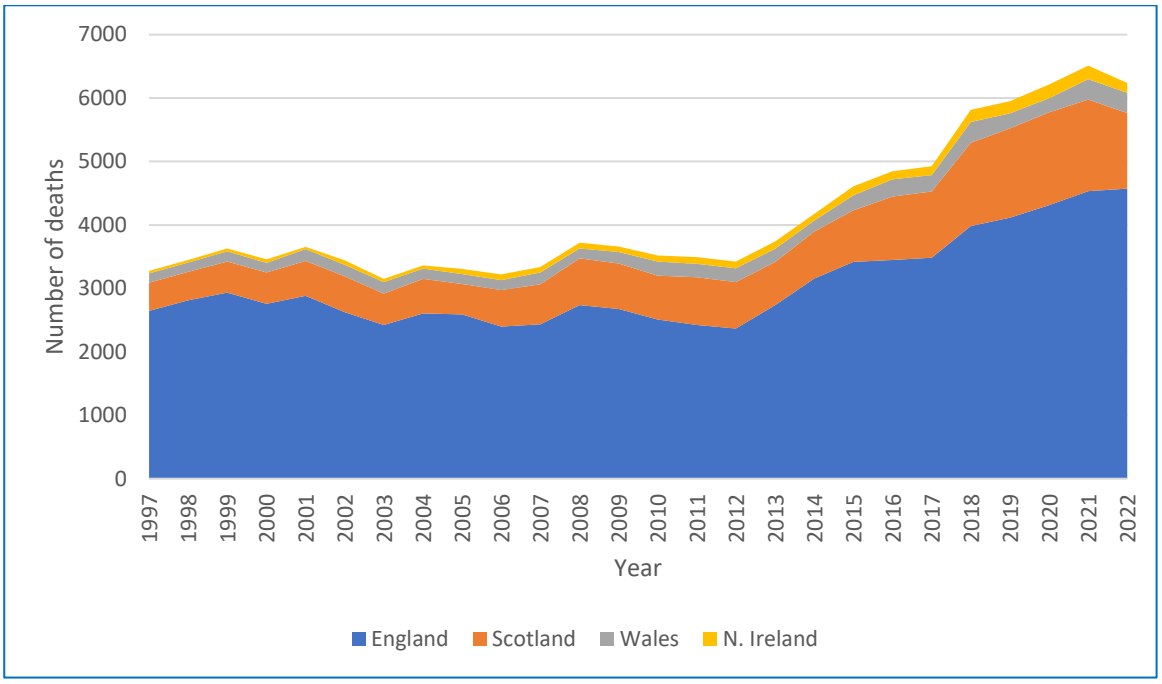

Figure 6.6: Contribution to overall drug death total by constituent parts of the United Kingdom, ONS definition, 1997-2022

Sources: ONS (2023); NRS (2023); NISRA (2024)

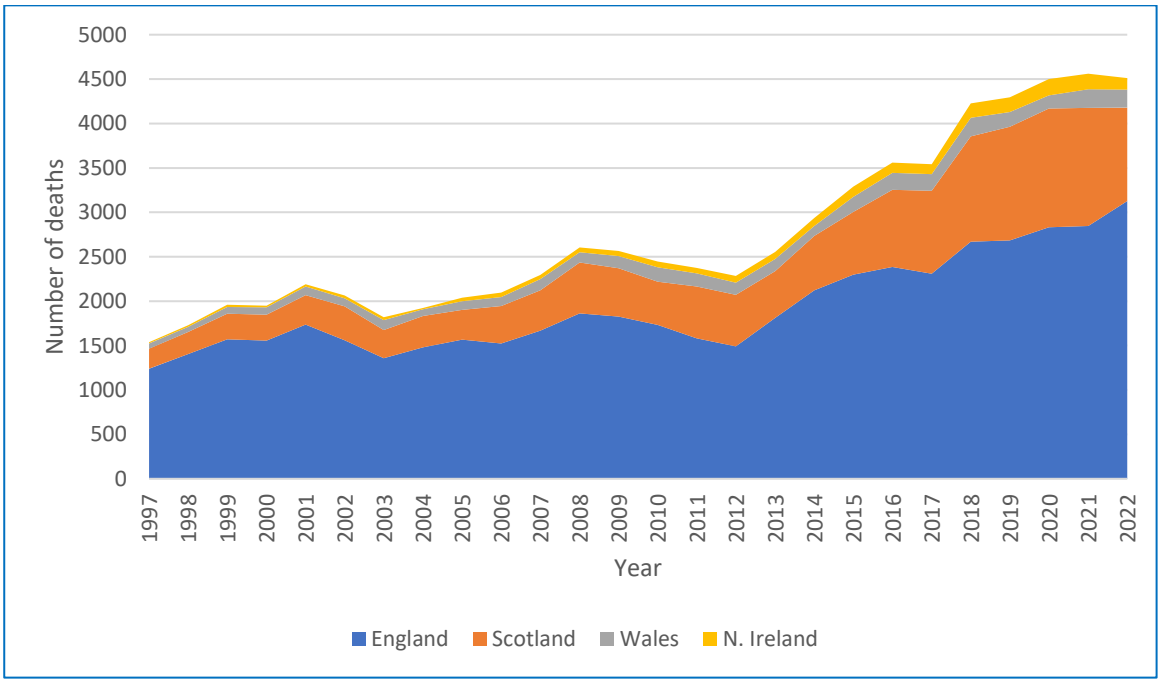

Figure 6.7: Contribution to overall drug death total by constituent parts of the United Kingdom, Drug Strategy definition, 1997-2022

Sources: ONS (2023); NRS (2023); NISRA (2024)

Table 6.1: Summary of contributions (%) to overall drug death total by constituent parts of the United Kingdom, 1997-2022

Definition and Country	*Measure*		
	Minimum	*Maximum*	*Mean*
ONS definition			
England	67.92	81.13	73.21
Wales	3.59	6.34	4.96
Scotland	12.96	23.47	18.82
Northern Ireland	0.95	3.49	2.51
Drug Strategy definition			
England	62.04	80.70	69.45
Wales	3.27	6.61	4.72
Scotland	14.30	29.64	22.58
Northern Ireland	0.83	4.03	2.70

Scotland and Northern Ireland have increased their respective contributions in recent years. Scotland's share in terms of the ONS definition has risen to just under one quarter especially since 2016; its contribution in terms of the Drug Strategy definition was over 29% in each year from 2019 to 2021, although falling to 24.41% in 2022. The proportion contributed by Northern Ireland in terms of the ONS definition has increased since 2005 reaching 3.49% in 2020, whereas its contribution to the Drug Strategy numbers is more evident since 2012, also peaking in 2020 at 4.03%. The contribution of Wales to the ONS definition totals is most evident since the mid-2000s, with the highest levels (in excess of 6%) being reached in 2010-2012; however, there is no clear pattern with regard to the Drug Strategy definition numbers. The upshot is that the contribution made by England has fallen overall for both definitions: from 80.05% in 1997 to 73.11% in 2022 for the ONS definition, and from 79.64% to 67.50% for the Drug Strategy definition over the same period.

Rates of death per 100,000 population

The patterns described in the preceding section become more understandable through an examination of both the number of deaths per 100,000 population and the types of drugs implicated. The latter aspect is examined a little later. Figures 6.8 and 6.9 present the number of deaths per 100,000 population (all ages) for the UK and its constituent parts using the ONS and Drug Strategy definitions, respectively. As foreshadowed in Chapter 5, the rate for Scotland is consistently higher than for any other part of the UK or indeed the UK average (mean). The gap has widened over time, using both definitions. Whereas the rate for Scotland increased from 9.78 in 1997 to 21.90 in 2022 (26.35 in 2021) using the ONS definition, the rates for other parts of the UK rose as follows: England from 5.60 to 8.01; Wales from 5.23 to 10.15 (10.37 in 2021); Northern Ireland from 3.15 to 8.06 (11.18 in 2021); the UK average from 5.91 to 9.25 (9.72 in 2021). A similar picture emerges using the Drug Strategy definition: Scotland from 5.77 to 19.29 (24.27 in 2021); England from 3.16 to 5.09; Wales from 2.79 to 6.55 (6.76 in 2021); Northern Ireland from 1.13 to 6.65 (9.19 in 2021); UK average from 3.34 to 6.37 (6.81 in 2021).

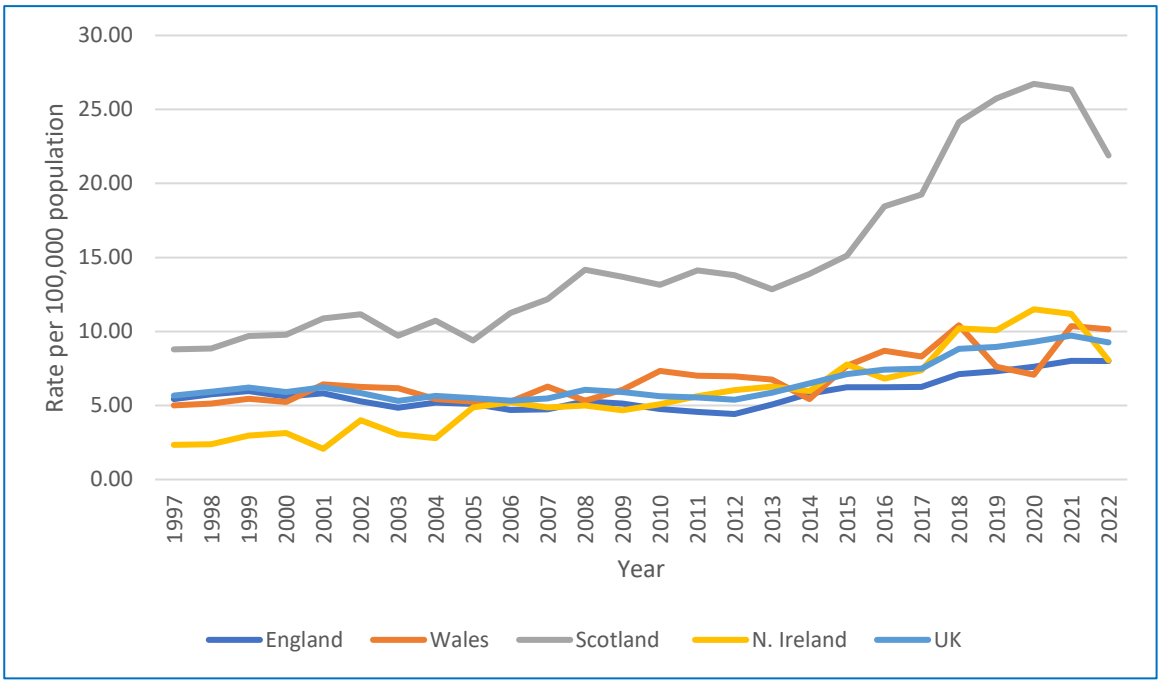

Figure 6.8: Rate of deaths per 100,000 population, United Kingdom and constituent countries, ONS definition, 1997-2022

Sources: ONS (2023, 2024); NRS (2023); NISRA (2024)

Whilst most attention has been paid to the extremely high rates in Scotland in comparison to the other parts of the UK (e.g., Major, 2022), and also to them being amongst, if not in fact, the highest in Europe (McAuley, 2019; EMCDDA, 2021), these statistics also reveal other matters of concern. Using the ONS definition, during the period 1997-2022 rates rose by 43% in England, 94% in Wales, 124% in Scotland, compared to 156% in Northern Ireland. The patterns using the Drug Strategy definition is even starker: an increase of 61% in England, 135% in Wales, 234% in Scotland, but 488% in Northern Ireland. However, the disparities were greater in 2021 (see previous paragraph).

Despite many attempts (e.g., Bloor et al., 2008; Minton et al., 2017; Parkinson et al., 2018; McDonald et al., 2021; Walsh et al., 2021) to try and get to the bottom of the issue of comparatively high numbers of deaths related to drugs, the conundrum remains: why are the rates in Scotland two to three times higher than the rest of the UK using the ONS definition, and four to five times using the Drug Strategy definition?

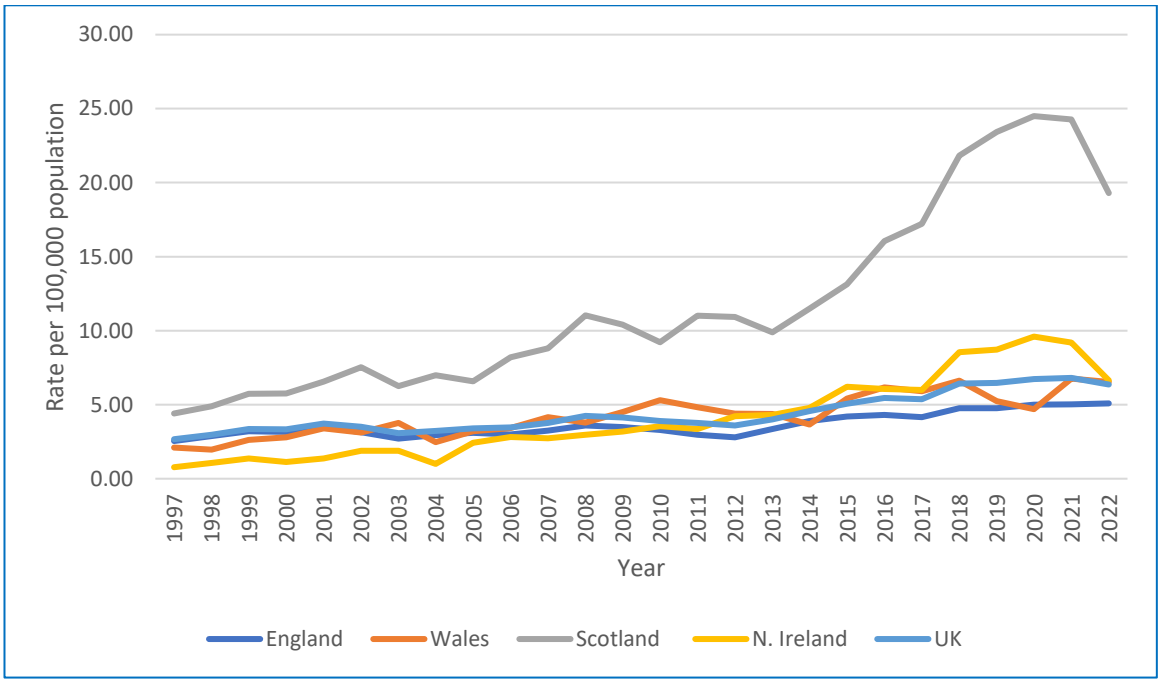

Figure 6.9: Rate of deaths per 100,000 population, United Kingdom and constituent countries, United Kingdom Drug Strategy definition, 1997-2022

Sources: ONS (2023, 2024); NRS (2023); NISRA (2024)

Walsh et al. (2021) made comparisons of drug-related poisoning death rates across Great Britain during the period 1981 to 2017. They found that:

"Male deaths from drug-related poisonings increased over most of the period in Scotland, starting in the mid-to-late-1980s; in E&W [England and Wales] rates also increased in the 1990s and early 2010s, but declined in-between those periods. Among women, previously flat (Scotland) or falling (E&W) rates started to increase from the mid-to-late-2000s." Walsh et al. (2021)

There were some similarities for males between England and Wales vs. Scotland in overall patterns in drug-related poisonings for Scotland in terms of the peak age (30-34 years) being the age cohorts most affected (e.g., 1975–1984 and 1965–1974). However, the crude mortality rate for the Scottish 1975-1984 cohort dying aged 40-44 years was 88.0 per 100,000 population compared to a rate of 23.5 for the same cohort south of the Border. For the equivalent female cohorts, the relative rates were 38.9 and 7.9 respectively; a five-fold difference. Walsh et al. (2021) conclude that "similar underlying influences on mortality have operated across all the countries, but that their effects have been greatest in Scotland. This tallies with previous research suggesting a greater vulnerability to these influences in Scotland." However, they do not venture to suggest what might be these influences.

This issue warrants further research, especially since only one-quarter of the higher level of all-cause mortality in Scotland compared to England could be explained by "socioeconomic, behavioural, anthropological or biological factors" (McCartney et al., 2015). It is probable that a range of factors are at work.

Challenges from changing classes of drugs

Like other nations and other parts of the world, the UK has experienced a series of challenges in respect of drug use and associated mortality over past decades arising from changes in the availability, popularity, prescribing, price, potency and purity, and purchasing of different classes of drugs.

For the past century (Kohn, 1997), or perhaps even longer, recreational drug use appears to have been cyclical in nature. Measham (2004) notes that some commentators have suggested that "these cycles of drug consumption may be heightened in contemporary society" citing, for example, Shapiro (1999:33) who proposes that "as drug use becomes increasingly a fashion accessory, it may be even more at the whim of fashion than in previous times" and Thornton (1995:122) who argues that "with mass media . . . affirmative coverage of the culture is the kiss of death, while disapproving coverage can breathe longevity into what would have been the most ephemeral of fads".

Cannabis has been a constant presence in the UK drug market since at least the 1930s. Whilst originally it was used as a recreational drug, in recent decades such use has fallen - yet remains the single most commonly used drug. On the other hand, cannabis and some of its extracts are being used for self-medication in terms of chronic pain. Licensed products are now available in the UK on prescription for the treatment of a limited number of specific conditions (NHS England, 2023).

'Generous' prescribing of barbiturates in the late 1970s and 1980s had an adverse impact on UK drug-related mortality. Making the connection between prescribing practices and resultant fatalities was an important public health event which eventually led to regulatory controls on the prescribing of this class of drug (Ghodse et al., 1998). These changes resulted in a sharp decline in barbiturate-related mortality. This is an example of how mortality data not only revealed a growing epidemic but demonstrate how these data can be used to evaluate the effectiveness of drug regulatory control policies (Chapter 13).

The author has previously identified different cocaine 'epidemics' from an analysis of notifications to the Home Office Addicts Index in the mid-1960s and from the mid-1980s through

to the mid-1990s (Corkery, 2001, 2002); the continuing contribution of cocaine to UK drug-related poisoning deaths is now a major concern (as will be seen later in this chapter).

Following the emergence of a 'crack' cocaine epidemic in the United Stated of America (USA) in the late 1980s, the UK braced itself for similar experience. Although 'crack use' spread in the UK, leading to increased numbers of 'problematic' drug users, it has never reached epidemic proportions (Bean, 1993; Hunter et al., 1995). Similarly, the UK has not experienced a methamphetamine ('ice') epidemic, probably because of the relatively high prevalence of amphetamine and 'ecstasy' use, thereby presenting a 'saturated' market (Griffiths et al., 2008a).

Since the 1960s, heroin has been the dominant 'problematic' drug in the UK, especially with regard to drug-related poisoning deaths, and acting as a vector for the transmission of HIV/AIDS and hepatitis C amongst injecting drug users. The 1980s and 1990s were the periods when heroin epidemics were major policy, health, and crime concerns (Morgan, 2014). Heroin shortages or 'droughts' have caused short-term changes in drug use, leading to substitution with other substances, adulteration, etc. (Harris et al., 2015; Simonson and Daly, 2011).

Changes in the availability, quality, and cost of cocaine in the mid- to late- 2000s contributed to the emergence of synthetic cathinones (Corkery et al., 2012; Moore et al., 2013). The UK has experienced different waves of other NPS - synthetic cannabinoids, 'designer' benzodiazepines, new synthetic opioids, etc. Some individual molecules (e.g., mephedrone) have become part of the everyday drug repertoire of some dealers and users, whilst others have disappeared as rapidly as they emerged.

Changes in drug use may have, inadvertently, prevented some premature deaths. For example, the heroin drought may have led to the use of less potent opioids or seeking maintenance on methadone or buprenorphine (Simonson and Daly, 2011). Deaths from stimulants such as cocaine and MDMA may have been reduced by the emergence of synthetic cathinones (Bird, 2010). On the other hand, control under the Misuse of Drugs Act 1971 and Temporary Class Drug Orders (Shapiro, 2016) may have led to more potent and toxic molecules being developed and marketed, with potentially fatal results, to avoid being caught by new legislative measures (Stevens et al., 2015). This could be conceived of as a 'cat and mouse' or 'whack a mole' approach. The introduction of the Psychoactive Substances Act 2016 does not appear to have led to a drop in NPS-related deaths notified to NPSAD (Deen et al., 2021) or in the proportion of NPS-related acute toxicity presentations to Emergency Departments (Webb et al., 2019). The possible effects of the 2016 Act on mortality will be examined later (Chapter 12).

Trends in United Kingdom deaths involving specific drugs and drug classes

Drawing on GMR data, this section provides an overview of the main index drugs and drug classes implicated in deaths registered in the UK. The definition used here is the ONS 'wide' definition of deaths related to drug-poisonings. Breakdowns by drug-type across the UK are only available on a consistent basis from 1997 onwards, Great Britain from 1993. The most recent year for which data on death registrations is available is 2022.

Deaths related exclusively to the use of solvents (volatile substances) and gases (e.g., helium, nitrogen and nitrous oxide) are excluded from analyses here in order to retain as narrow a focus as possible. For the same reason, the range of drugs examined here is comprehensive but not exhaustive. As data are unavailable in some parts of the UK for some classes of drugs of interest, e.g., antidepressants, antipsychotics, synthetic cannabinoids, gabapentinoids, 'street/designer' benzodiazepines, etc. the author has decided to concentrate on the drug classes and specific drugs set out in Table 6.2.

Table 6.2: Drug classes and specific drugs selected for analysis

Drug class	*Specific drug(s)*
Opiates/opioids	Any opiate/opioid, heroin/morphine, methadone, tramadol, codeine, dihydrocodeine, oxycodone, fentanyl
Benzodiazepines	Any benzodiazepine, diazepam, temazepam
Stimulants	Cocaine (including 'crack'), amphetamines, 'ecstasy' (MDA, MDMA), synthetic cathinones (including mephedrone)
Cannabinoids	Cannabis, synthetic cannabinoids
Anaesthetics/Dissociatives	Ketamine
Antidepressants	Barbiturates
Central nervous system depressants	GHB/GBL
Gabapentinoids	Gabapentin, pregabalin
Novel Psychoactive Substances (NPS)	Any molecule classified as an NPS

Figures 6.10 to 6.13 present the number of UK deaths for the main drug classes for the period 1997-2022. The breakdowns are provided in this way otherwise the figures would be far too 'busy' to distinguish the data represented. It should be noted that the numbers provided for NPS are for any substances considered as an NPS at any time, regardless of whether or not they have subsequently become controlled under the Misuse of Drugs Act 1971. Thus, whilst the definition has remained unchanged, its implementation has not remained consistent over time.

Looking at the opiate/opioid class (Figure 6.10), it is immediately apparent that it is dominated by heroin/morphine and methadone, with the other five drugs examined showing less of a contribution.

Most of the deaths covered by heroin/morphine are the result of consumption of 'street' heroin; in fact, very low volumes of pharmaceutical heroin (diamorphine) are prescribed in the UK.

There was a steep rise in these deaths between 1997 and the turn of the century, followed by considerable variations until the start of the 2010s. The following decade saw a further rapid increase in deaths, although a noticeable fall has occurred in recent years.

Deaths involving methadone fell in the late 1990s and remained stable for several years before starting to show an overall increase up until 2021, albeit with some year-on-year variation. A drop was observed in 2022; it remains to be seen if this fall will be sustained. There is no illicit manufacture of methadone in the UK and no large scale importation, licit or otherwise (Fountain et al., 2000). There has been an overall increase in the UK prescribing of methadone (see Chapter 9), thereby facilitating availability. Despite various attempts (e.g., supervised dispensing) to try and prevent 'diversion' over the last three decades or so (Dickinson, et al., 2006; Anthony et al., 2012), the published evidence (especially NPSAD annual reports compiled by the author and his successors) consistently shows that only about one-third of individuals whose deaths involved methadone had been in receipt of prescribed methadone at the time. This means that up to two-thirds of methadone-related deaths involved 'diverted' supplies (Marteau et al., 2015, Corkery et al., 2004).

The five other opioids considered here are: codeine, dihydrocodeine, fentanyl, oxycodone, and tramadol. Some of these substances, e.g., dihydrocodeine and oxycodone, are used for both pain relief and in treating drug dependence. The number of deaths in which these drugs have been implicated have increased overall during the last three decades, but at far lower rates than observed for heroin/morphine and methadone. In recent years, there was increased concern about the involvement of tramadol in deaths (ACMD, 2013, 2016) as well as the possibility of the 'opioid epidemic' – mainly fuelled by fentanyl and oxycodone - causing many thousands of deaths in North America coming to the UK (Basler, 2017; Roberts and Richards, 2023). Fortunately, at the time of writing, this has not occurred.

The fear of fentanyl analogues and other very potent synthetic opioids (such as 'nitazenes'; Holland et al., 2024) causing large numbers of deaths in the UK has, to date, not been realised. Although these are a major concern in North America, very few deaths involving these substances have been reported in the UK (ACMD, 2020, 2022).

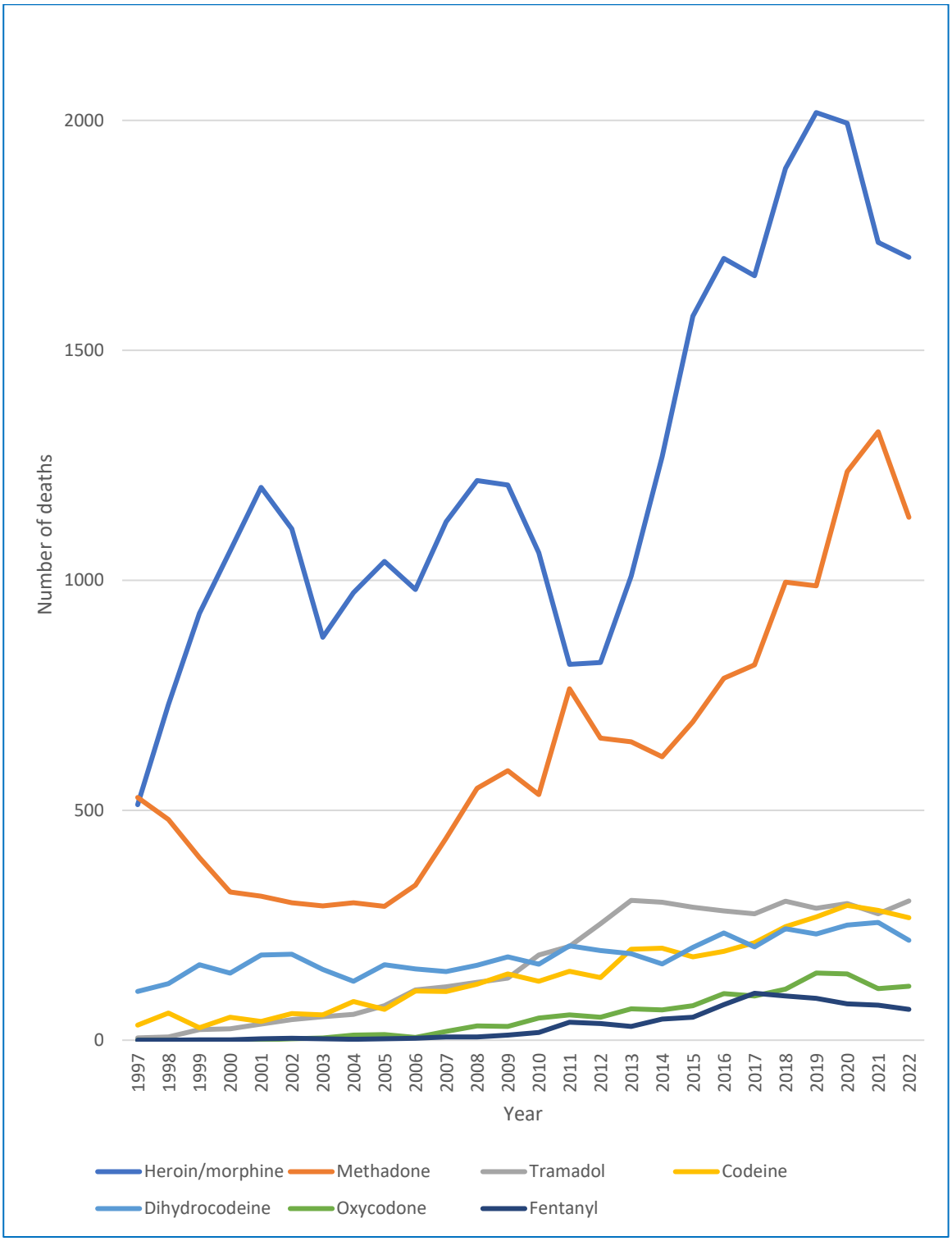

Figure 6.10: Number of drug poisoning deaths by main opiate/opioid drugs, United Kingdom, 1997-2022

Sources: ONS (2023); NRS (2023); NISRA (2024)

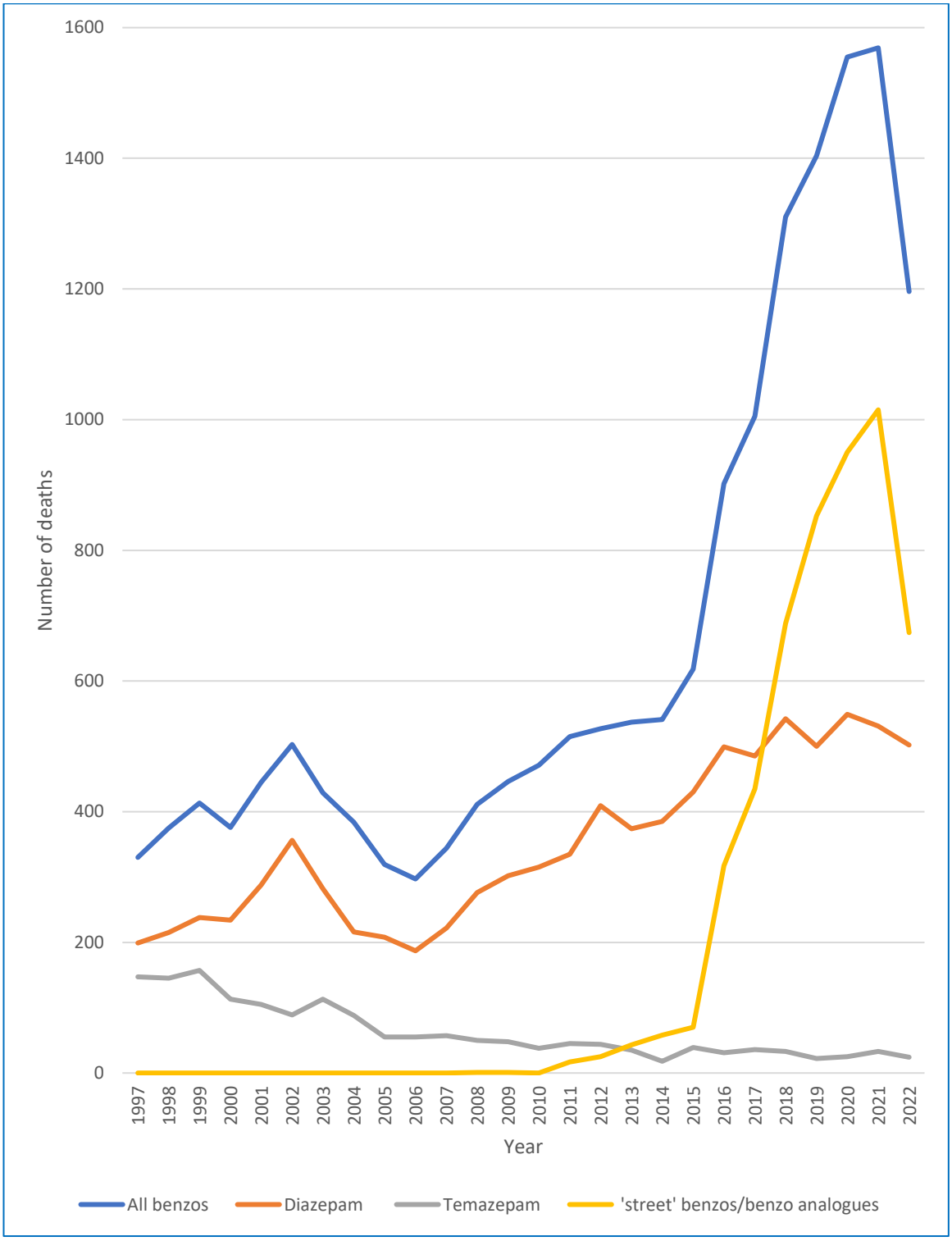

Figure 6.11: Number of drug poisoning deaths by main benzodiazepine drugs, United Kingdom, 1997-2022

Sources: ONS (2023); NRS (2023); NISRA (2024)

Another class of drugs implicated in many deaths are the benzodiazepines. Figure 6.11 presents information on the number of deaths for all benzodiazepines as well as individually for

the main prescribed benzodiazepines (diazepam and temazepam) and for ‘street benzos’ and benzodiazepine analogues (‘designer benzos’).

The overall trend seen for benzodiazepines was an increase from 1997 to about 2002, followed by a fall that lasted until 2006, followed by an accelerating increase to the present time. Within this wider picture, there are different patterns for the selected drugs and ‘street benzos’.

There has been an overall increase in the number of deaths involving diazepam, mirrored by increased prescribing of the drug (see Chapter 9). The trend for temazepam has been in the opposite direction, accompanied by a corresponding fall in its prescribing (see Chapter 9).

So-called ‘designer benzos’, now also referred to as ‘street benzos’, began to be recorded as being involved in UK deaths in 2011, increasing moderately up to 2015. However, after that the rate of increase in such deaths was very rapid, peaking in 2021, followed by a fall in 2022. This increased volume has been the main driver for the overall number of benzodiazepine deaths, especially in Scotland. The majority of these deaths are driven by substances such as etizolam (Corkery et al., 2020) and alprazolam (Corkery et al., 2022).

Trends for the main stimulant drugs are presented in Figure 6.12. The drugs/ drug classes considered here are cocaine, amphetamines, amphetamine/methamphetamine, and 3,4-Methyl enedioxymethamphetamine (MDMA).

Cocaine deaths include some cases where ‘crack’ had been used; unfortunately, no accurate information is available to UK GMRs (apart from NRS) on what specific cocaine metabolites were found in postmortem toxicology, and thus does not usually appear in the ‘cause of death’ information. In the author’s own experience with NPSAD, it is necessary to have access to detailed toxicology so that the specific cocaine metabolites caused by smoking ‘crack’, i.e., pyrolytic products, can be screened for to ascertain if ‘crack’ had been used. There are occasional mentions of ‘crack’ *per se* in death certificates.

Cocaine dominates the stimulant-related class of deaths. Numbers rose steadily in the decade up to 2008 but fell over the next three years, possibly due to falls in purity and the emergence of synthetic cathinones (see Chapter 10). However, between 2012 and 2020 there was a very highly accelerated rise in numbers, before an apparent stabilisation in 2021 and 2022.

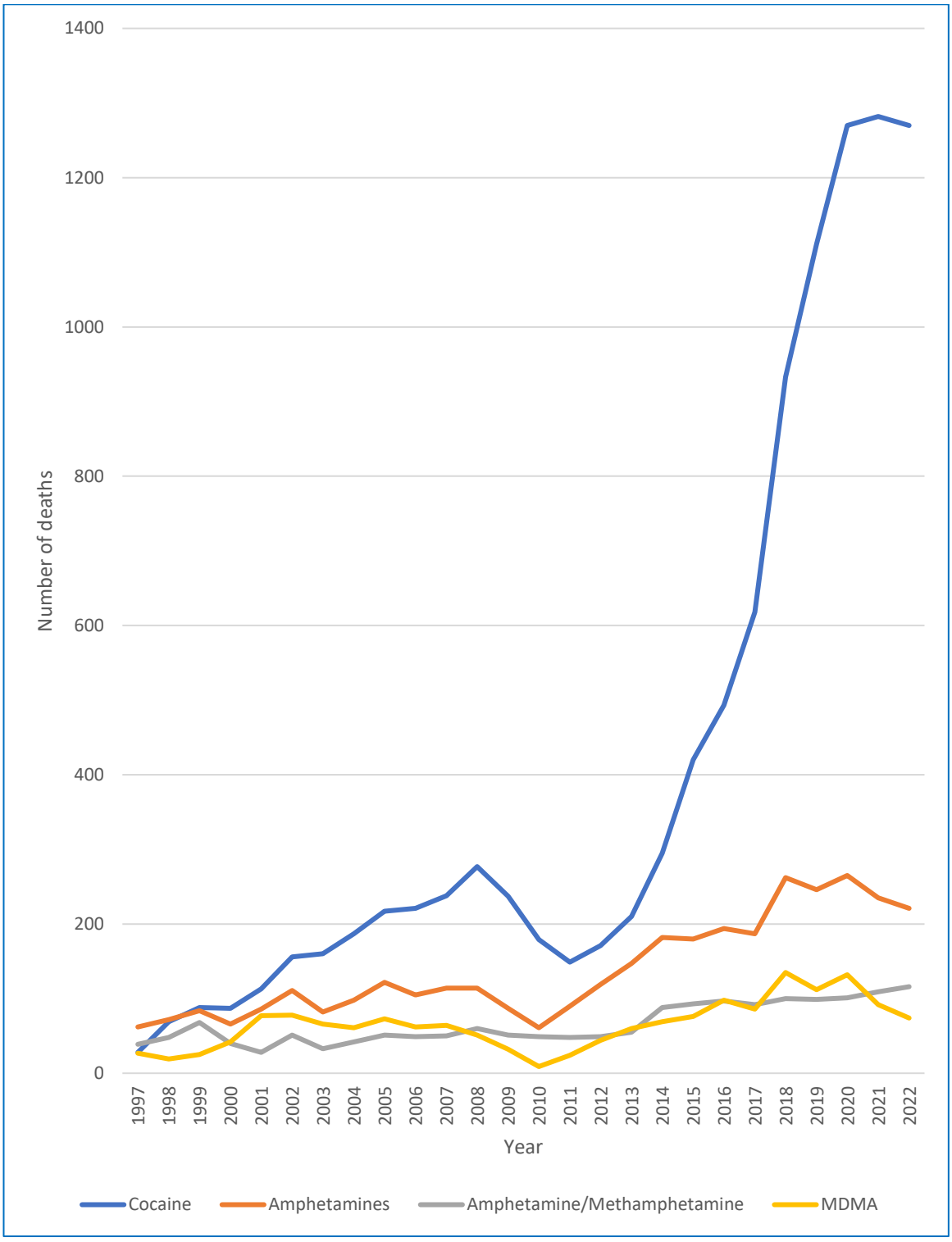

Figure 6.12: Number of drug poisoning deaths by main stimulant drugs, United Kingdom, 1997-2022

Sources: ONS (2023); NRS (2023); NISRA (2024)

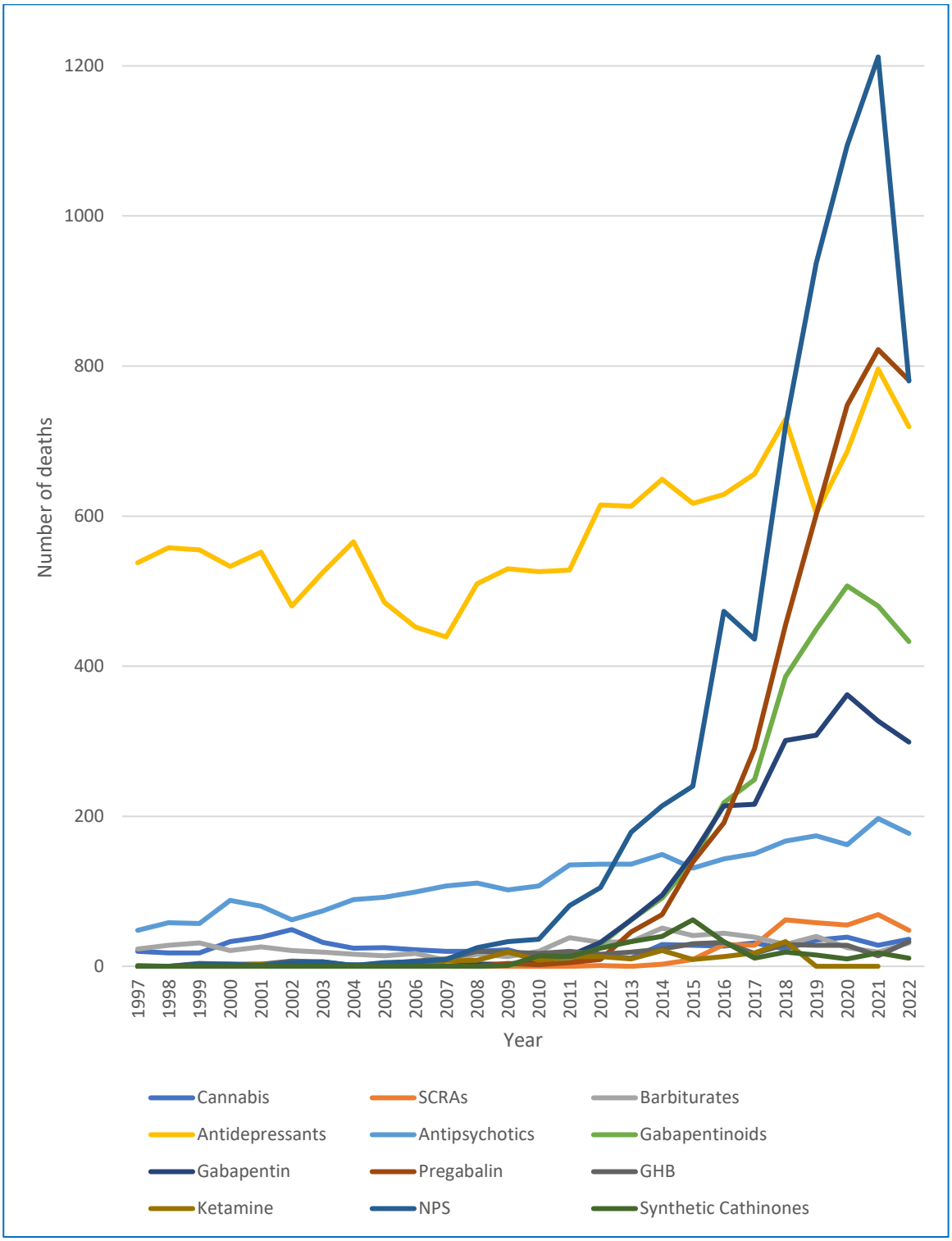

Figure 6.13: Number of drug poisoning deaths by selected other drugs, United Kingdom, 1997-2022

Sources: ONS (2023); NRS (2023); NISRA (2024)

Amphetamines as a class have increased over the last three decades, with MDMA (ecstasy) appearing to be the main driver, especially since 2010; since then, these trends have moved in parallel. The dip for MDMA (and hence overall amphetamine deaths) between 2008 and 2010 could also be due to the same factors that affected cocaine (see Chapter 10). Amphetamine/ methamphetamine-related deaths have also increased but at a more consistent rate.

Figure 6.13 presents information on a range of other selected drugs. The number of lines may be excessive but helps to provide a more complete picture of developments. In terms of number of deaths, many drugs have remained relatively stable. The role of antidepressants and antipsychotics have increased steadily over the timeframe considered here. Gabapentinoids, gabapentin and especially pregabalin, deaths have shown a very steep increase over the last decade or so. However, the most noteworthy increase has been that of NPS, especially since 2009 when the first synthetic cathinones and cannabinoids started to emerge. However, a noticeable fall was observed in 2022 NPS registrations. Falls in the number of other substances have occurred since 2020 or 2021.

Figures 6.14 to 6.17 present the number of UK deaths in England for the main drug classes for the period 1997-2022. It should also be remembered that 84.5% of the UK population resides in England (ONS, 2024); thus, the patterns in deaths presented here dominate many of the classes of drugs across the UK as a whole – but there are exceptions, as will be seen with regard to Scotland.

The patterns noted for opiate/opioid deaths at the UK level also apply to England (Figure 6.14). There was a steep rise in heroin/morphine deaths between 1997 and the turn of the century, followed by considerable variations until the start of the 2010s. The very noticeable fall in 2010-11 is probably due to a heroin ‘drought’ which obviously impacted at the UK level (see Chapters 9 and 12). The following decade saw a further rapid increase in deaths, although a drop occurred in recent years.

Deaths involving methadone fell in the late 1990s and remained stable for several years before starting to show an overall increase, albeit with some year-on-year variation. There was a rapid rise in registrations of methadone-related deaths between 2019 and 2021, followed by a levelling off in 2022.

The number of deaths in which most of the other opioid drugs (codeine, fentanyl, oxycodone, and tramadol) have been implicated have increased overall during the last three decades, but at far lower rates than observed for heroin/morphine and methadone. By contrast, dihydrocodeine involvement has remained fairly stable.

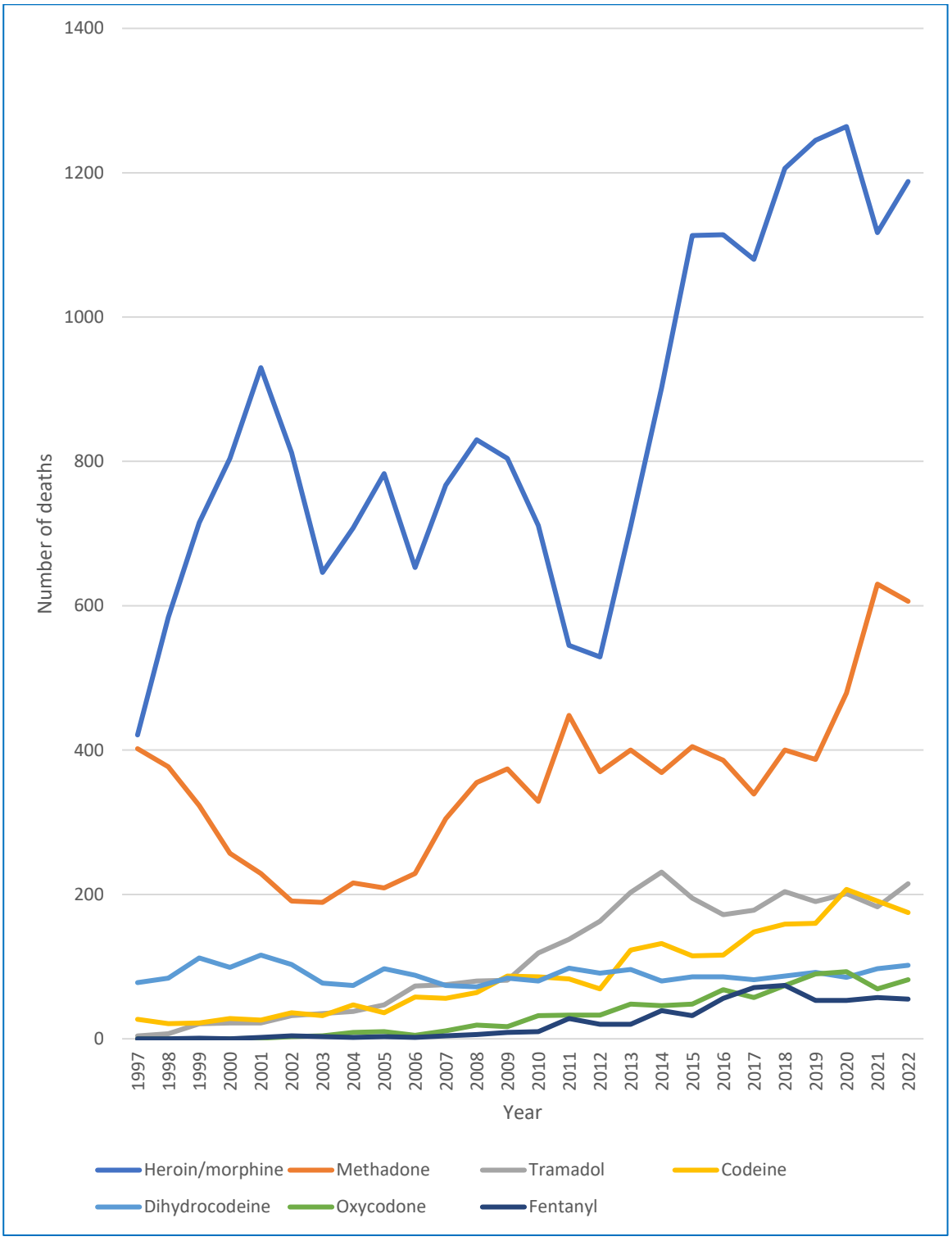

Figure 6.14: Number of drug poisoning deaths by main opiate/opioid drugs, England, 1997-2022

Source: ONS (2023)

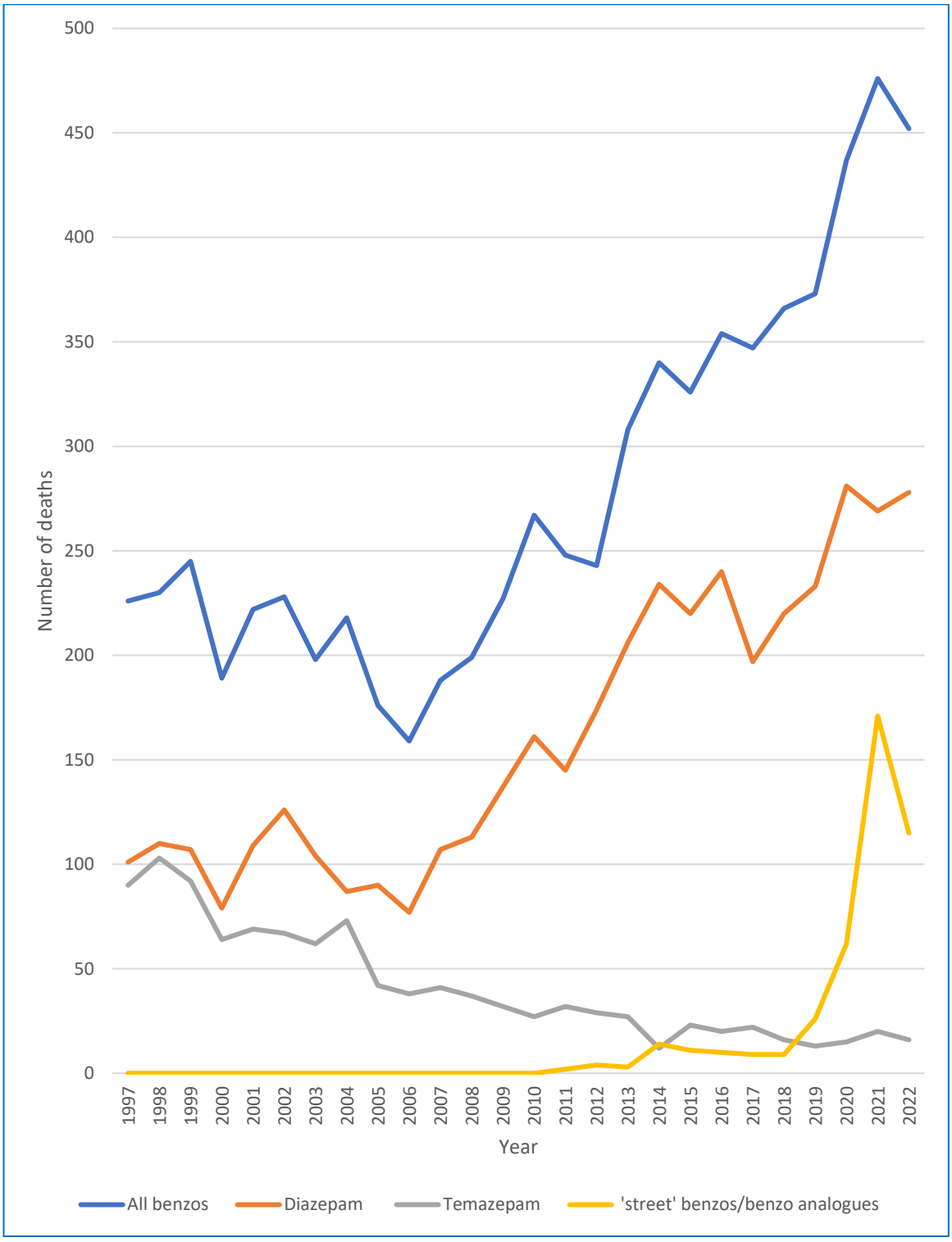

Figure 6.15: Number of drug poisoning deaths by main benzodiazepine drugs, England, 1997-2022

Source: ONS (2023)

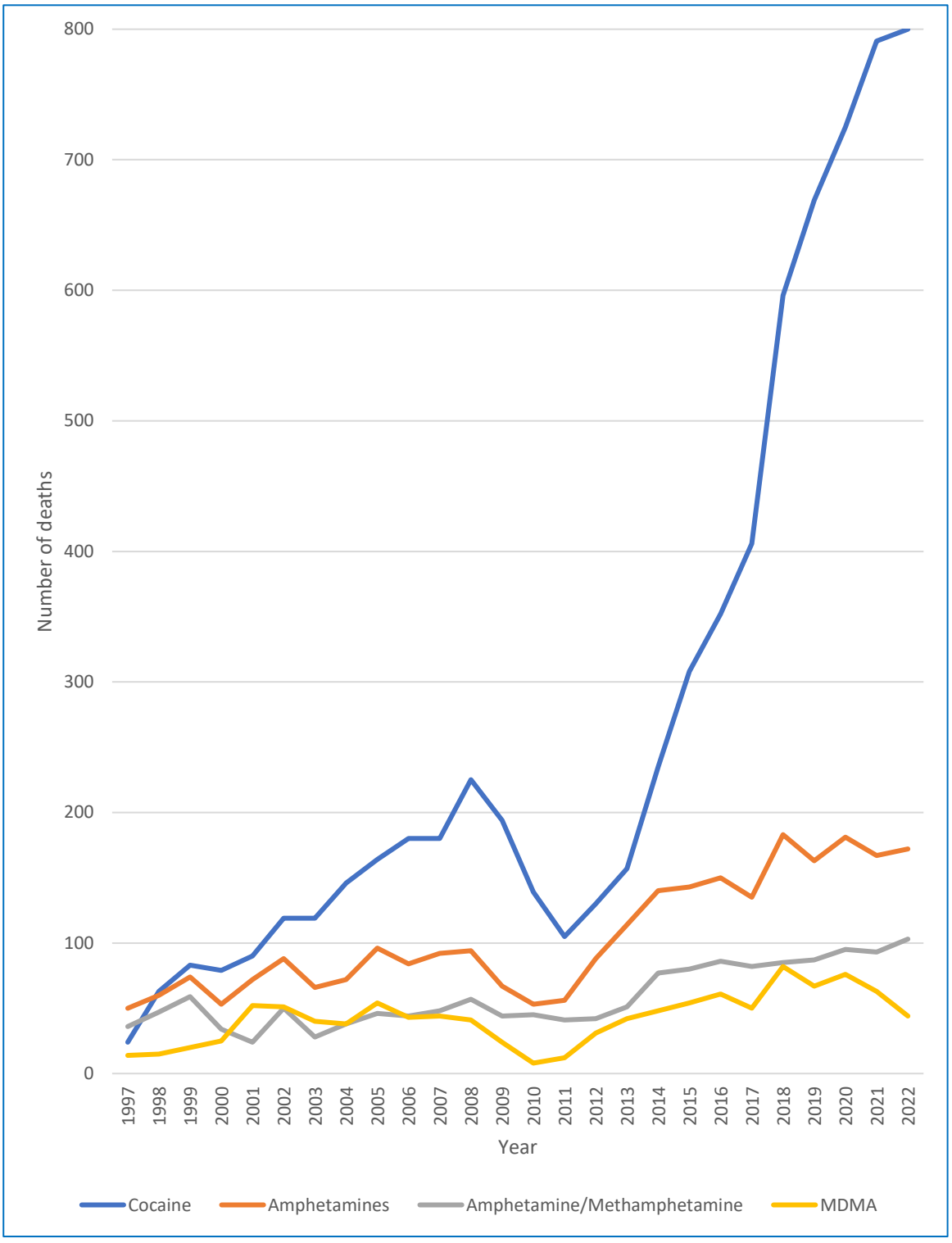

Figure 6.16: Number of drug poisoning deaths by main stimulant drugs, England, 1997-2022

Source: ONS (2023)

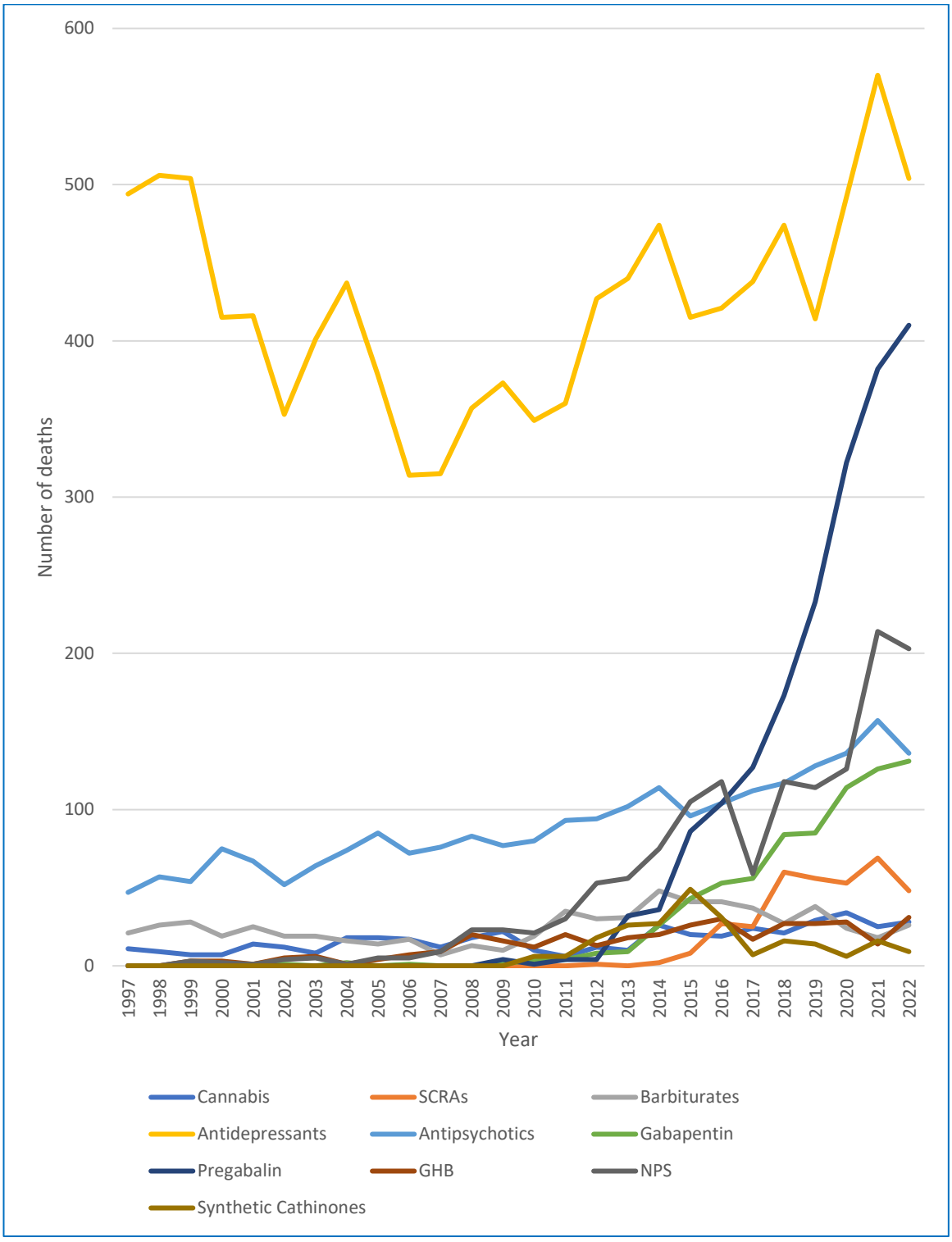

Figure 6.17: Number of drug poisoning deaths by selected other drugs, England, 1997-2022

Source: ONS (2023)

The overall trend seen for benzodiazepines in England (Figure 6.15) was an increase from 1997 to 1999, followed by a fall that lasted until 2006, followed by an accelerating increase to the present time. Much of these changes until about 2019 were driven by deaths involving diazepam, which was the dominant benzodiazepine. Part of the overall early decline was due to a decreasing number of temazepam-related deaths. The increase in the overall number of benzodiazepine deaths registered in the last few years to record levels is largely due to 'street benzos'. However, a fall in the registrations of such deaths was observed in 2022.

Trends for deaths in England involving stimulant drugs are presented in Figure 6.16. As for the UK as a whole, cocaine deaths dominate stimulant deaths in the English context. The period 1997-2008 was marked by an overall increase in deaths, at a much higher rate and level than those for amphetamine-type stimulants. All these stimulants experienced a fall between 2008 and 2010-11, a period when synthetic cathinones were emerging. Whilst the number of deaths for all these substances then rose at a higher rate, cocaine-related deaths exhibited a highly accelerated trajectory from 2011; one that continued unabated until 2021. Deaths involving MDMA have declined a little in recent years whilst amphetamine/methylamphetamine ones have increased a little.

Antidepressants, especially tricyclics and selective serotonin re-uptake inhibitors, dominate the deaths involving other substances in England (Figure 6.17). However, they do not display any particular pattern, varying considerably over the past three decades, although trending upwards since 2019. Antipsychotic-related deaths run at a lower level than antidepressants but at a considerably higher level than the rest of the other substances considered here. Whilst synthetic cannabinoid or synthetic cannabinoid receptor agonist (SCRA) and gabapentin deaths have risen since about 2014, the numbers for NPS and pregabalin have risen more rapidly. The latter two now lie third and second respectively behind antidepressants.

Figures 6.18 to 6.21 present the number of deaths in Wales for the main drug classes for the period 1997-2022. The same provisos outlined earlier also apply here.

Deaths involving heroin/morphine have shown an overall increase over the last three decades but have also exhibited several very noticeable swings in either direction, i.e., rises and falls (Figure 6.18). As in England, opioid-related deaths are lower than those associated with heroin. Methadone has been the second highest contributor (after heroin/morphine) to opiate/opioid deaths since 2006. The other opioids mostly show no discernible trends. However, absolute numbers are relatively low compared to England.

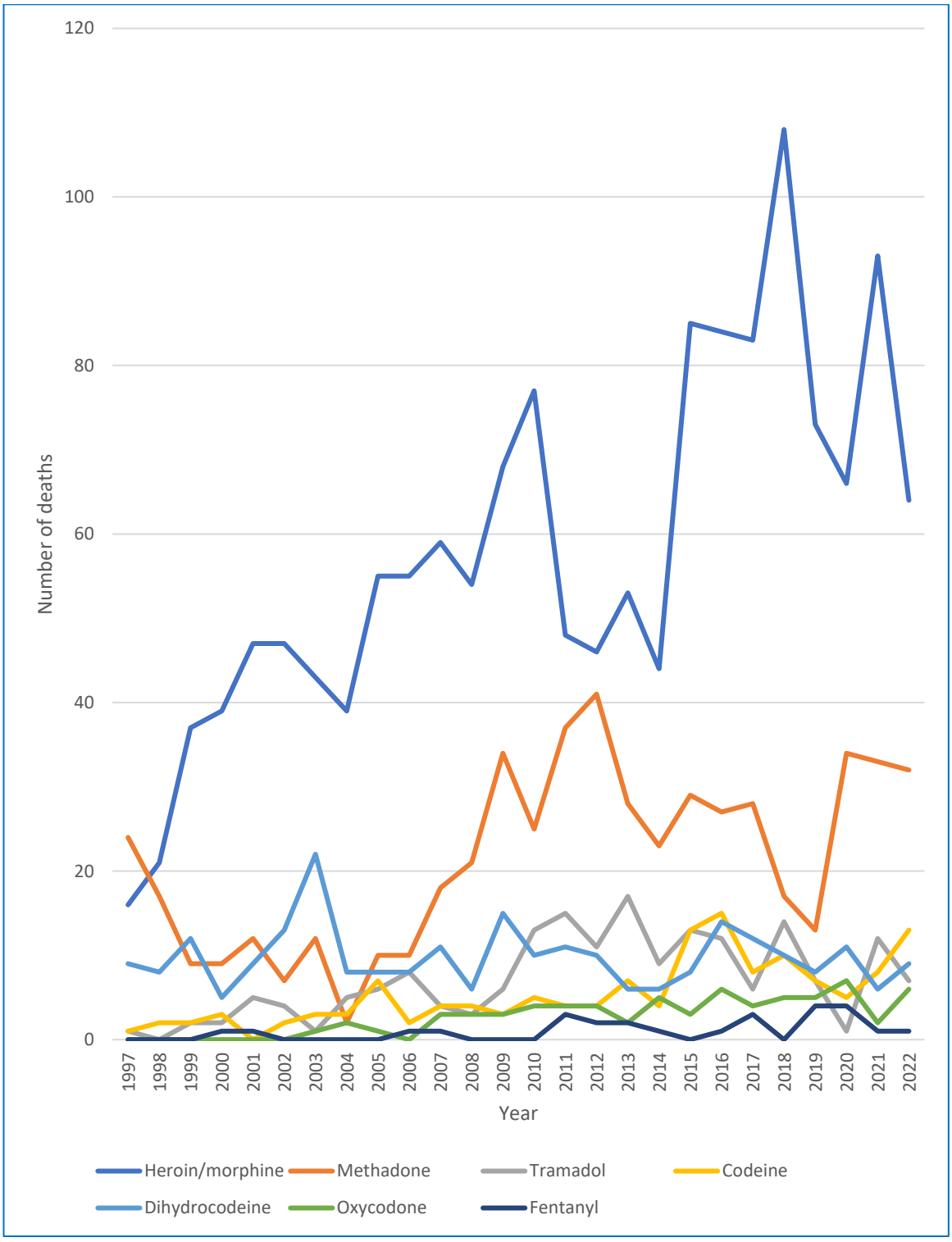

Figure 6.18: Number of drug poisoning deaths by main opiate/opioid drugs, Wales, 1997-2022

Source: ONS (2023)

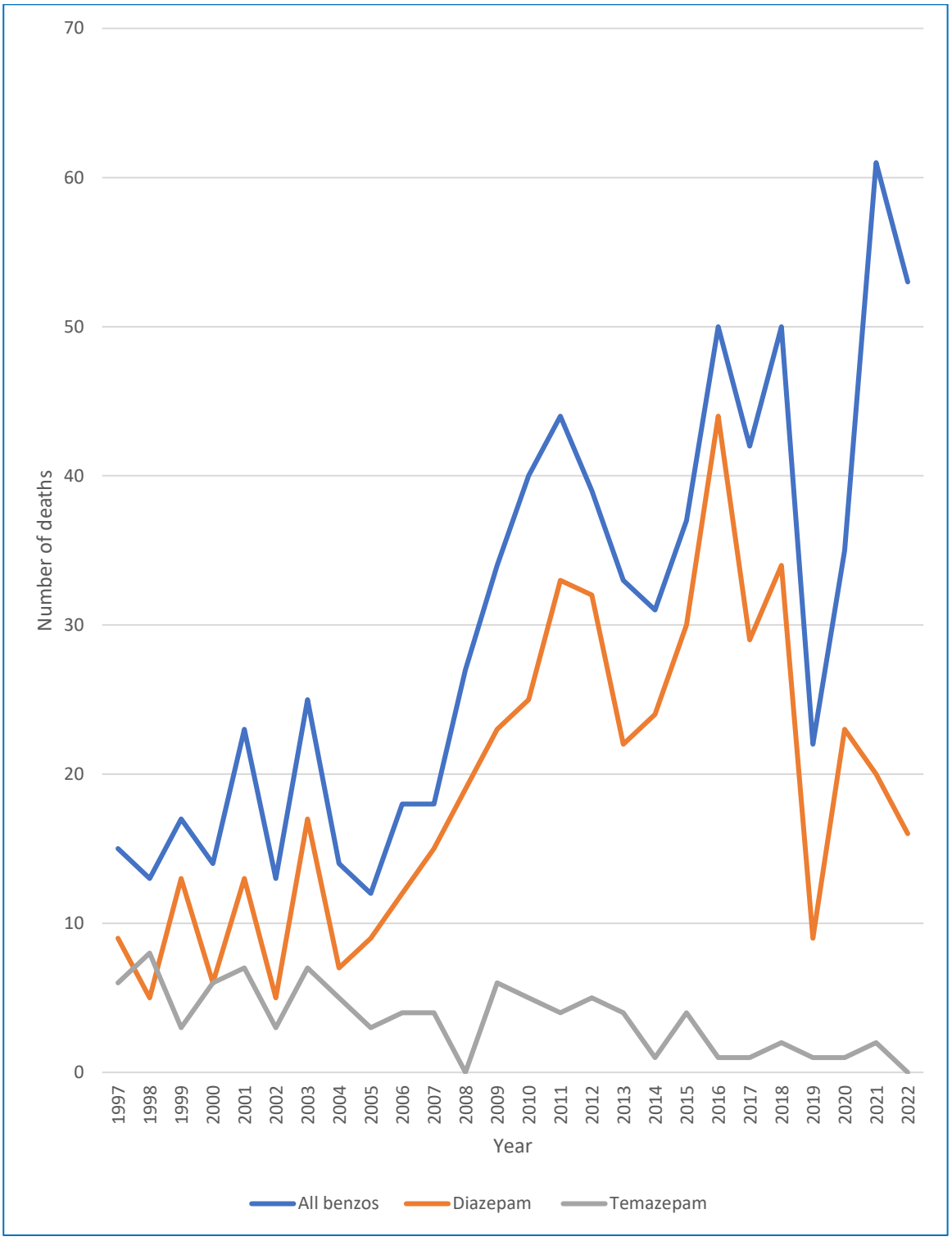

Figure 6.19: Number of drug poisoning deaths by main benzodiazepine drugs, Wales, 1997-2022

Source: ONS (2023)

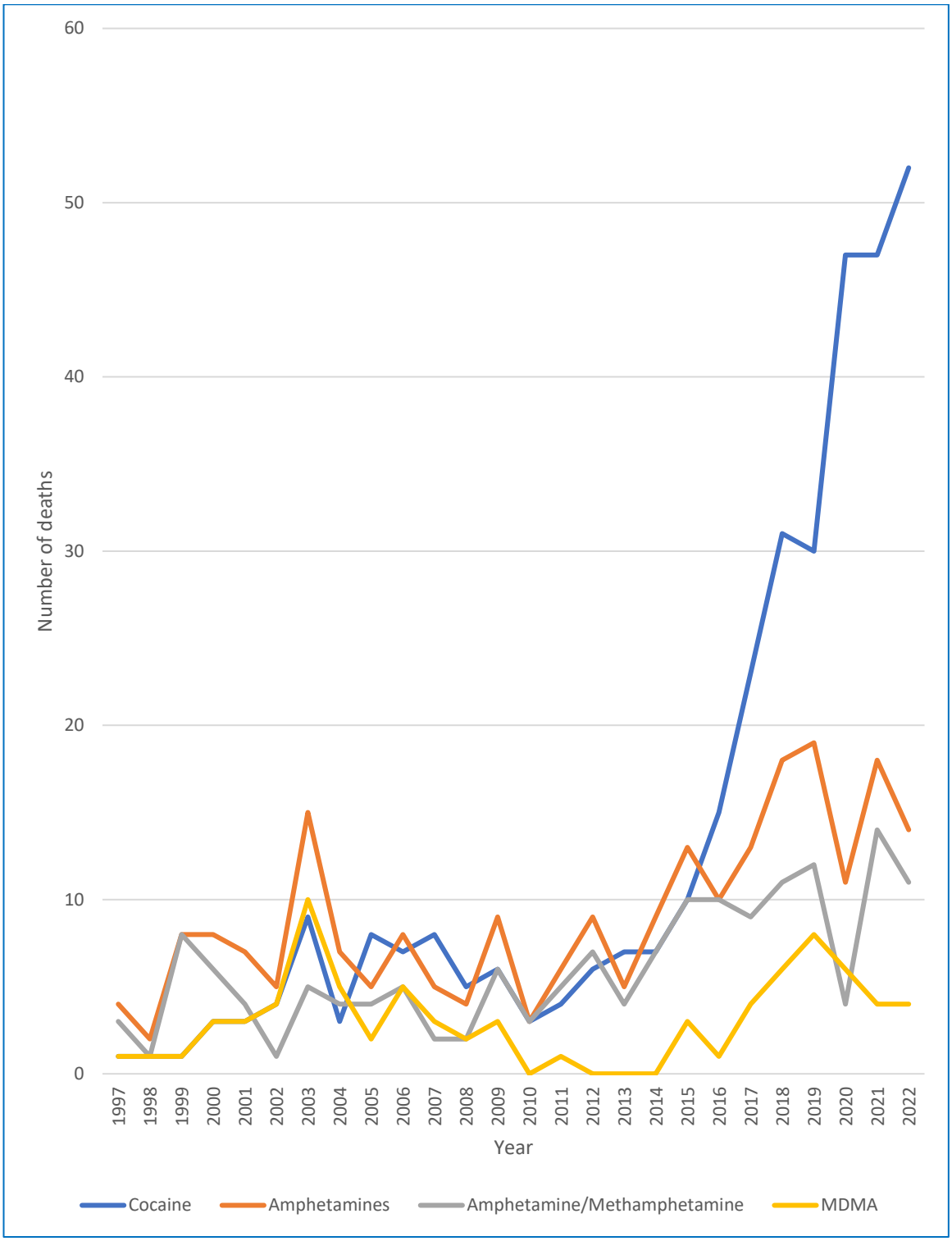

Figure 6.20: Number of drug poisoning deaths by main stimulant drugs, Wales, 1997-2022

Source: ONS (2023)

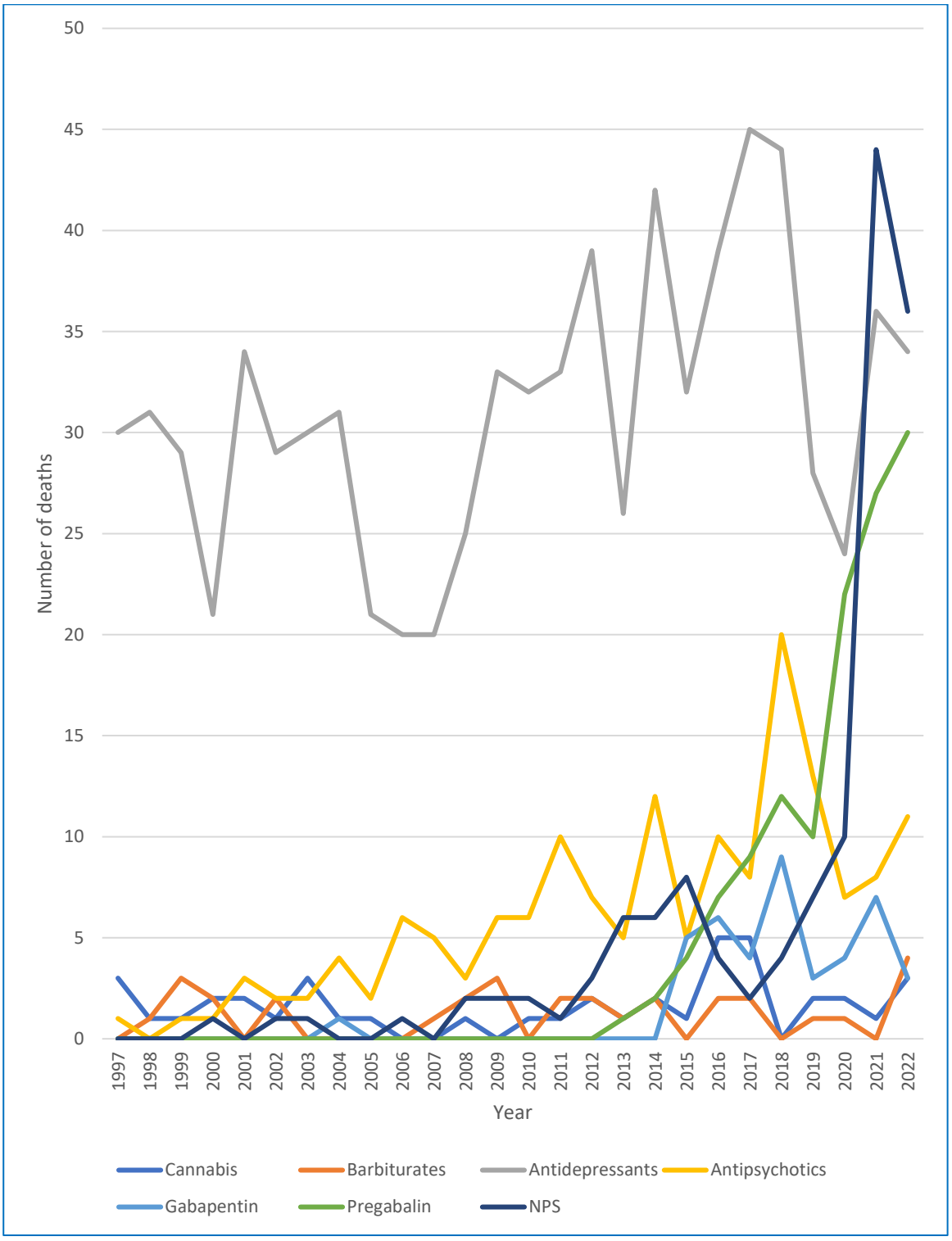

Figure 6.21: Number of drug poisoning deaths by selected other drugs, Wales, 1997-2022

Source: ONS (2023)

Limited information is available on benzodiazepine-related deaths in Wales; only for benzodiazepines as a class and individually for diazepam and temazepam. There are no data available for ‘street benzos’. The overall trend over this period was upwards, but very noticeable swings are demonstrated here (Figure 6.19). Whilst most of this is attributable to rising numbers of deaths involving diazepam, this does not explain the sudden increase in 2019-2021. This likely to have been caused by ‘street benzos’. Deaths involving temazepam have generally trended downwards.

Deaths involving stimulants remained fairly stable (allowing for many year-on-year fluctuations) until about 2013-2014 (Figure 6.20). Since that period, amphetamine-related deaths have risen overall but MDMA-related ones peaked in 2019. Cocaine-related deaths started to increase in 2013 but accelerated rapidly from 2015 to peak in 2020, levelling off in 2021 but rising again in 2022.

In terms of the other selected substances examined, Figure 6.21 indicates that antidepressants were the main feature of deaths across the whole period, except for the latest year when NPS overtook them. NPS rapidly increased their contribution to deaths from 2017 to 2021. Pregabalin has made an increasingly important contribution to deaths in Wales since 2012. The other main player has been antipsychotic drugs.

Figures 6.22 to 6.25 present the number of deaths in Scotland for the main drug classes for the period 1997-2022. The caveats outlined earlier also apply here.

Heroin/morphine and methadone also dominate the opiate/opioid class of drug deaths in Scotland (Figure 6.22). However, very different patterns are demonstrated compared to England and Wales in respect of heroin/morphine and other parts of the UK in respect of methadone. In Scotland, both drugs show overall upward trends, but at accelerated rates from 2013 to 2019 for heroin/morphine and from 2014 to 2020 for methadone. These peaks were followed by sharp falls. There appears to be a time-lag of a year between heroin/morphine and methadone trajectories. Methadone-related deaths have surpassed those for heroin/morphine in recent years.

Whilst diazepam-related deaths increased initially from 1997 to 2002 they experienced some movement in terms of falls and rises until about 2017 since when they have stabilised. On the other hand, temazepam-related deaths have fallen steadily over the last three decades and have all but disappeared. By contrast, ‘street benzos’ only emerged as an issue about 2015 but have since dominated the benzodiazepine contribution to drug poisoning deaths in Scotland, despite a fall since 2021 (Figure 6.23).

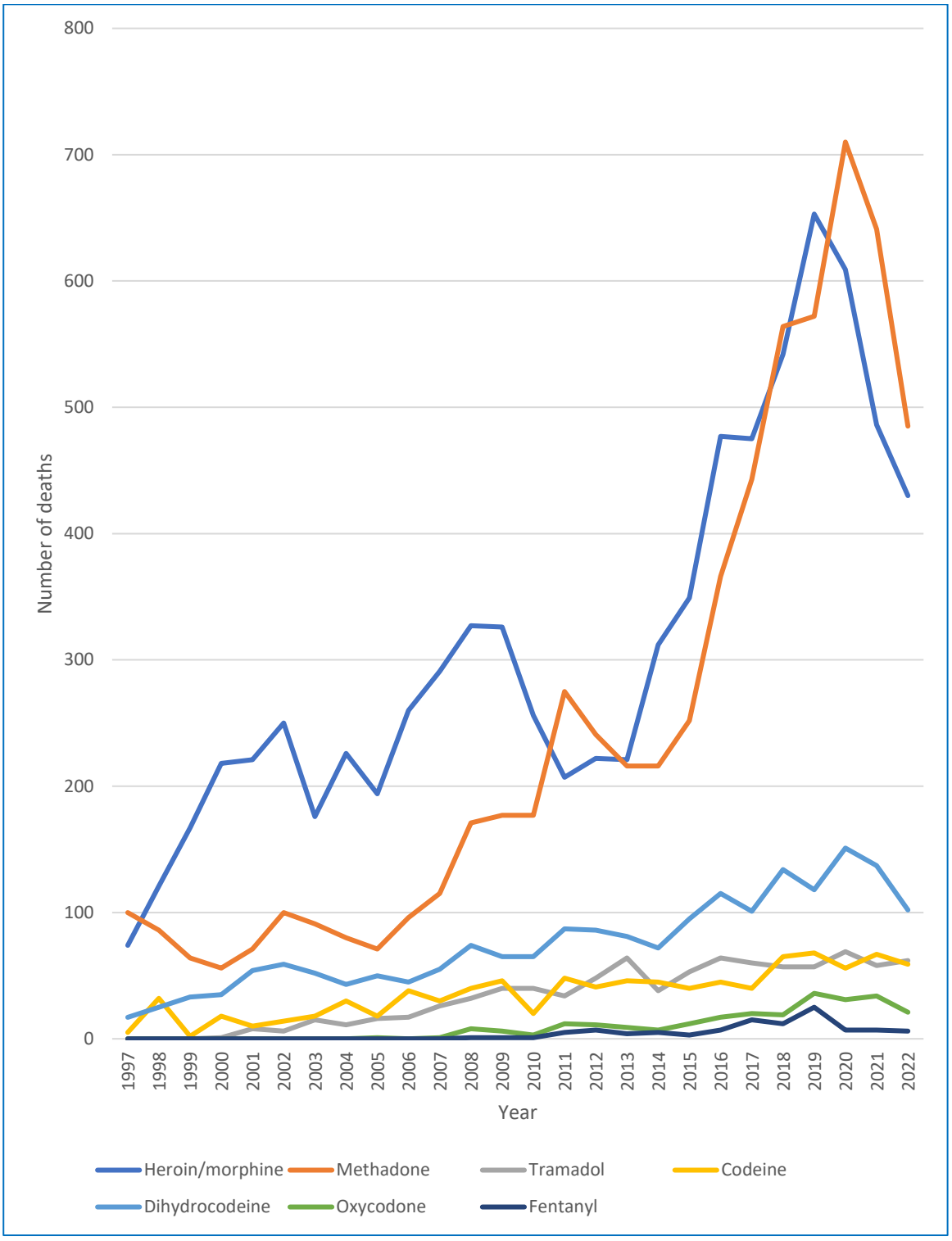

Figure 6.22: Number of drug poisoning deaths by main opiate/opioid drugs, Scotland, 1997-2022

Source: NRS (2023)

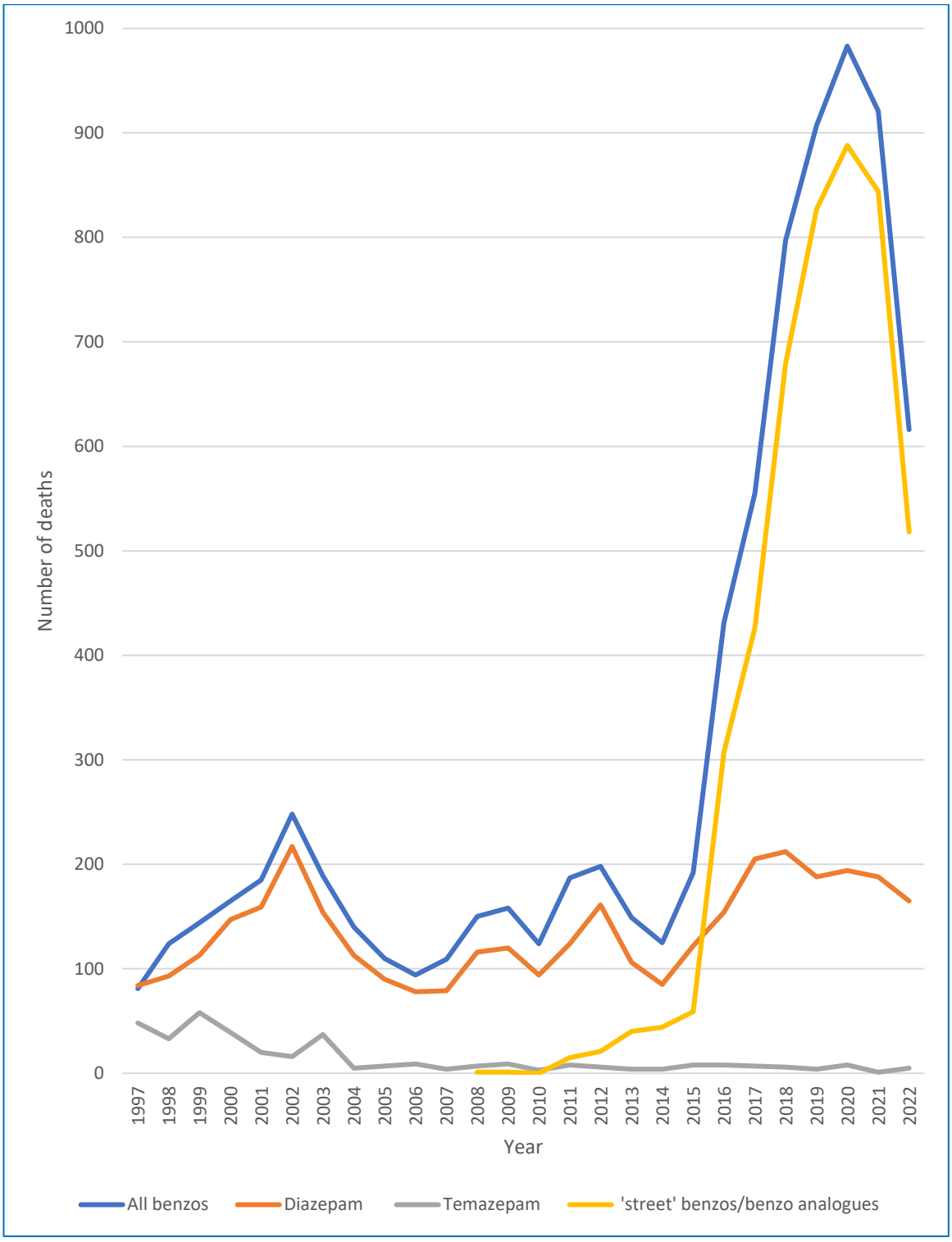

Figure 6.23: Number of drug poisoning deaths by main benzodiazepine drugs, Scotland, 1997-2022

Source: NRS (2023)

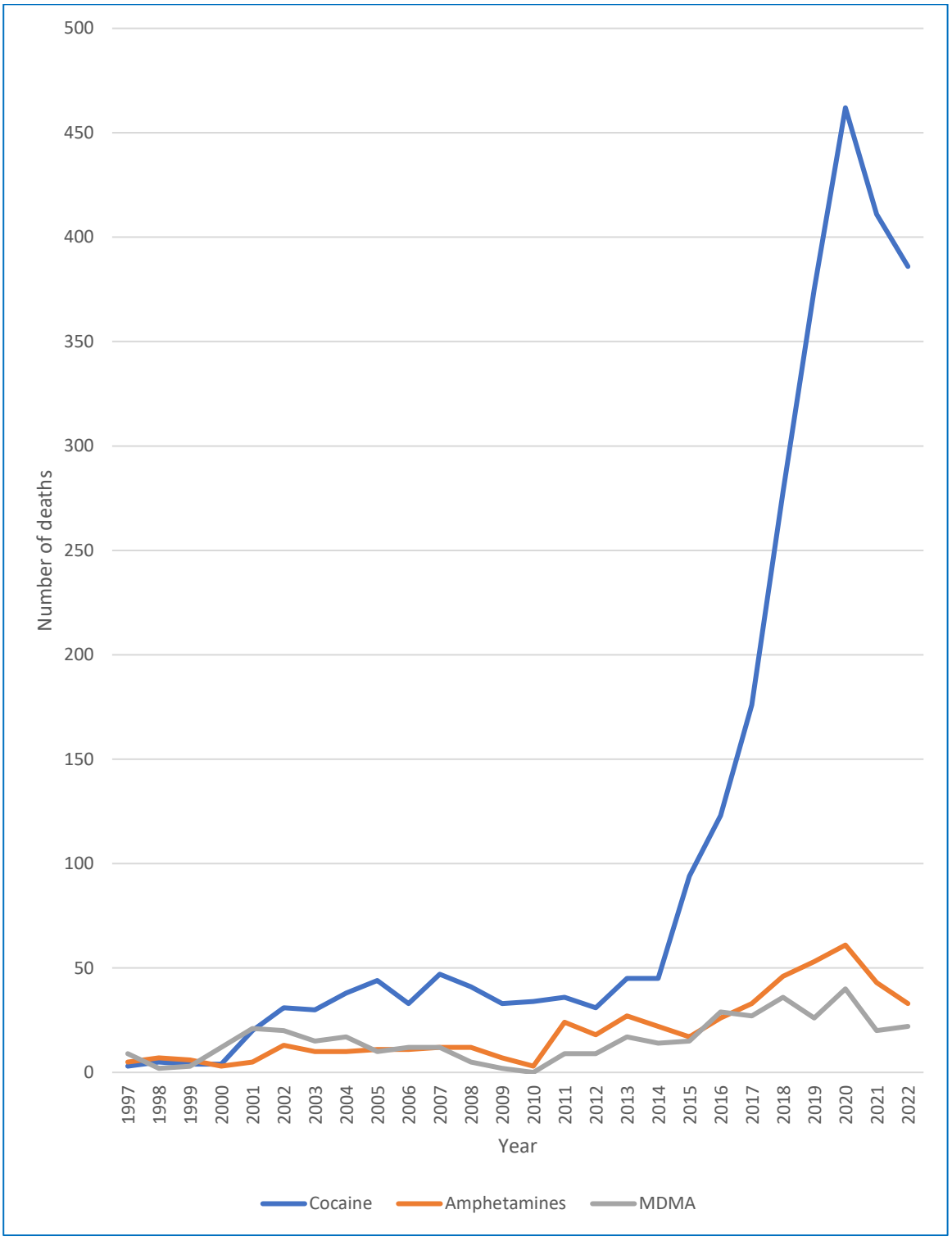

Figure 6.24: Number of drug poisoning deaths by main stimulant drugs, Scotland, 1997-2022

Source: NRS (2023)

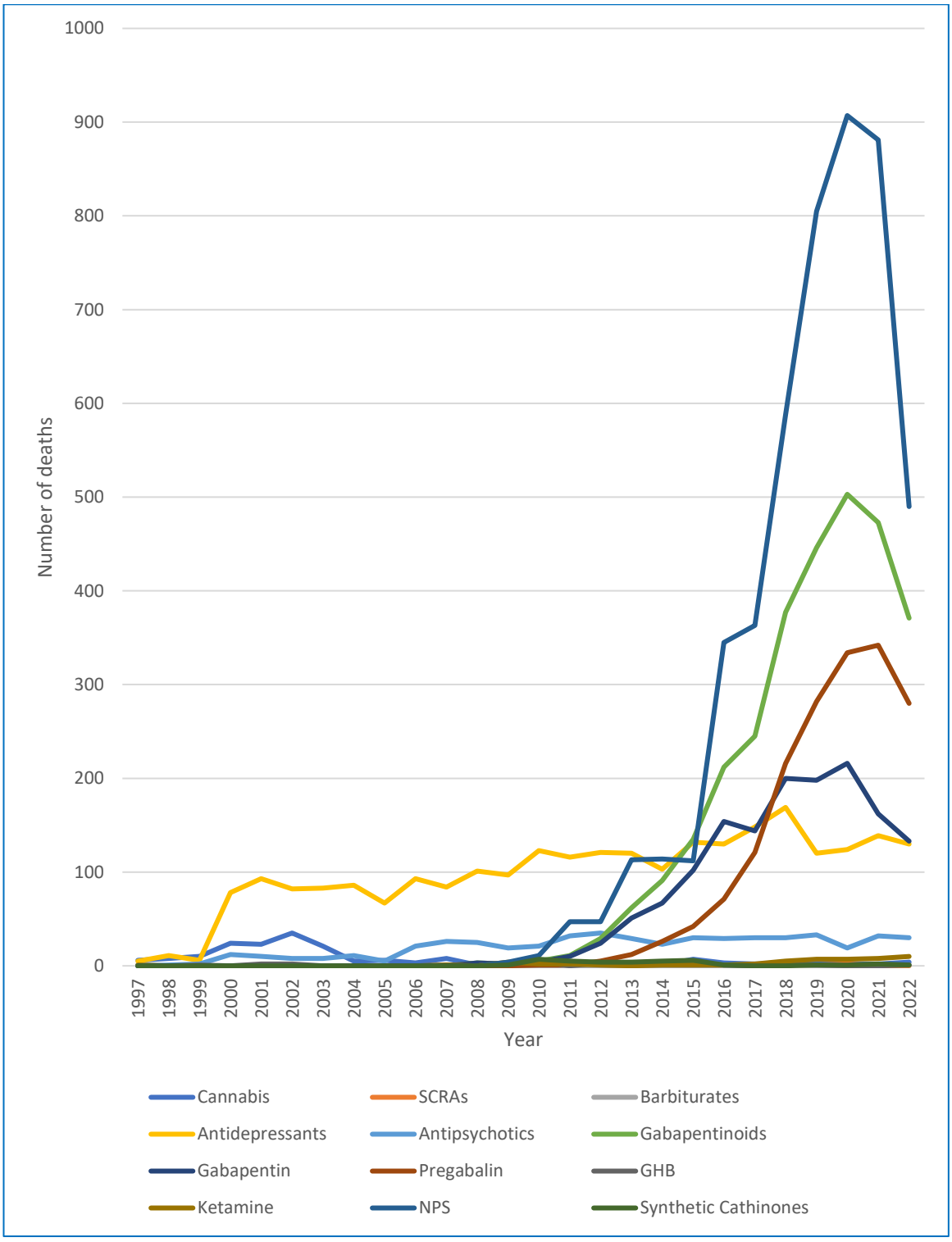

Figure 6.25: Number of drug poisoning deaths by selected other drugs, Scotland, 1997-2022

Source: NRS (2023)

Whilst amphetamine- and MDMA-related deaths have increased at a moderate rate in Scotland, cocaine dominates the contribution of stimulants to drug deaths (Figure 6.24). Most of the very steep increase in death registration numbers occurred between 2014 and 2020, with a slight fall from 2021.

Antidepressants have contributed to drug deaths consistently in Scotland since 2000 (Figure 6.25). However, the contribution of gabapentinoids has increased rapidly since 2011-2012, against a background of increased prescribing (Torrance et al., 2020) as has been the case in the other parts of the UK. However, the most dominant drug class that has emerged, since 2015, is that of NPS; however, much of this class includes 'street benzos'.

Figures 6.26 to 6.29 present the number of deaths in Northern Ireland for the main drug classes for the period 1997-2022. The same warnings outlined earlier also apply here.

Most types of opiate/opioid-related deaths have increased overall during the period since 1997. However, it can be difficult to tease out clear trends for the majority of them due to frequent changes in trajectory and relatively low absolute numbers (Figure 6.26). Heroin/morphine deaths play a less dominant role than opioid-related deaths in the rest of the UK. A spike in heroin deaths registered occurred in 2020 but they have now returned to their 2015 level; this was mirrored by deaths registered involving codeine. Relatively high contributions are made by methadone, codeine and tramadol. Methadone-related deaths appear to be generally increasing.

In terms of benzodiazepine-related deaths, temazepam has played a relatively stable role, whilst diazepam-related fatalities increased up until 2018 since when they have fallen back (Figure 6.27). Most of the increase in overall benzodiazepine-related deaths was accounted for by diazepam up until this date, but the rise to 2021 is probably due to 'street benzos' which are included in this overarching group. A fall in these may underlay the overall fall seen in 2022 registrations.

MDMA has been the major component of amphetamine-type stimulant deaths over the timeframe considered here, peaking about 2018 since when falls have been recorded (Figure 6.28). As in the rest of the UK, cocaine-related fatalities dominate stimulant-related deaths, exhibiting a very rapid rise between 2016 and 2019, since when they have fallen.

When it comes to the other drugs considered here (Figure 6.29), of note is the overall increased contribution of antidepressants, and in more recent years (since 2016) the very much increased role of pregabalin and NPS. However, pregabalin registrations peaked in 2019 and those for NPS in 2021.

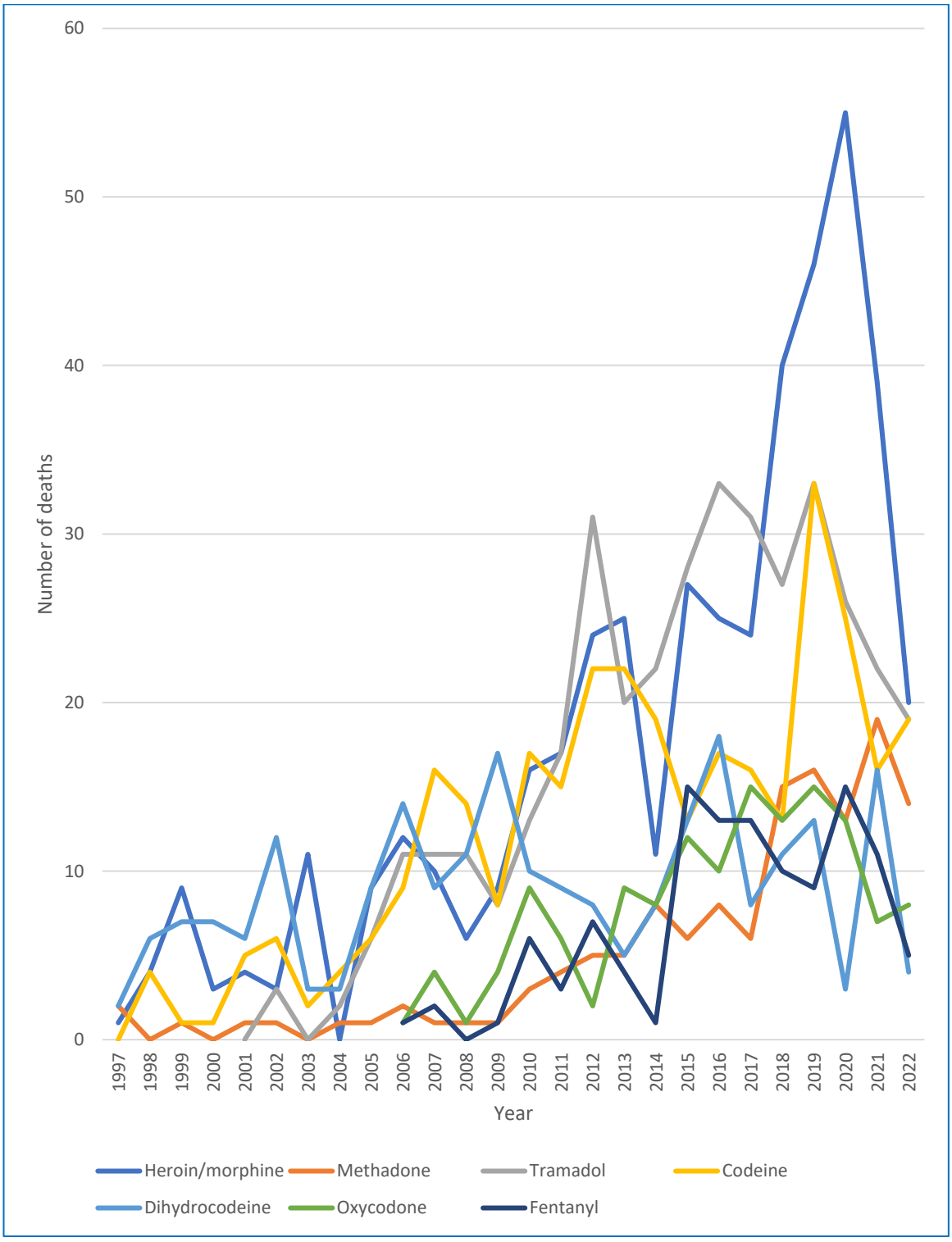

Figure 6.26: Number of drug poisoning deaths by main opiate/opioid drugs, Northern Ireland, 1997-2022

Source: NISRA (2024)

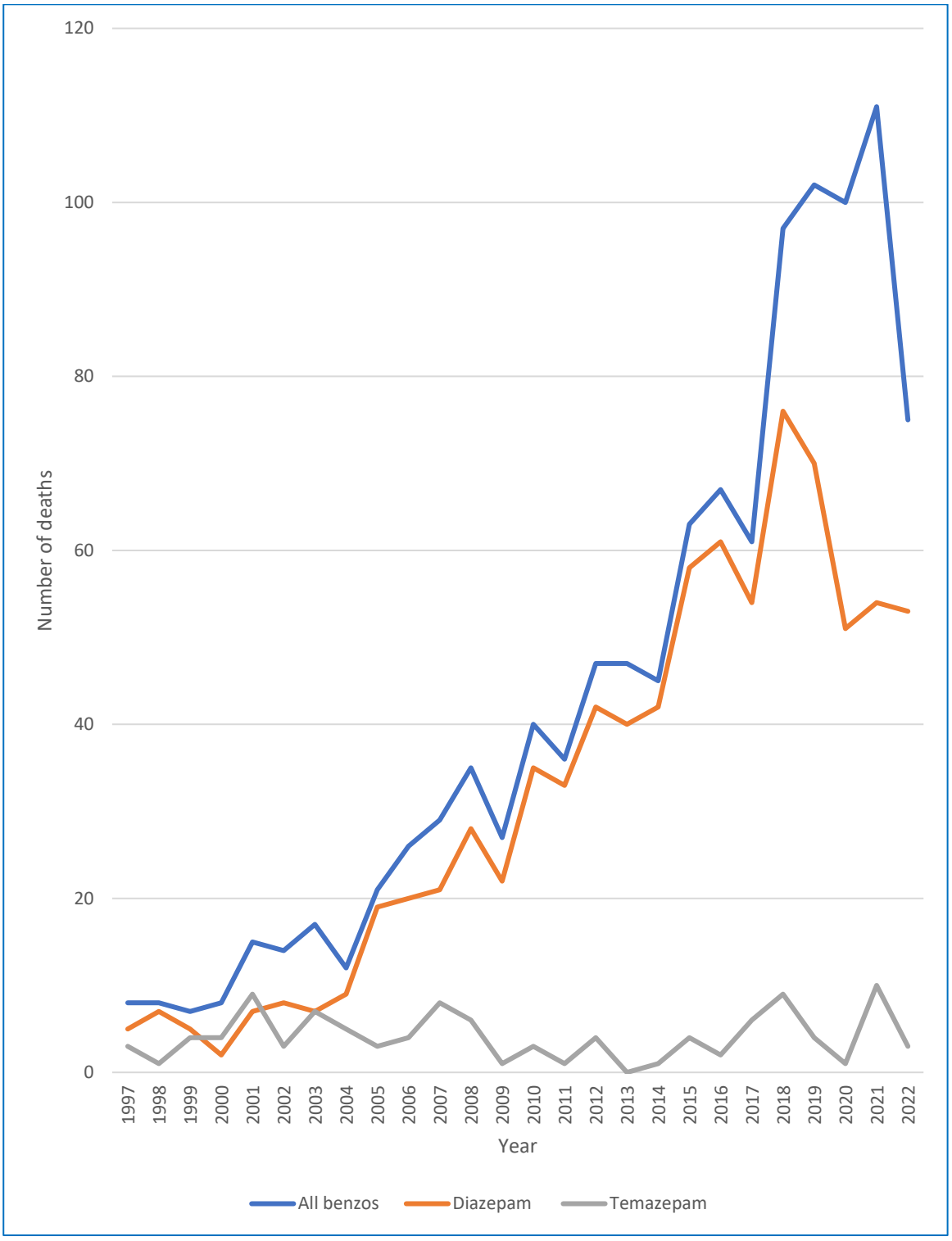

Figure 6.27: Number of drug poisoning deaths by main benzodiazepine drugs, Northern Ireland, 1997-2022

Source: NISRA (2024)

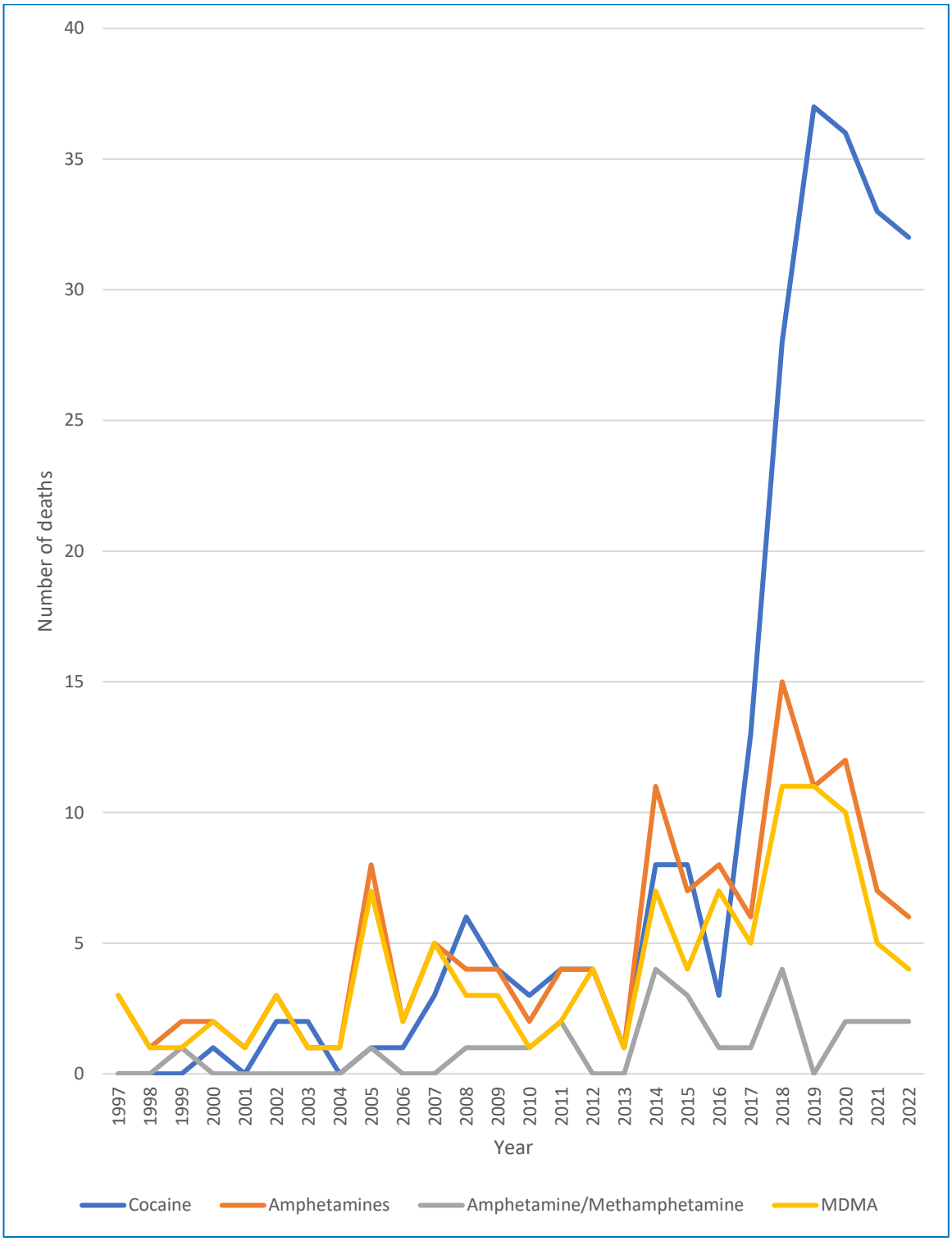

Figure 6.28: Number of drug poisoning deaths by main stimulant drugs, Northern Ireland, 1997-2022

Source: NISRA (2024)

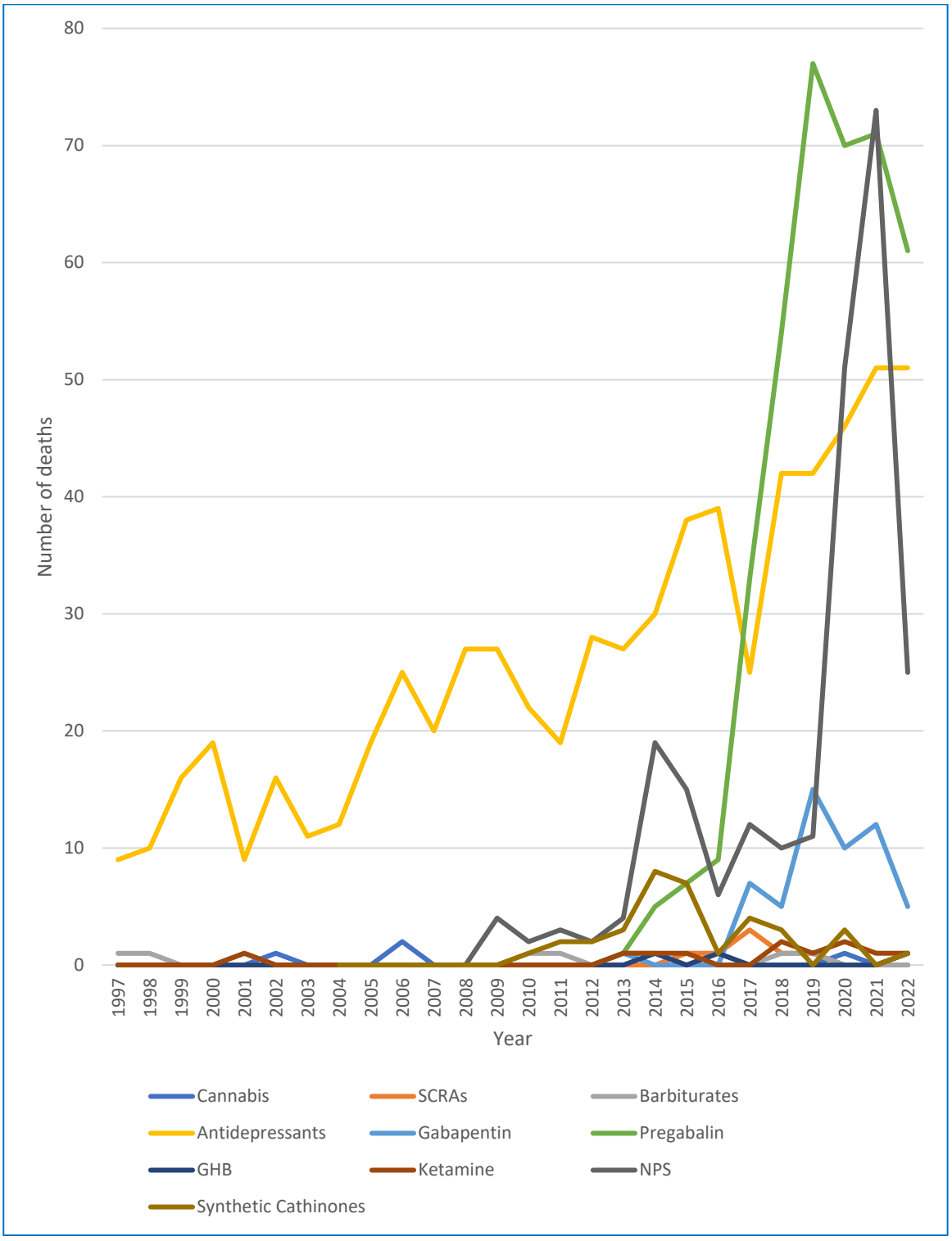

Figure 6.29: Number of drug poisoning deaths by selected other drugs, Northern Ireland, 1997-2022

Source: NISRA (2024)

Figures 6.30 to 6.34 present information, at the UK and sub-national levels, on the proportions of all deaths involving selected index substances/drug classes for the period 1997-2022. Line graphs were chosen in preference to stacked area graphs as the latter would add up to more than 100% (due to polydrug deaths). In addition, individual substances can be more easily distinguished than if stacked areas were used.

At the UK level, not unsurprisingly given earlier comments, heroin/morphine deaths have contributed most to the overall patterns (Figure 6.30). There was an increase in the proportion for which they accounted between 1997 and 2002, followed some fluctuations to 2009. There was a sharp drop in 2010 and 2011, likely due to the 'heroin drought'; this was followed by a return to the previous levels by 2016, but a fall is noticeable since 2019. Methadone proportions appear to go in the opposite direction to movements in heroin/morphine deaths

The antidepressant contribution appears to have stayed relatively stable, albeit with some variations in direction. Benzodiazepines have shown an increasing contribution over the timeframe examined here. Significant increases have been exhibited by NPS since 2010 (soon after they had emerged onto the markets) and cocaine since 2011 (following a fall in purity). Of increasing importance in recent years has been the contribution of the gabapentinoids, particularly pregabalin. However, it appears that benzodiazepines peaked in 2020, and NPS and pregabalin in 2021. The contributions made by other substances examined here have remained at low levels.

Turning to the sub-national level, i.e., constituent countries, of the UK, it is no surprise (given its population size) that the patterns exhibited in England largely replicates the patterns outlined in the previous two paragraphs. The main exception is the antidepressant drug class which has seen an overall decrease in its contribution (Figure 6.31). The proportions contributed by the other main substances, such as cocaine, NPS and pregabalin are considerably lower than for the UK as a whole.

The opiate/opioid and methadone profiles in England are mirrored by those in Wales but that for heroin/morphine is at a slightly higher level (Figure 6.32). Antidepressants' contribution has generally fallen over time whereas that of benzodiazepines has increased overall. The contributions made by cocaine, NPS and pregabalin have all increased in the last 8 to 10 years.

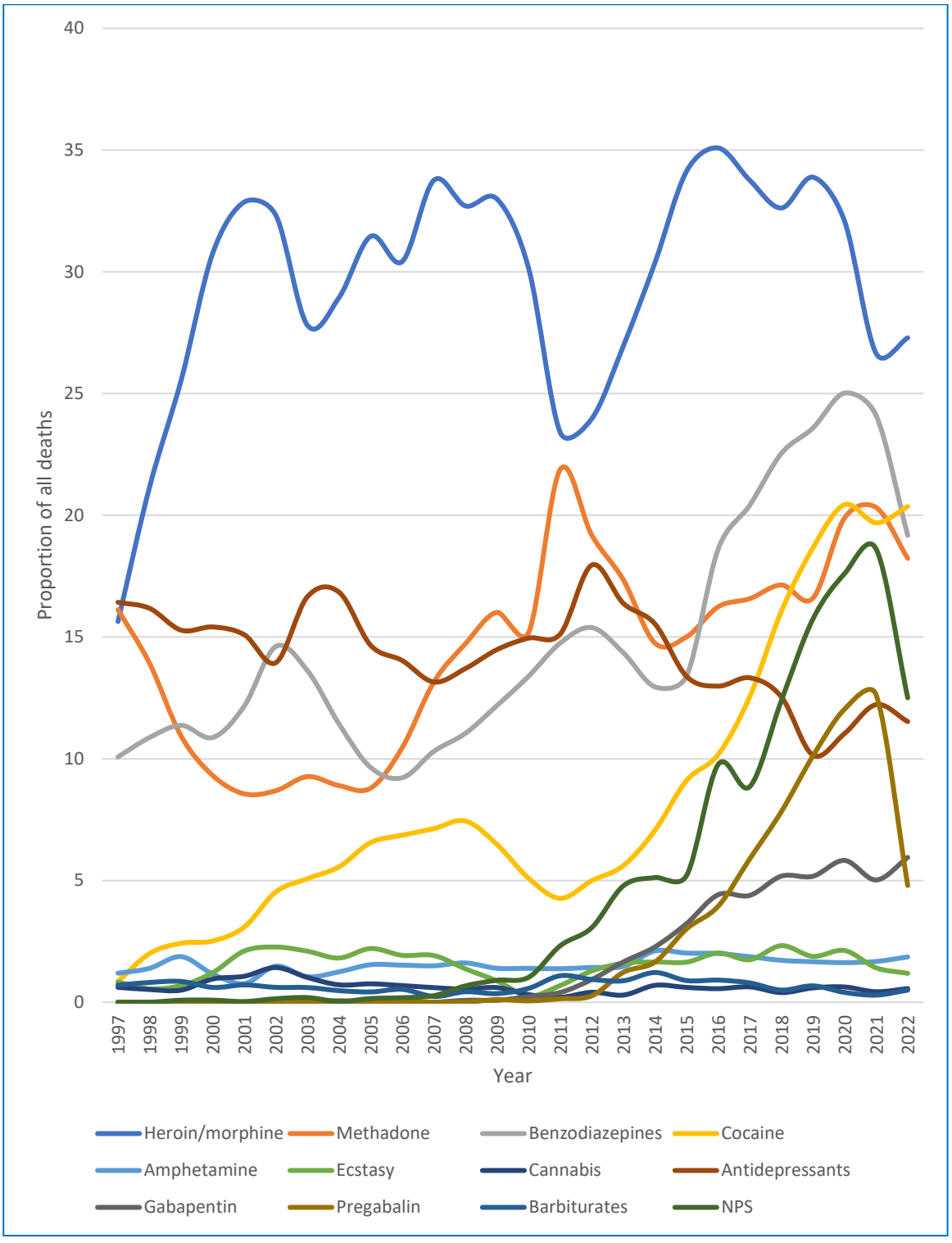

Figure 6.30: Trends in proportions of deaths accounted for by drug classes/index drugs, United Kingdom, 1997-2022

Sources: ONS (2023); NRS (2023); NISRA (2024)

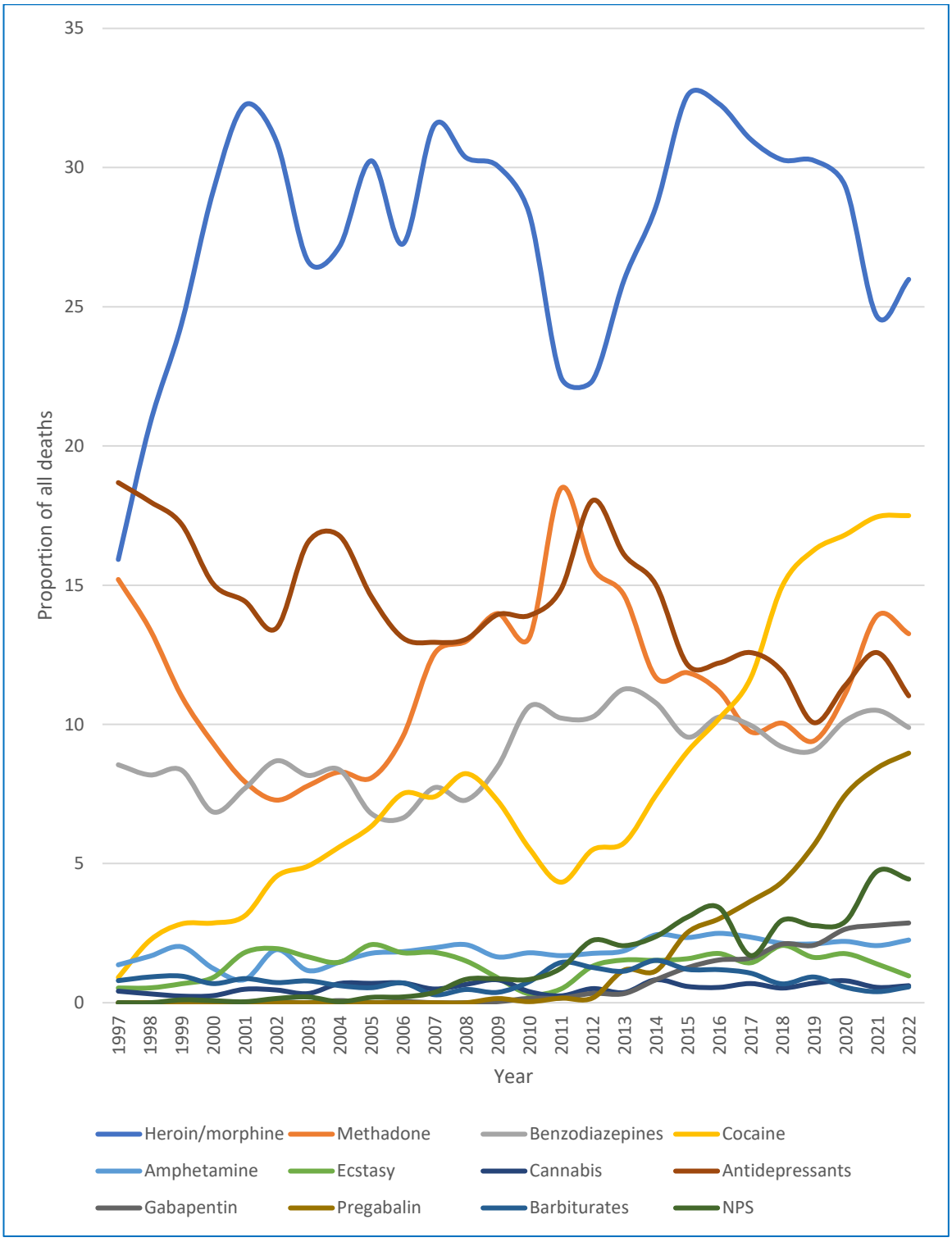

Figure 6.31: Trends in proportions of deaths accounted for by drug classes/index drugs, England, 1997-2022

Source: ONS (2023)

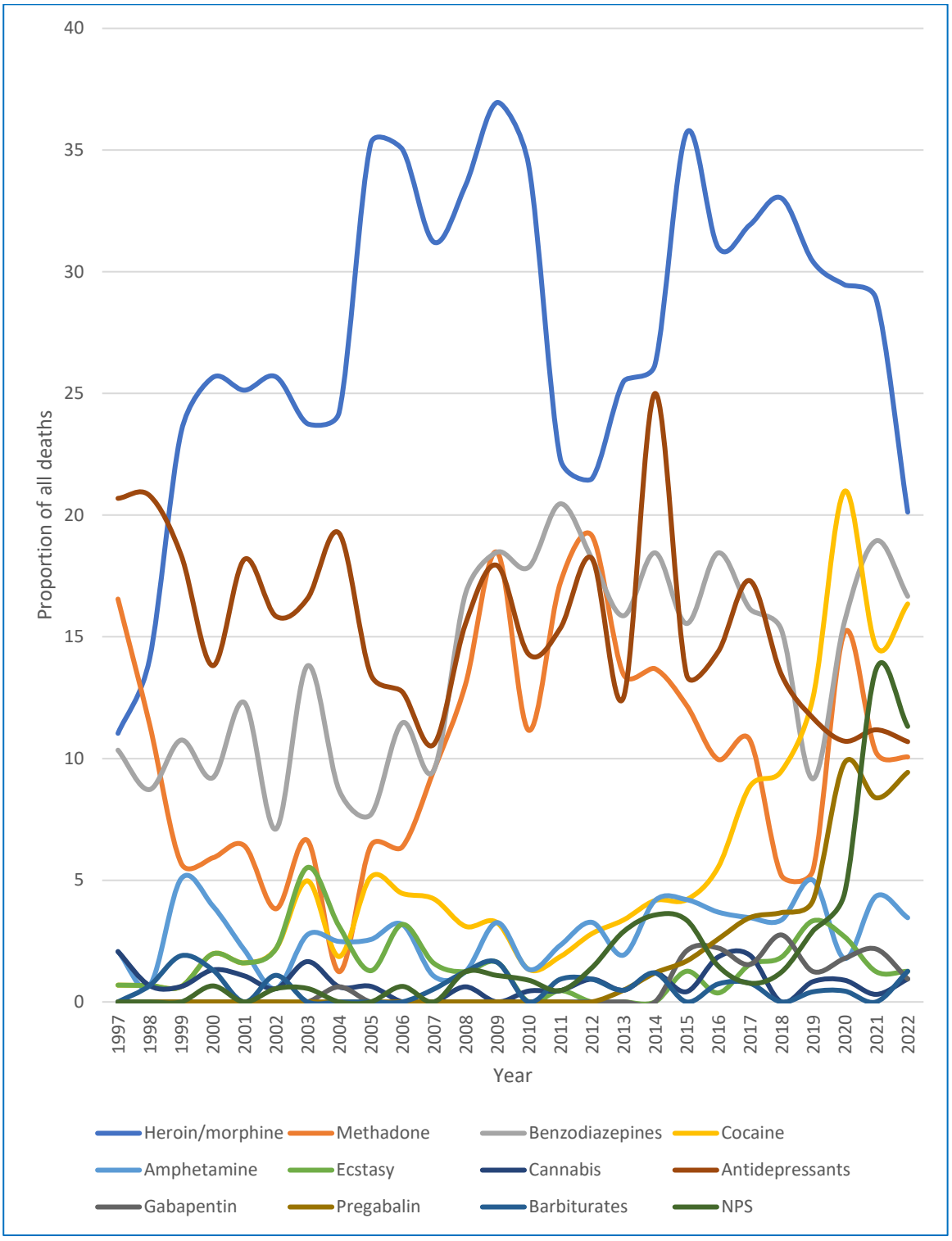

Figure 6.32: Trends in proportions of deaths accounted for by drug classes/index drugs, Wales, 1997-2022

Source: ONS (2023)

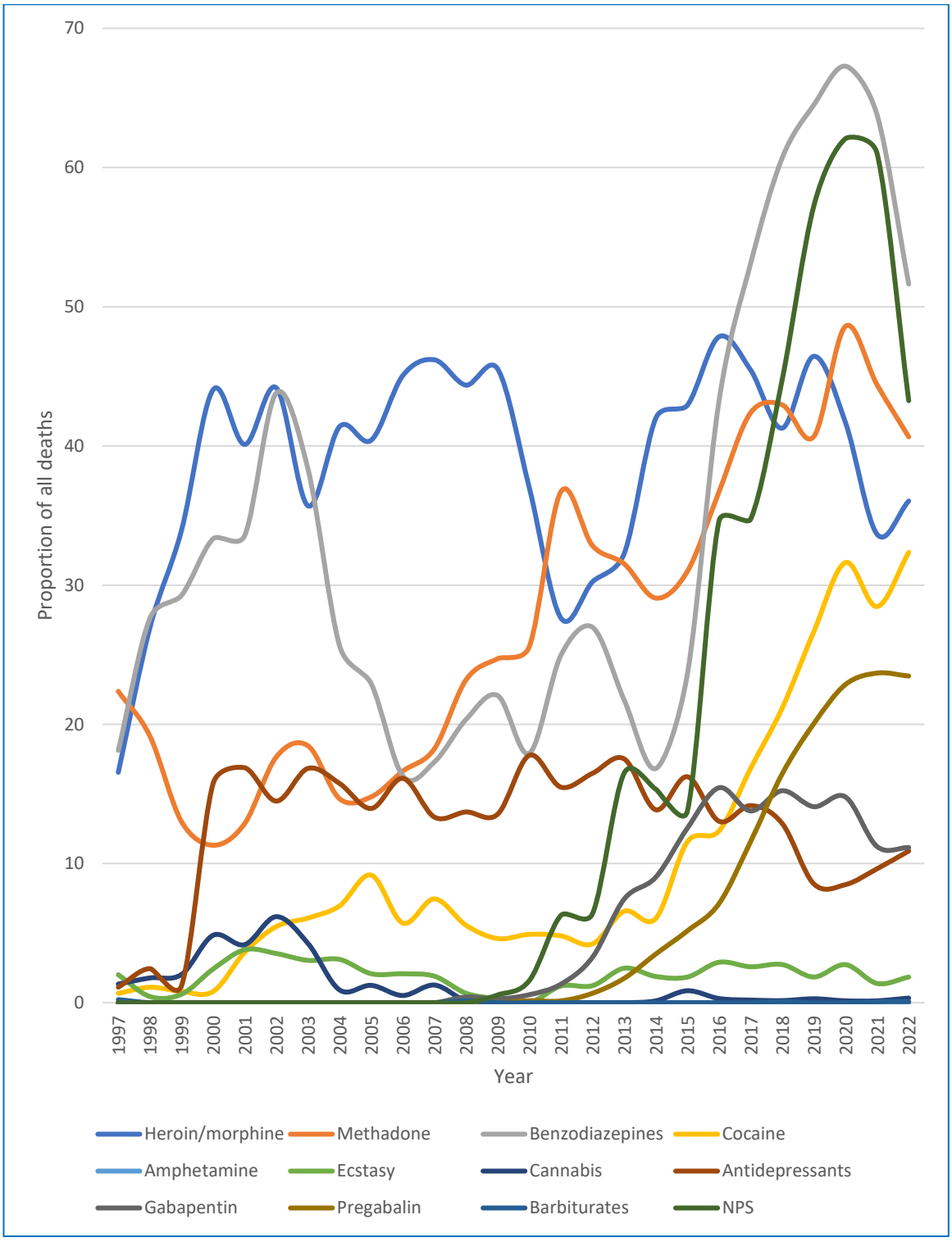

Figure 6.33: Trends in proportions of deaths accounted for by drug classes/index drugs, Scotland, 1997-2022

Source: NRS (2023)

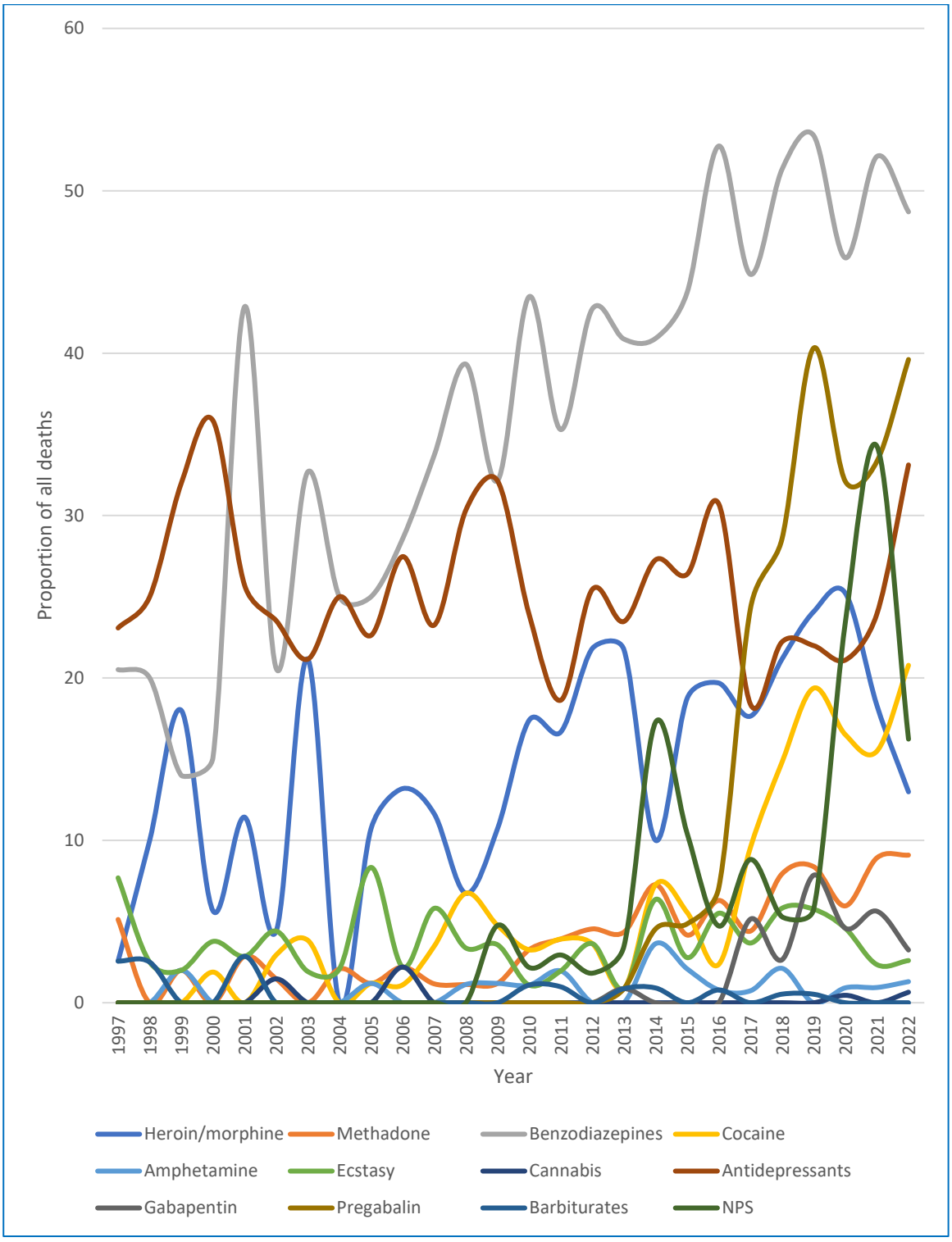

Figure 6.34: Trends in proportions of deaths accounted for by drug classes/index drugs, Northern Ireland, 1997-2022

Source: NISRA (2024)

In Scotland, the overall pattern of heroin/morphine deaths is similar to that observed south of the border, but at a considerably higher level (about 50%). The overall contribution made by methadone has increased across time (Figure 6.33). However, the most salient development is the very rapid and major contribution made by NPS, mostly 'street benzos', from 2015 to 2020. During this period, they accounted for higher contributions than the opiate/opioid class. However, the contributions made by benzodiazepines which including 'street' benzodiazepines/'designer benzos') and NPS have fallen since 2020. As in England and Wales, pregabalin has had an increasing part to play in deaths in recent years. Cocaine's contribution has also increased rapidly in the last decade or so, but at about twice the level seen in England.

Very different trends are evident in Northern Ireland (Figure 6.34). Benzodiazepines and antidepressants are the dominant drug classes, followed by heroin/morphine. Unlike other parts of the UK, methadone does not feature very highly; probably to relatively low levels of prescribing. Developments of note are the increasing contributions made by pregabalin, NPS and cocaine since 2016. There appears to have been a fall in the NPS contribution in 2022.

Tables 6.3 to 6.7 present the overall UK and sub-national proportions of all drug poisoning deaths accounted for by 11 specific drug classes/substances at the start and end of the period 1997-2022, changes over time, and whether these changes are statistically significant. The ratio of proportions was used to compare the 2021 data against that for 1997, using MedCalc (2023). MedCalc employs the "N-1" Chi-square test recommended by Campbell (2007) and Richardson (2011). The confidence interval was calculated following the method recommended by Altman et al. (2000). It was not possible to make comparisons for NPS and gabapentin or pregabalin as these were absent from deaths at the start of the time-frame considered here; gabapentin was licensed for use in the UK in 1997, followed by pregabalin in 2004. These limitations apply also to Tables 6.4 to 6.7.

At the UK level (Table 6.3), where it is possible to make a comparison between 1997 and 2022, 6/9 classes/substances showed an increase; the proportion contributed by barbiturates fell (by 35%). Against a background of the number of drug poisoning deaths nearly doubling, antidepressants (34%) and cannabis (80%) exhibited moderate increases, whilst methadone (115%), ecstasy (174%), heroin/morphine (232%), amphetamines (256%) and benzodiazepines (262%) displayed strong increases, cocaine increased its share 44-fold! The majority of these differences were statistically significant at the $P < 0.0001$ level; that for methadone was significant at the $P < 0.01$ level. Differences for barbiturates, cannabis and ecstasy were not statically significant.

Table 6.3: Change in proportions of drug classes/index drugs between 1997 and 2022, United Kingdom

Main drug class/index drug	*1997*		*2022*		*Change*		*Difference in proportions (2022 vs. 1997)*	*Chi-square value*	*Difference in proportions statistically significant*
	Number of deaths	*% of all drug-related deaths*	*Number of deaths*	*% of all drug-related deaths*	*Number*	*%*			
Heroin/Morphine	512	15.63	1702	27.29	1190	232.42	11.66	163.469	P < 0.0001
Methadone	528	16.12	1137	18.23	609	115.34	2.11	6.620	P = 0.0101
Benzodiazepines	330	10.08	1196	19.18	866	262.42	9.10	131.985	P < 0.0001
Cocaine (in. 'crack')	28	0.85	1270	20.36	1242	4435.71	19.51	693.722	P < 0.0001
All amphetamines	62	1.89	221	3.54	159	256.45	1.65	20.272	P < 0.0001
Ecstasy (MDA/MDMA)	27	0.82	74	1.19	47	174.07	0.37	2.796	P = 0.0945
Cannabis	20	0.61	36	0.58	16	80.00	-0.03	0.033	P = 0.8560
Antidepressants	538	16.43	719	11.53	181	33.64	-4.90	44.946	P < 0.0001
Gabapentin	0	0.00	299	4.79	299	-	4.79	161.942	P < 0.0001
Barbiturates	23	0.70	31	0.50	8	34.78	-0.20	1.518	P = 0.2179
Novel Psychoactive Substances	0	0.00	780	12.51	780	-	12.51	446.266	P < 0.0001
Total number of deaths (N)	3275	100.00	6237	100.00	2962	90.44	-	-	-

Looking at England (Table 6.4), the number of deaths increased by 73%. A slight increase was exhibited by antidepressants (2%) and barbiturates (24%), and a moderate increase by methadone (51%). Stronger increases were demonstrated by benzodiazepines (100%), cannabis (155%), heroin/morphine (182%), ecstasy (214%), and amphetamines (244%). Again, cocaine's role was the outstanding change - a 32-fold increase. Compared to the UK level, fewer changes were statistically significant at the P < 0.0001 level (heroin/morphine, cocaine, amphetamines, antidepressants, gabapentin, and NPS). However, ecstasy changes were statistically significant at the P < 0.05 level.

Table 6.4: Change in proportions of drug classes/index drugs between 1997 and 2022, England

Main drug class/index drug	*1997*		*2022*		*Change*		*Difference in proportions (2022 vs. 1997)*	*Chi-square value*	*Difference in proportions statistically significant*
	Number of deaths	*% of all deaths*	*Number of deaths*	*% of all deaths*	*Number*	*%*			
Heroin/Morphine	421	15.92	1188	25.98	767	182.19	10.06	97.851	P < 0.0001
Methadone	402	15.20	606	13.25	204	50.75	-1.95	5.301	P = 0.0213
Benzodiazepines	226	8.55	452	9.89	226	100.00	1.34	3.532	P = 0.0602
Cocaine (in. 'crack')	24	0.91	800	17.50	776	3233.33	16.59	455.679	P < 0.0001
All amphetamines	50	1.89	172	3.76	122	244.00	1.87	19.653	P < 0.0001
Ecstasy (MDA/MDMA)	14	0.53	44	0.96	30	214.29	0.43	3.891	P = 0.0486
Cannabis	11	0.42	28	0.61	17	154.54	0.19	1.125	P = 0.2888
Antidepressants	494	18.68	504	11.02	10	2.02	- 7.66	82.486	P < 0.0001
Gabapentin	0	0.00	131	2.87	131	-	2.87	77.278	P < 0.0001
Barbiturates	21	0.79	26	0.57	5	23.81	- 0.22	1.254	P = 0.2627
Novel Psychoactive substances	0	0.00	203	4.44	203	-	4.44	120.775	P < 0.0001
Total number of deaths (N)	2644	100.00	4572	100.00	1928	72.92	-	-	-

The situation in Wales (Table 6.5) is more difficult to interpret because of the relatively low numbers of deaths. For example, barbiturates increased from 0 to 4 deaths whereas cannabis remained unchanged at 3 deaths. Antidepressants showed a slight increase (13%), as did methadone (33%). Stronger increases can be observed for amphetamines (250%), heroin/morphine (300%), ecstasy (333%), and benzodiazepines (489%). Yet again, cocaine is the most noteworthy a 51-fold increase, against an increase of 119% in the overall number of deaths. Only two drug classes/substances (cocaine and NPS) exhibited changes that were statistically significant at the P < 0.0001 level. There were no drug classes/substances that showed changes significant at the P < 0.001 level.

Table 6.5: Change in proportions of drug classes/index drugs between 1997 and 2022, Wales

Main drug class/index drug	*1997*		*2022*		*Change*		*Difference in proportions (2022 vs. 1997)*	*Chi-square value*	*Difference in proportions statistically significant*
	Number of deaths	*% of all deaths*	*Number of deaths*	*% of all deaths*	*Number*	*%*			
Heroin/Morphine	16	11.03	64	20.13	48	300.00	9.10	5.757	P = 0.0164
Methadone	24	16.55	32	10.06	8	33.33	-6.49	3.938	P = 0.0472
Benzodiazepines	9	10.34	53	16.67	44	488.89	6.33	3.178	P = 0.0746
Cocaine (in. 'crack')	1	0.69	52	16.35	51	5100.00	15.66	24.044	P < 0.0001
All amphetamines	4	2.76	14	4.40	10	250.00	1.64	0.716	P = 0.3976
Ecstasy (MDA/MDMA)	1	0.69	4	1.26	3	333.33	0.57	0.302	P = 0.5828
Cannabis	3	2.07	3	0.94	0	0.00	-1.13	0.994	P = 0.3189
Antidepressants	30	20.69	34	10.69	4	13.33	-10.00	8.343	P = 0.0039
Gabapentin	0	0.00	3	0.94	3	-	0.94	1.369	P = 0.2420
Barbiturates	0	0.00	4	1.26	4	-	1.26	1.839	P = 0.1751
Novel Psychoactive substances	0	0.00	36	11.32	36	-	11.32	17.759	P < 0.0001
Total number of deaths (N)	145	100.00	318	100.00	173	119.31	-	-	-

The situation in Scotland (Table 6.6) shows that barbiturate deaths remained unchanged, whilst cannabis fell by two-thirds (albeit from 6 to 4). There were strong changes for ecstasy (144%), methadone 385%) and heroin/morphine (481%). Very strong changes can be noted for both benzodiazepines (660%) and antidepressants (2500%). However, it is cocaine, once more, that demands most interest/concern – a 127-fold increase. Not unsurprisingly, most of these changes were statistically significant at the P < 0.0001 level (heroin/morphine, methadone, benzodiazepines, cocaine, antidepressants, gabapentin, and NPS); cannabis was also significant at the P < 0.001 level. This is against an overall increase of 167% in drug poisoning deaths in this timeframe.

Table 6.6: Change in proportions of drug classes/index drugs between 1997 and 2022, Scotland

Main drug class/index drug	*1997*		*2022*		*Change*		*Difference in proportions (2022 vs. 1997)*	*Chi-square value*	*Difference in proportions statistically significant*
	Number of deaths	*% of all deaths*	*Number of deaths*	*% of all deaths*	*Number*	*%*			
Heroin/Morphine	74	16.55	430	36.04	356	481.08	19.49	57.993	P < 0.0001
Methadone	100	22.37	485	40.65	385	385.00	18.28	47.325	P < 0.0001
Benzodiazepines	81	18.12	616	51.63	535	660.49	33.51	149.328	P < 0.0001
Cocaine (in. 'crack')	3	0.67	386	32.36	383	12766.67	31.69	180.354	P < 0.0001
All amphetamines	5	1.12	29	2.43	24	480.00	1.31	2.747	P = 0.0974
Ecstasy (MDA/MDMA)	9	2.01	22	1.84	13	144.44	-0.17	0.051	P = 0.8218
Cannabis	6	1.34	4	0.34	- 2	-33.33	-1.00	5.338	P = 0.0209
Antidepressants	5	1.12	130	10.90	125	2500.00	9.78	41.135	P < 0.0001
Gabapentin	0	0.00	133	11.15	133	-	11.15	54.207	P < 0.0001
Barbiturates	1	0.22	1	0.08	0	0.00	0.14	54.207	P = 0.4626
Novel Psychoactive substances	0	0.00	516	43.25	516	-	43.25	281.900	P < 0.0001
Total number of deaths (N)	447	100.00	1193	100.00	746	166.89	-	-	-

Northern Ireland experienced the highest rate of increase in such deaths - 295% (Table 6.7). Barbiturate deaths fell by 100% (one death) but cannabis fatalities increased by the same amount (from zero to one death). Cocaine deaths increased from 0 to 32. A moderate increase was shown by ecstasy (33%). Very strong increases can be noted for antidepressants (467%), methadone (600%), and benzodiazepines (838%). The principal change to comment on here is the 19-fold increase for heroin/morphine. Due to the relative low Chi-square values, changes for only three drug classes were statistically significant at the P < 0.01 level: benzodiazepines, cocaine, and NPS.

Table 6.7: Change in proportions of drug classes/index drugs between 1997 and 2022, Northern Ireland

Main drug class/index drug	*1997*		*2022*		*Change*		*Difference in proportions (2022 vs. 1997)*	*Chi-square value*	*Difference in proportions statistically significant*
	Number of deaths	*% of all deaths*	*Number of deaths*	*% of all deaths*	*Number*	*%*			
Heroin/Morphine	1	2.56	20	12.99	19	1900.00	10.43	3.473	P = 0.0624
Methadone	2	5.13	14	9.09	12	600.00	3.96	0.639	P = 0.4242
Benzodiazepines	8	20.51	75	48.70	67	837.50	28.19	10.037	P = 0.0015
Cocaine (in. 'crack')	0	0.00	32	20.78	32	-	20.78	9.665	P = 0.0019
All amphetamines	3	7.69	6	3.90	3	100.00	-3.79	1.000	P = 0.3174
Ecstasy (MDA/MDMA)	3	7.69	4	2.60	1	33.33	- 5.09	2.294	P = 0.1299
Cannabis	0	0.00	1	0.65	1	100.00	0.65	0.254	P = 0.6146
Antidepressants	9	23.08	51	33.12	42	466.67	10.04	1.457	P = 0.2275
Gabapentin	0	0.00	5	3.25	5	-	3.25	1.295	P = 0.2552
Barbiturates	1	2.56	0	0.00	-1	- 100.00	- 2.56	3.942	P = 0.0471
Novel Psychoactive substances	0	0.00	25	16.23	25	-	16.23	7.234	P = 0.0072
Total number of deaths (N)	39	100.00	154	100.00	115	294.87	-	-	-

The analysis presented in the tables above underline that there are important differences between the constituent parts of the UK in terms of both the absolute proportions of deaths accounted for by specific drug classes/substances but also their evolutions over time.

Temporal and spatial patterns of Drug-Related Deaths

Globally, relatively little research has been conducted on drug poisoning deaths and how they may be affected by short-term or cyclical factors.

"There may be demand-side drivers such as stress during holidays or monthly financial pressures and supply-side drivers such as regular changes in the availability and potency of drugs... These cycles could be an important part of the 'risk environment' … for drug-related deaths. An understanding of these patterns could contribute to the planning of public health and clinical services that aim to prevent drug-related deaths."
Lewer et al. (2023)

Most research on these dimensions seems to have occurred in just a few countries: the USA, Italy, and the UK. The interest in such phenomena has also been sporadic, the 1970s, mid-2000s, and the last year or so. The findings reported below fail to demonstrate any sort of consistency.

Deaths in New York City's 'narcotic addicts' in the 1964-1968 period increased during the summer and autumn; the summer peak possibly being caused by increased 'addiction activity' during the warmer months (Cherubin et al., 1972). By contrast, Abraham et al. (2021) found that

the most consistent increases in Delaware overdose deaths occurred in spring months. Han et al. (2022) report a much longer period for higher intentional overdose death rates for both genders - spring and summer, when days are longer. They also note a lower death rate in December, suggesting that social and cultural influences, such as increased social interactions and collective community optimism during the holiday season, may reduce the likelihood of suicide; these factors could also play a protective role in fewer suicides on Saturdays. Yet a different pattern was reported by Sadler and Furr-Holden (2019): fatal opioid drug overdoses in Michigan during 2013-2015 were lowest in summer and highest in spring. More recently, Slade et al. (2023) report higher overdose rates in winter, rather than the summer, in the state of Kentucky.

Italian research found that deaths from unintentional overdose occurred at specific times of the year (December-January and August), but the causes were unclear (Rocchi et al., 2003, 2004). However, there may be an association between them and the Christmas and peak holiday season (August) in Italy.

In terms of the UK, Barraclough and White (1978) found no evidence of seasonal variation in poisoning deaths of undetermined intent. Some seasonal variation may have occurred in accidental poisoning deaths, but low numbers made this finding statistically non-significant. Suicides by poisoning showed yet a different pattern and may have been caused by seasonal variation in the incidence of depressive illnesses.

Following their study, little research was undertaken by ONS or its predecessors on seasonality until the mid-2000s. Johnson et al. (2005) found that opioid-related deaths in England and Wales were highest on Saturdays in the period 1993-2002. However, this pattern seemed to vanish shortly thereafter (Morgan et al., 2006). Suicides by intentional drug overdose peaked on 1 January (New Year's Day) in England and Wales (Johnson et al., 2005). Higher rates of intentional overdose deaths in England and Wales (Johnson et al., 2005) and suicides in England (Cavanagh et al., (2016) were found to occur on Mondays. This is a period when individuals are transitioning from the weekend to the working week (Han et al, 2022).

The author's recent research (see Chapter 2) on drownings in Scotland involving drugs (conducted during the course of this PhD programme) found that such deaths are fewer during the 'spring' and 'summer' months March to August compared with the 'autumn' and 'winter' months September to February. This difference is statistically significant (Corkery et al., 2023). Lewer et al. (2023) used ONS data to look at season, weekday, week-of-month and public holiday patterns in drug poisoning deaths in England and Wales between 1993 and 2018. Their main finding was that the daily rate of death was highest in Spring, that this pattern had only emerged in the decade since 1998 and was only present for opioid-related deaths. The daily

death rate at New Year was 1.28 times higher than on non-holidays, but only for non-opioid related deaths. The daily death rate was at its highest on Saturdays, in line with earlier UK (Johnson et al., 2005) and USA studies (Goedel et al., 2019). Lewer et al. (2023) found no evidence that the week-of-month caused variation in the daily death rate. They concluded that their findings suggest a role for external triggers in drug poisoning deaths but noted that "these seasonal variations are small compared with long-term increases in drug-related deaths" (Lewer et al., 2023).

Spatial or geographical patterns have been examined in the past, see, for example Tables 5.1 and 5.2: drug misuse (HSQ 11; Griffiths et al., 2008b); antidepressant drugs (HSQ 27); occupation and geography (Population Trends 80). Subsequently, these have become part of the annual analyses published by ONS and its other UK counterparts. In the most recent statistics, it was reported that the North East region of England had had the highest death rate for 10 (ten) consecutive years (ONS, 2023). Congdon (2019) looked at a range of geography-related issues to try and understand differences in patterns of drug-related deaths and suicide in England, including deprivation, fragmentation and rurality. The other GMRs also publish geographical breakdowns of death rates, etc. An examination of such patterns and their possible causes would provide ample material for further studies by the author and his research group.

ONS and its predecessors occasionally published information regarding temporal patterns or trends for specific (classes of) substances/drugs, e.g., paracetamol (HSQ 7); antidepressants (HSQ 23). (See Tables 5.1 and 5.2 for further details.) In due course, trend data for specific classes/substances became part of the annual statistical analyses, e.g., opioids, methadone, cocaine, NPS (e.g., ONS, 2023). Such trend data are presented earlier in this chapter (Figures 6.30 to 6.34).

ONS data have also been used to examine both temporal trends and geographic aspects of so-called 'deaths of despair' (suicide, drug poisoning, and alcohol-related conditions). Augarde et al. (2022) found that whilst such deaths had increased in England and Wales in the 2001-2016 timeframe, there was limited evidence of commonalities in the epidemiology of the three different components.

Factors influencing patterns on index substances and classes of drug deaths

As indicated in previous paragraphs, understanding and explaining the overall patterns in deaths involving particular index substances or drug classes is a very complex process, given that the patterns are constantly changing over time, across geographies, and populations.

Different types of factors or characteristics at an individual level (e.g., socio-demographics, substance use history, physical and mental health history, genetics, etc.) as well as at a social level (e.g., drug prescribing, drug laws and controls, policy (see Chapters 8 to 12); service provision, education, social *mores*, economic drivers (availability, price, purity - see Chapters 8 to 12); pandemics; etc.) can combine in a myriad of different ways to both cause and prevent death.

An overview of some of the factors available in the GMR published statistics is now presented. However, other factors can only be examined from an exploration of data from SMRs, such as NPSAD. See Chapter 7 for a more detailed description of risk factors, including: marital status, living arrangements, ethnicity, employment status, deprivation, and prescribed psychoactive substances.

Gender and age

Unfortunately, due to differences in the definitions of death and age-groups across the three UK GMRs, it is not possible to make detailed comparisons between all parts of the UK. However, as with drug use generally, the majority of individuals dying in the UK of drug-related deaths are males. For example, with regard to deaths caused by drug poisonings registered in 2022 in England and Wales, the overall rate was 84.4 deaths per million population (4,907 deaths); among males the rate was 114.3 (3,240 deaths) compared to 55.8 (1,667 deaths) for females; the ratio of male to female deaths was 2.00:1 (ONS, 2023). The corresponding ratio in Northern Ireland was 2.28:1 (NISRA, 2024). In Scotland, there were 1.93 times more males than females whose drug misuse deaths were registered in 2022 (NRS, 2023).

At the UK level, it is possible to present information using the European DRD definition for the period 1996-2017 on the mean age at death of males and females, based on data published in the EMCDDA's annual statistical bulletins and on unpublished data prepared by the author for the UK's annual returns to the agency. Although unpublished data are available to the author using the drug-poisoning and drug misuse death definitions, these only cover part of the above period. Figure 6.35 shows that over the course of these two decades, the mean age at death for both males and females rose very rapidly, for males from 31.0 to 42.0 years and for females from 34.3 to 45.2 years. The profile of these increases appears to be in step with each other.

According to the ONS (2023), mortality rates, from drug poisonings registered, rose for both males and females in England and Wales over the period 1993-2022, although the rate for males peaked in 2021. As can be seen from Table 6.8, in both countries, males accounted for slightly over two-thirds of such deaths registered in 2022. Similar increases have occurred for drug misuse deaths over the same period, with males accounting for around seven out ten deaths in 2022 in both countries.

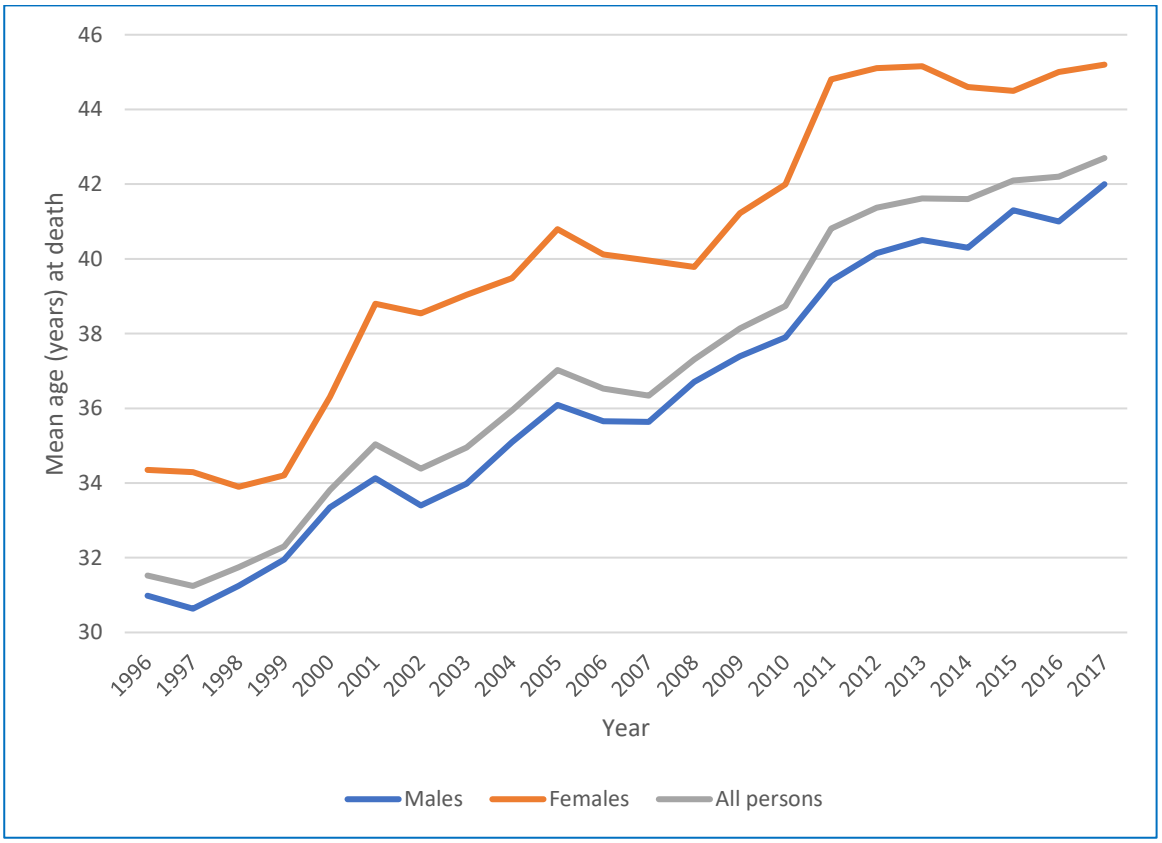

Figure 6.35: Mean age (years) at death, using EMCDDA DRD definition, by gender and year, United Kingdom, 1996-2017

Sources: EMCDDA annual reports

Table 6.8: Number (%) of drug-poisoning and drug misuse deaths by gender and age-groups registered in England and Wales, 2022

	Drug poisoning						*Drug misuse*					
	England			*Wales*			*England*			*Wales*		
	Gender			*Gender*			*Gender*			*Gender*		
Age-group (years)	*Male*	*Female*	*All*	*Male*	*Female*	*All*	*Male*	*Female*	*All*	*Male*	*Female*	*All*
Number												
<20	41	28	69	2	2	4	27	17	44	1	1	2
20-29	291	122	413	30	7	37	212	65	277	24	7	31
30-39	692	299	991	53	21	74	465	173	638	38	13	51
40-49	926	434	1,360	76	29	105	632	282	914	51	18	69
50-69	929	527	1,456	47	29	76	625	290	915	32	11	43
>69	136	147	283	8	14	22	59	59	118	4	5	9
All ages	3,015	1,557	4,572	216	102	318	2,020	886	2,906	150	55	205
%												
	Gender		*Age*	*Gender*		*Age*	*Gender*		*Age*	*Gender*		*Age*
	Male	*Female*		*Male*	*Female*		*Male*	*Female*		*Male*	*Female*	
<20	59.42	40.58	1.51	50.00	50.00	1.26	61.36	38.64	1.51	50.00	50.00	0.98
20-29	70.46	29.54	9.03	81.08	18.92	11.63	76.53	23.47	9.53	77.42	22.58	15.12
30-39	69.83	30.17	21.68	71.62	28.38	23.27	72.88	27.12	21.95	74.51	25.49	24.88
40-49	68.09	31.91	29.75	72.38	27.62	33.02	69.15	30.85	31.45	73.91	26.09	33.66
50-69	63.80	36.20	31.85	61.84	38.16	23.90	68.31	31.69	31.49	74.42	25.58	20.98
>69	51.94	48.06	6.19	36.36	63.64	6.92	50.00	50.00	4.06	44.44	55.56	4.39
All ages	65.94	34.06	100.00	67.92	32.08	100.00	69.51	30.49	100.00	73.17	26.83	100.00

Source: Table 2, ONS (2023)

In Scotland, deaths involving males have outnumbered those of females since 1996. Males accounted for 66% of drug misuse deaths in 2022 (Table 6.9). In that year, the age-standardised mortality rates (deaths per 100,000 population) were: males 26.6 (35.8 in 2021), females 13.3 (14.7 in 2021). This ratio for males to females was 2.0 (2.4 in 2021), compared to more than 4 in the early 2000s (NRS, 2023).

Table 6.9: Number (%) of drug misuse deaths by gender and age-groups, registered in Scotland, 2022

	Number			*%*		
	Gender			*Gender*		*Age*
Age-group (years)	*Male*	*Female*	*All*	*Male*	*Female*	
<25	44	18	62	70.97	29.03	5.90
25-34	90	46	136	66.18	33.82	12.94
35-44	209	115	324	64.51	35.49	30.83
45-54	227	109	336	67.56	32.44	31.97
>54	122	71	193	63.21	36.39	18.36
All ages	692	359	1,051	65.84	34.16	100.00

Source: NRS (2023)

In 2022, the age-standardised mortality rate for males using the drug-related death definition registered in Northern Ireland was 11.8 (17.3 in 2021) compared to 5.0 (6.0 in 2021) for females; the respective rates using the drug misuse definition were 9.6 (14.6 in 2021) and 4.1 (4.4 in 2021). For both genders, these rates increased markedly over the past decade: the drug-related death rates in 2011 stood at 6.9 for males and 4.0 for females; the corresponding drug misuse rates were 4.4 and 2.2 (NISRA, 2024).

Turning to age at death, in terms of 2022 registrations in England and Wales, drug misuse death rates were highest in the 40-49 years age-group (ONS, 2023). This age-group is part of the cohort born between [1965] and 1980 (essentially the 1970s), often referred to as ‘Generation X’. Over time, this cohort has consistently exhibited a higher mortality rate than other cohorts. Table 6.8 also reflects the fact that, for deaths registered in 2022, the highest number of deaths for drug misuse in Wales was in the 40-49 age-group, whereas in England this age-group accounted for almost the same number as in the 50-59 age group. In terms of drug poisoning deaths, the 40-49 years age-group accounted for most deaths in Wales, whereas in England it was the next age-group (50-59 years) that accounted for most deaths using this definition.

In Scotland. the average age at death from drug misuse increased from 32 years in 2000 to 45 in 2022 (NRS, 2023). This phenomenon is reflected by the fact that those aged < 35 years accounted for 68% of such deaths in 2000 but by 2022 this proportion had fallen to 19%. By contrast, the proportions for those in the 35-54 age-groups went from 29% to 63% of drug misuse deaths.

In Northern Ireland, using the drug-related death definition, the age-group accounting for most deaths registered in 2022 was the 25-34 years one (Table 6.10). This was true for most of the

previous decade, apart from 2013 and 2014 when the 35-44 years age-group accounted for most deaths (NISRA, 2024).

Table 6.10: Number (%) of drug-poisoning deaths by gender and age-groups registered in Northern Ireland, 2022

	Number			*%*		
	Gender			*Gender*		*Age*
Age-group (years)	*Male*	*Female*	*All*	*Male*	*Female*	
<25	11	7	18	61.11	38.89	11.69
25-34	38	8	46	82.61	17.39	29.87
35-44	27	13	40	67.50	32.50	25.97
45-54	17	6	23	73.91	26.09	14.94
55-64	9	10	19	47.37	52.63	12.34
>64	5	3	8	62.50	37.50	5.19
All ages	107	47	154	69.48	30.52	100.00

Source: NISRA (2024)

Combining the age and gender parameters, we can see that in terms of 2022 death registrations, in England, using the drug-poisoning definition, most males were in the 50-59 years age-group whereas in Wales it was the 40-49 years age-group which accounts for most males. For females, most were in the 50-69 years age-group in England, whereas in Wales the same number of deaths occurred in the 40-49 and 50-59 years age-groups. These patterns were slightly different for the drug misuse definition. Most males were in the 40-49 years age-group in both England and Wales, as were females in Wales; however, in England most females were in the 50-59 years age-group.

Individuals aged 45-54 years accounted for most male deaths in Scotland using the drug-misuse definition in 2022; for females, the dominant age-group was 35-44 years. In Northern Ireland in 2022, most male drug-poisoning deaths were accounted for by those in the 25-34 years age-group, whereas most female deaths occurred in the 35-44 years age-group.

A comparison of age-standardised mortality rates for deaths registered in England and Wales during 2022 shows that males tend to have a higher rate than females in most specific drug types/classes (see Table 6.11). The proportions are closest for fentanyl, paracetamol and antidepressants; the rates are slightly higher for females for the latter two drugs. The rates for males are typically about twice that of females; however, for stimulants (excluding ecstasy) and NPS the rates are three to four times higher.

Table 6.11: Age-standardised mortality rates for selected substances by gender, England and Wales, 2022

	Male		*Female*		*All persons*		*Male:female ratio for mortality rate*
Drug/drug class	*Number of deaths*	*Mortality rate*	*Number of deaths*	*Mortality rate*	*Number of deaths*	*Mortality rate*	
Any opiate*	1,535	54.3	726	24.5	2,261	39.1	2.22:1
Heroin/morphine	884	31.3	372	12.6	1,256	21.8	2.48:1
Methadone	456	16.3	184	6.3	640	11.2	2.59:1
Tramadol	121	4.3	102	3.4	223	3.8	1.26:1
Codeine**	101	3.5	87	2.9	188	3.2	1.21:1
Dihydrocodeine**	75	2.6	36	1.2	111	1.9	2.17:1
Fentanyl	32	1.1	25	0.8	57	1.0	1.38:1
Cocaine	672	23.5	185	6.3	857	14.7	3.73:1
Any amphetamine	140	4.9	49	1.6	189	3.2	3.06:1
Ecstasy/MDMA	37	1.2	14	0.5	51	0.9	2.40:1
Cannabis	21	0.7	11	0.4	32	0.5	1.75:1
New Psychoactive Substance	192	6.7	49	1.6	241	4.1	4.19:1
Any benzodiazepines	365	12.9	144	4.9	509	8.8	2.63:1
Zopiclone/Zolpidem	98	3.5	83	2.7	181	3.1	1.30:1
Any antidepressant	242	8.5	297	10.0	539	9.2	0.85:1
Any antipsychotic	84	3.0	63	2.1	147	2.5	1.43:1
Paracetamol	117	4.2	144	4.7	261	4.5	0.89:1
All drug poisonings***	3,240	114.3	1,667	55.8	4,907	84.4	2.05:1
Notes: * Includes unspecified opiates and excludes paracetamol compounds; ** Not from compound formulation. *** Rows should not be added together.							

Source: Table 4, ONS (2023)

Deprivation

Deprivation emerged over recent decades as an aspect that the GMRs have explored in explaining regional differences (see Chapter 7 for information on this topic from SMRs). For instance, Romeri et al. (2006) found that deprivation In England and Wales was associated with increased all-cause mortality rates for both males and females, especially the former. Deprivation can cause differences between different part of the UK in respect of drug use (Parkinson et al., 2018) and drug deaths (Schofield et al., 2016; Walsh et al., 2021).

Looking at deprivation quintiles based on the Scottish Index of Multiple Deprivation (Scottish Government, 2020), the NRS (2023) reported that drug misuse death rates in 2022 were 15.9 times higher in the most deprived compared to the least deprived areas (52.4 vs. 3.3 deaths per 100,000 population). In the early 2000s the differential was about ten times.

Using the English Index of Multiple Deprivation (MHCLG, 2019), ONS (2023) reported that for 2021 drug poisoning death registrations, the rate for males in the most deprived areas of England was 242.1 vs. 40.8 in the least deprived areas; for females, the corresponding rates were 115.4 vs. 26.1. These differentials are 5.9 for males and 4.4 for females.

Using the Welsh Index of Multiple Deprivation (StatsWales, 2019), ONS (2023) noted for drug poisoning deaths registered in Wales in 2020-2022, the rate for males in the most deprived areas was 281.4 vs. 55.1 in the least deprived areas; for females, the corresponding rates were: 101.2 vs. 29.2 These differentials are 5.1 for males and 3.5 for females.

Using the Northern Ireland Multiple deprivation Measure (NISRA, 2017), NISRA (2024) also report that the areas of highest deprivation continue to experience the highest number of drug-related and drug-misuse deaths. In the most deprived areas, the number of drug-related deaths registered in 2018-2022 was 431 vs. 74 in the least deprived areas; the numbers for drug-misuse deaths were 360 vs. 58, respectively.

Manner, intent, and mechanism(s) of death

As previously mentioned in Chapter 3, the UK GMRs code the information on the Medical Certificate of Cause of Death (MCCD) using ICD codes (WHO, 1978, 1992). Typically, the published statistics only present information on the underlying (distal) cause of death, i.e., the incident which started the train of events that eventually led to death, rather than the immediate (proximal) event.

The reader is reminded that there have been ongoing changes during the last half century in opinions about how to classify suicide, i.e., whether deaths whose intent is unclear/unknown should be regarded as (potential) suicides or as accidental fatalities (see, for example, Beck et al., 1975; Katz et al., 2016; Silverman and De Leo, 2016). The author's position is that, at a high level, it is useful to maintain the distinctions that have been made in the published GMR data. At a lower level, where more granularity is needed, then it is necessary to use SMR databases to ascertain with more accuracy the potential intention(s) of the individual decedent. This can be done by examining the documentary evidence collected as well as interviewing witnesses, family members and friends, i.e., using a 'psychological autopsy' approach (Shneidman, 1981).

Information on how the UK GMRs classify the underlying cause of death is given in Chapter 2 (Tables 2.1 and 2.2). It is reproduced here for convenience (Tables 6.12 and 6.13).

Table 6.12: International Classification of Diseases codes used for ONS 'standard' definition of drug poisoning deaths

Description	ICD-9 codes	ICD-10 codes
Mental and behavioural disorders due to drug use (excluding alcohol and tobacco)	292, 304, 305.2–305.9	F11–F16, F18–F19
Accidental poisoning by drugs, medicaments, and biological substances	E850–E858	X40–X44
Intentional self-poisoning by drugs, medicaments, and biological substances	E950.0–E950.5	X60–X64
Assault by drugs, medicaments, and biological substances	E962.0	X85
Poisoning by drugs, medicaments, and biological substances, undetermined intent	E980.0–E980.5	Y10–Y14

Table 6.13: Cause of death categories included in the ONS 'drug misuse' definition

(a) deaths where the underlying cause of death has been coded to the following categories of mental and behavioural disorders due to psychoactive substance use (excluding alcohol, tobacco, and volatile solvents):	
(i)	Opioids (F11)
(ii)	Cannabinoids (F12)
(iii)	Sedatives or hypnotics (F13)
(iv)	Cocaine (F14)
(v)	Other stimulants, including caffeine (F15)
(vi)	Hallucinogens (F16)
(vii)	Multiple drug use and use of other psychoactive substances (F19)
(b) deaths coded to the following categories and where a drug controlled under the Misuse of Drugs Act 1971 was mentioned on the death record:	
(i)	Accidental poisoning by drugs, medicaments, and biological substances (X40–X44)
(ii)	Intentional self-poisoning by drugs, medicaments, and biological substances (X60–X64)
(iii)	Poisoning by drugs, medicaments, and biological substances, undetermined intent (Y10–Y14)
(iv)	Assault by drugs, medicaments, and biological substances (X85)
(v)	Mental and behavioural disorders due to use of volatile solvents (F18)
Notes	
1: Deaths coded to opiate abuse which resulted from the injection of contaminated heroin have been included in the indicator. This differs from the approach taken in Scotland, where these deaths have been excluded. This is because the General Register Office for Scotland (GROS) is able to identify deaths which occurred as a result of the use of contaminated heroin, whereas in England and Wales, these deaths cannot be readily identified. In practice, in England and Wales, they will only be included where the drug was mentioned on the death record and the death was coded to one of the ICD codes on the ONS database of drug-related poisonings and not to an infection code.	
2: Specific rules were adopted for dealing with compound analgesics which contain relatively small quantities of drugs listed under the Misuse of Drugs Act, the major ones being dextropropoxyphene, dihydrocodeine and codeine. Where these drugs are mentioned on a death record, they have been excluded if they are part of a compound analgesic (such as co-proxamol, co-dydramol or co-codamol) or cold remedy. Dextropropoxyphene has been excluded on all occasions, whether or not paracetamol or a compound analgesic was mentioned. This is because dextropropoxyphene is rarely, if ever, available other than as part of a paracetamol compound. However, codeine or dihydrocodeine mentioned alone were included in the indicator. This is because they are routinely available and known to be abused in this form. This approach is the same as that taken by GROS.	
3: ICD-10 codes are given in brackets. Information ICD-9 codes are in Health Statistics Quarterly 13. Available at: www.ons.gov.uk/ons/rel/hsq/health-statistics-quarterly/no--13--spring-2002/index.html	
Adapted from ONS (2021)	

Figures 6.36 to 6.38 present breakdowns by underlying cause for drug poisoning deaths in England, Wales and Northern Ireland, respectively; such information is not published for Scotland. ONS presents combined data for suicides and deaths of undetermined intent.

The beginning of 2011 saw the implementation by the UK GMRs of updated WHO rules for identifying underlying cause of death. This did not have much of an impact on the way the overall number of drug poisoning and drug misuse deaths were calculated. However, these changes did result in a discontinuity between 2010 and 2011 which is visible in the following data visualisations (Figures 6.36 - 6.42). The main effect was a sudden drop in the number of deaths ascribed to 'Mental and behavioural disorders due to drug use'. This was offset by an increase in deaths from 'accidental poisoning'.

In England, the number of registered deaths due to mental and behavioural disorders rose steadily from 1993 to 1999 and remained stable until 2006, followed by a fall over the next few years (Figure 6.36). Suicides and deaths of undetermined intent appear to have remained stable from 1993 to the mid-2000s when they seem to have fallen but have since remained stable. Most of the overall increase in drug poisoning deaths appears to have been driven by more accidental poisoning fatalities occurring from about 2007-2008. Ignoring the changes in WHO coding rules implemented in 2011, it is likely that much of this increase is due to greater use of stimulants including many NPS, which started to emerge around this time, and cocaine. (These relationships are examined in Chapters 8 to 12.) Deaths resulting from assault and homicide are relatively rare.

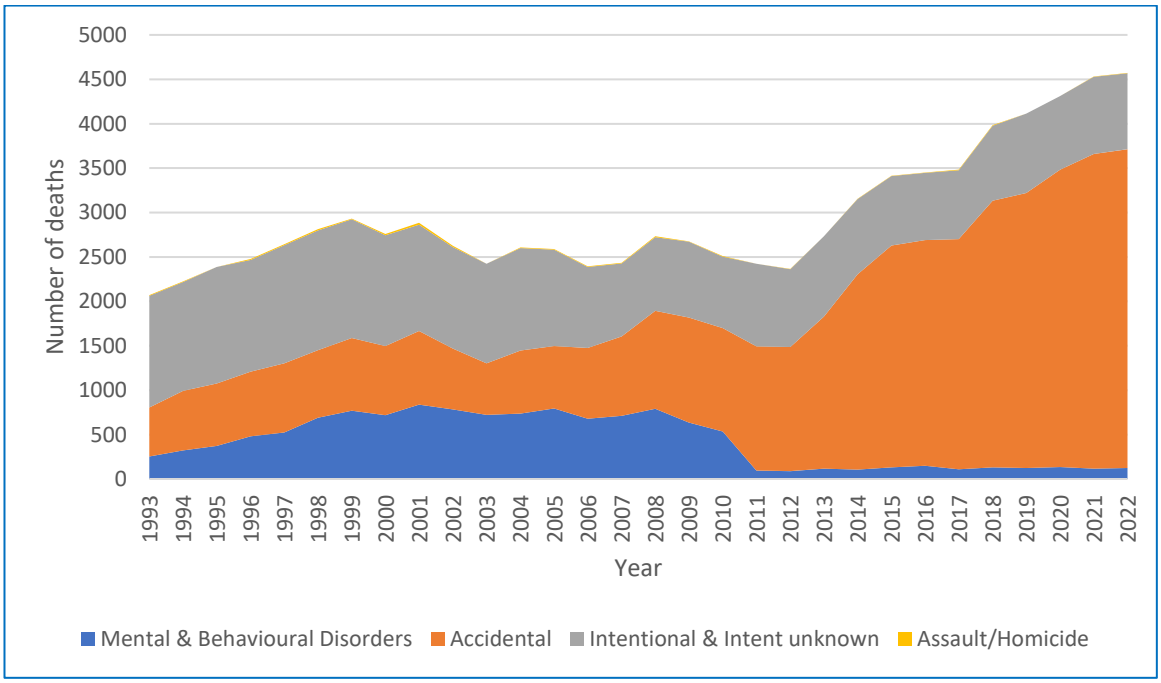

Figure 6.36: Drug poisoning deaths, by underlying cause, England, 1993-2022

Source: ONS (2023)

As the number of deaths is far lower in Wales than in England, the relative importance of trends is more difficult to interpret; the same observation can also be applied to Northern Ireland. The increase in deaths ascribed to mental and behavioural disorders was more gradual in Wales and initially peaked about 2001, remaining at this level until about 2010 (Figure 6.37). Both accidental deaths and suicides/undetermined intent deaths also increased in number, with some year on year variation, over the same period. However, since then, the number of suicides/deaths of undetermined intent have remained stable. The dip in accidental deaths in 2019-20 may be due to the impact of the Covid-19 pandemic. As with England, most of the increases in drug poisoning deaths appear to have been driven by rising accidental deaths, probably driven by the factors mentioned above for England. As elsewhere in the UK, deaths from assault or homicide are rare in Wales.

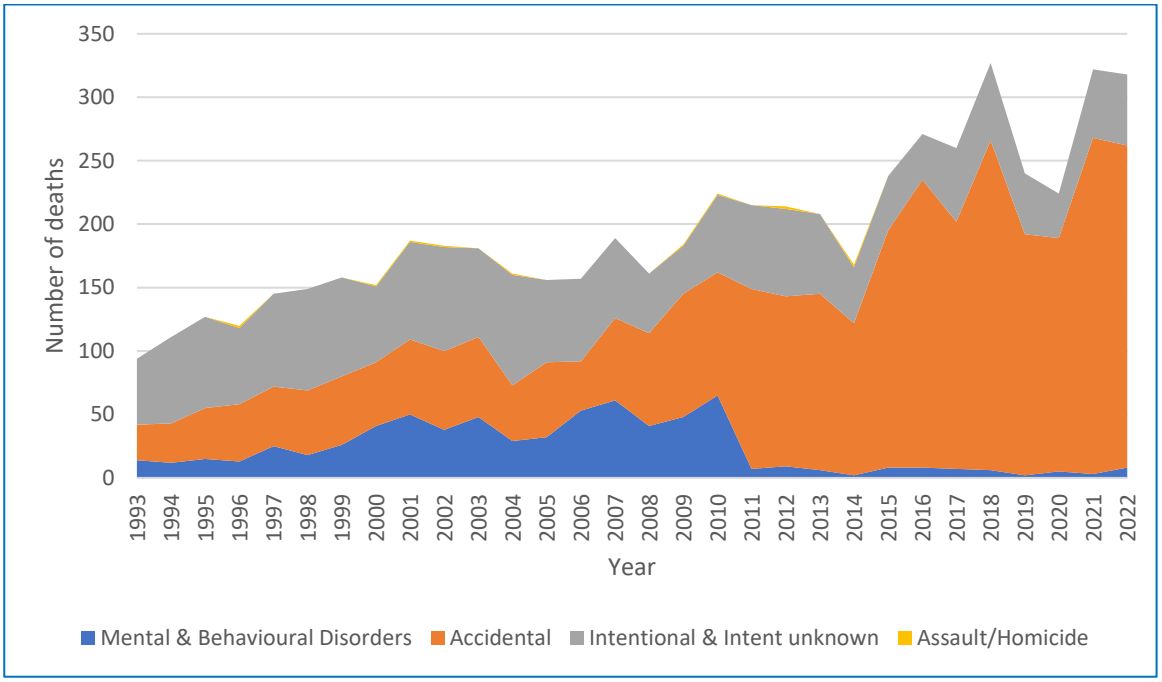

Figure 6.37: Drug poisoning deaths, by underlying cause, Wales, 1993-2022

Source: ONS (2023)

The picture in Northern Ireland is even more complex (Figure 6.38). The mental and behavioural disorders and the assault and homicide categories have accounted for very few deaths in this part of the UK. The change in WHO coding rules seems to have no effect. Suicides appear to have occurred at higher levels in the period up to 2006 than afterwards, or at least until the last few years - especially during the peak of the Covid-19 pandemic. Deaths of undetermined intent were more common in the period 2009-2014. Taken together, suicides and deaths of undetermined intent accounted for most deaths until 2014. The increase in deaths observed from 2015 is almost entirely driven by accidental deaths.

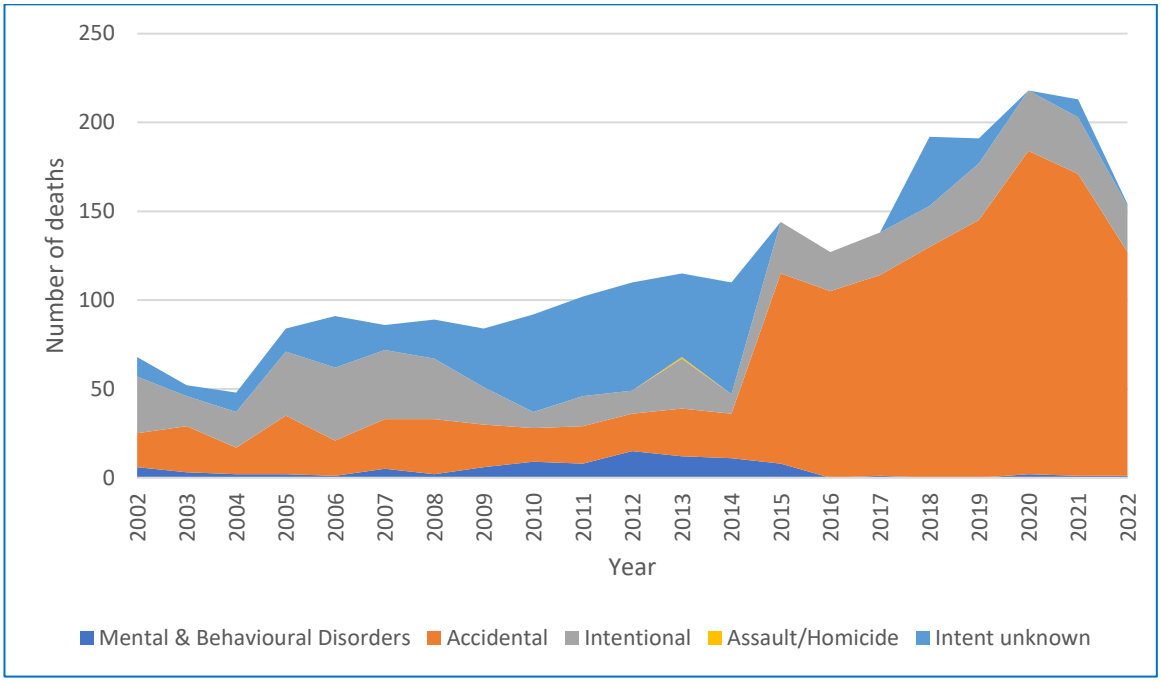

Figure 6.38: Drug poisoning deaths, by underlying cause, Northern Ireland, 2002-2022

Source: NISRA (2024)

Figures 6.39 to 6.42 provide breakdowns by underlying cause for drug misuse deaths in the four constituent parts of the UK. ONS presents combined data for suicides and deaths of undetermined intent.

The trends in England (Figure 6.39) are even clearer for this definition of drug-related death. Most of the increase in numbers of deaths to 2001 is accounted for by mental and behavioural disorders, their level remaining stable to about 2008. Around this time, there is an increase in accidental deaths which has continued to the present day. The WHO ICD coding rule changes in 2011 also contributed to this shift. Suicides and deaths of undetermined intent have remained stable across the period examined here. Deaths resulting from assault or homicide account for only a handful of deaths across the entire period.

Almost identical patterns can be observed for Wales (Figure 6.40), although the absolute numbers are considerably lower. Thus, the same comments as for England should be applied here. The observations made above about the dip in accidental death registrations in 2019-20 being perhaps due to the impact of the Covid-19 pandemic apply here also.

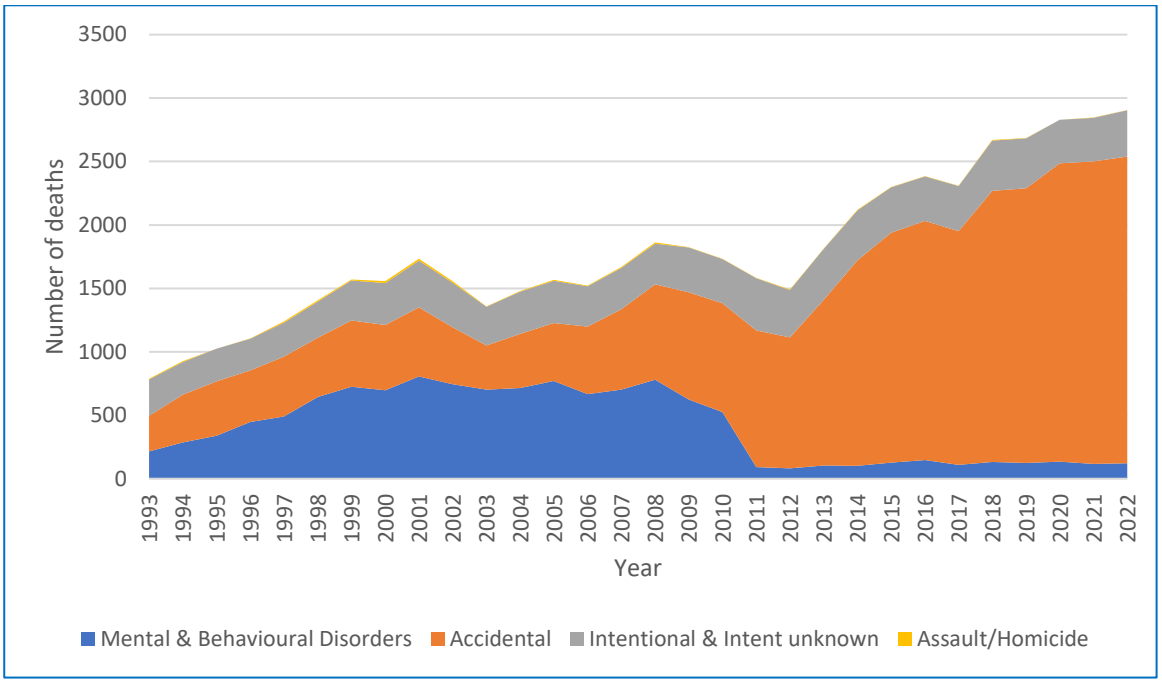

Figure 6.39: Drug misuse deaths, by underlying cause, England, 1993-2022

Source: ONS (2023)

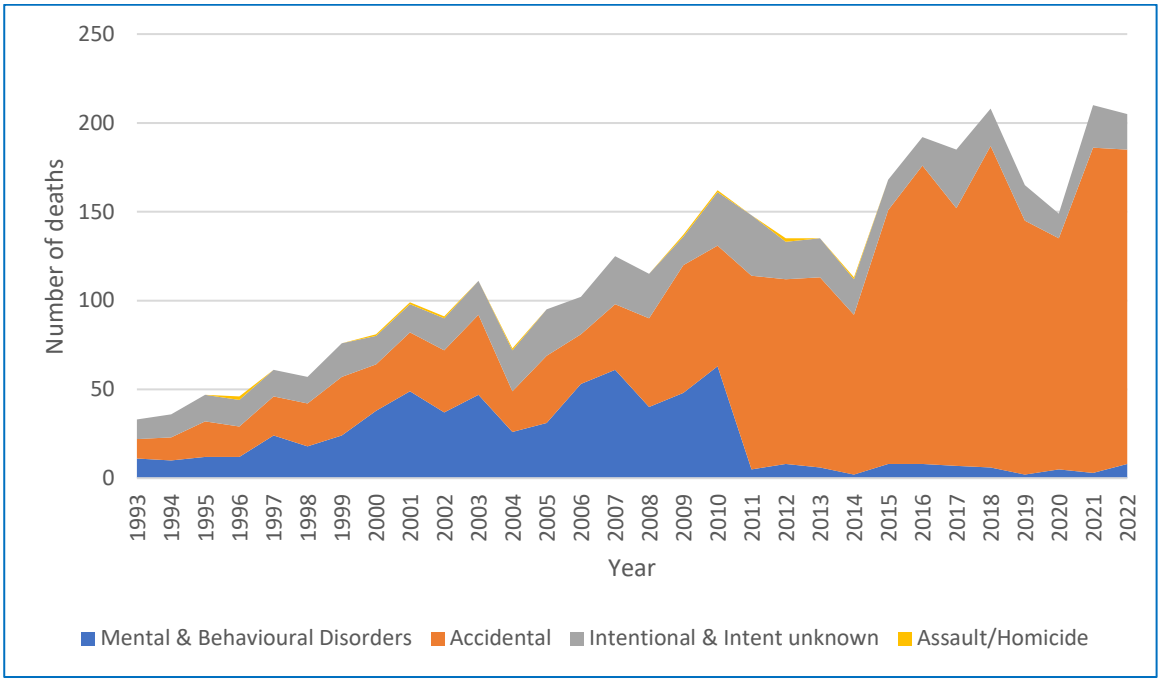

Figure 6.40: Drug misuse deaths, by underlying cause, Wales, 1993-2022

Source: ONS (2023)

Overall, in Northern Ireland there is a much smoother increase in the number of drug misuse deaths over time (Figure 6.41). Deaths due to mental and behavioural disorders play less of a role than in other parts of the UK, and do not seem to have been affected by the changes in WHO coding rules. In the period up to 2014, most deaths were classified as suicides or deaths of undetermined intent, mostly the latter between 2009 and 2014. As was observed for drug poisoning deaths in Northern Ireland, there was a parallel increase in accidental deaths from 2015 to 2020, since when there has been a decline. Such deaths have driven the rises and falls since 2015. The contribution to the overall picture made by assaults and homicides is negligible.

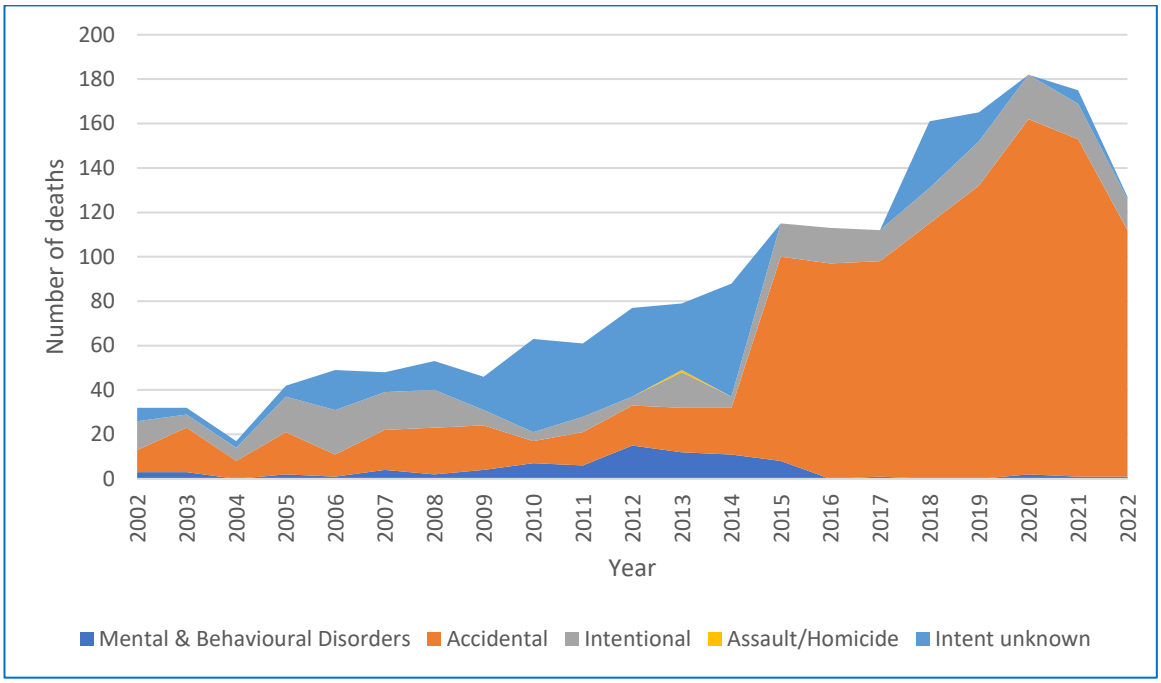

Figure 6.41: Drug misuse deaths, by underlying cause, Northern Ireland, 2002-2022

Source: NISRA (2024)

Scotland displays yet another, very different, pattern in its drug misuse deaths (Figure 6.42). Most deaths up to 2010 were ascribed to mental and behavioural disorders, followed by deaths of undetermined intent and suicides. Suicides increased in number between 2007 and 2014 but have since remained stable at lower levels, as have deaths of undetermined intent. Accidental deaths played a very small role until 2008-2009. One can assume that the increase in accidental deaths in 2011 is due to the ICD coding rules changes since the overall level of such deaths remained stable until 2013. The following years have seen increasing numbers of accidental deaths which, in turn, has driven the overall increase in drug misuse deaths. The actual components of this change need further exploration, for example, the emergence of 'street benzos' and/or increased use of cocaine (see Chapters 8 to 12). The overall fall in DRDs registered in 2021-22 would appear to be as result of fewer 'street' benzodiazepines being

implicated in accidental deaths. Assaults/homicides account for very small numbers of deaths in Scotland.

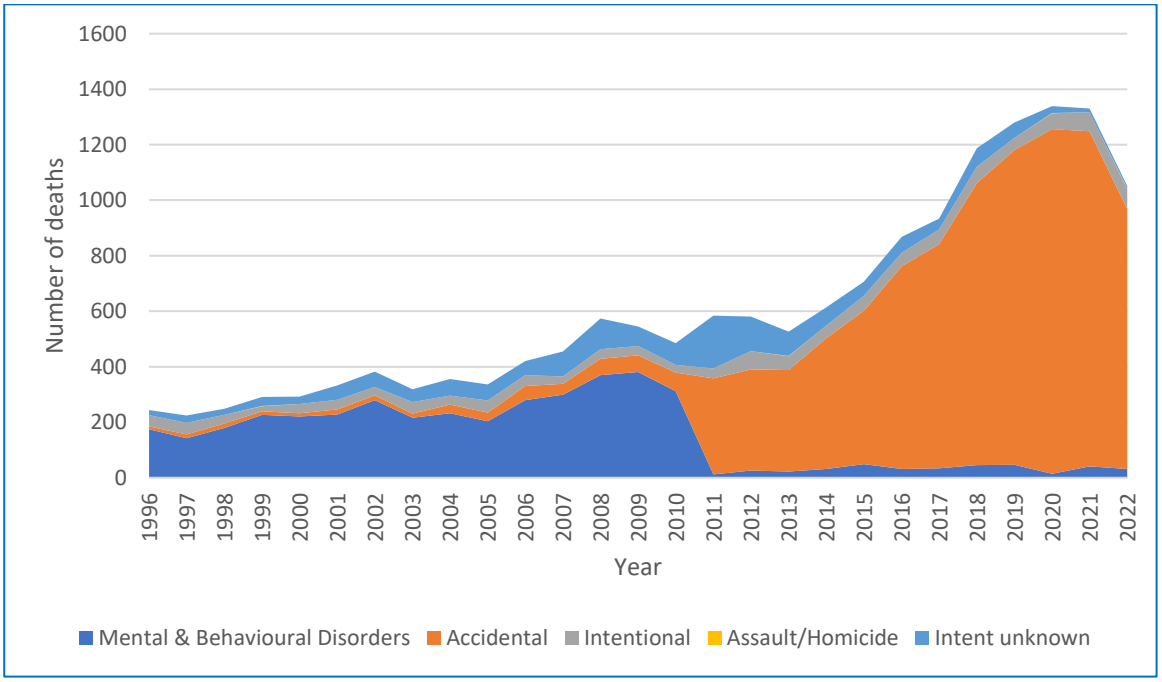

Figure 6.42: Drug misuse deaths, by underlying cause, Scotland, 1996-2022

Source: NRS (2023)

Since the cause of death fields in the MCCDs do not always specify information on mechanism(s), or, if they do, inconsistently, it is necessary to look at SMR data for such detailed information via autopsy/postmortem reports. This is equally true for understanding intent and the relationship between that and the means used to cause death.

There are a range of factors which can influence the patterns of death examined at a macro level above. Unfortunately, UK GMRs lack the required detailed information on them, so SMRs become an important means of understanding the interplay between factors at a micro level, where granularity can be observed and explored. These can help to profile ‘at risk’ groups (Chapter 7) and understand wider connections to external influences, such as the COVID-19 pandemic, ‘drug market’ forces, drug policy and law, etc. (Chapters 8 to 12).

Chapter overview

This chapter has outlined and explored the changes in UK drug-related deaths over the past three decades from several angles: socio-demographic, spatial; temporal; toxicological (drug involvement); and intention This has been at a high or macro level, relying on the published outputs of the General Mortality Registers. Comparisons have been made, where possible, between the constituent parts of the UK; differences as well as similarities have been noted and explored.

The limitations of the published data have been noted in respect of gaining an in-depth understanding of all the factors at work and the interplay between them. For this, it is necessary to drill down into the more comprehensive and detailed information available to Special Mortality Registers. The next chapter (Chapter 7) looks at the profiling of 'at risk' groups, and Chapters 8 to 12 explore the relationships between drug-related deaths and other drug indicators.

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CHAPTER 7 – ANALYSING SPECIAL MORTALITY REGISTER DATA TO IDENTIFY AND PROFILE 'AT RISK' GROUPS

"Little research has been conducted on risk factors for fatal accidental overdose, in clinical or other settings. Much of the available data come from surveillance systems …, which have limited data on the characteristics of individuals who died from overdose. …
Although understanding risk factors for accidental overdose among chronic drug users is important, questions regarding risk for accidental overdose in broader clinical populations remain unanswered."
Bohnert et al. (2012)

"Assessing the mortality rate in a population which in the literature is characterized as "hidden", and where maybe just a minority of the abusers establish contact with a drug surveillance system, is difficult. Predicting future mortality rates and future proportion of overdose deaths for such a population is clearly no less difficult. The mortality rate is affected by complex set of factors. There are factors with multiplicative effects and there are factors counteracting each other's effects. To understand such a complexity causal conceptualization is needed. Furthermore, if we at some time ahead are to be able to in some extent to foresee changes in mortality, not only reliable data of the drug abuse population must be available, the model for prediction must include parameters expressing the actual causal processes."
Ødegård et al. (2007)

The previous chapter (6) provides high or macro level information from UK General Mortality Registers (GMRs) on drug-related deaths (DRDs) and insights into their nature and extent. This chapter (7) uses findings from Special Mortality Registers (SMRs) to provide low level explorations of the more detailed data on a wider range of information and how they can assist in identifying those groups 'at risk' of a drug-related death.

In the UK context the main SMRs that facilitate such explorations are the National Programme on Substance Abuse Deaths (NPSAD) and the Scottish Drug-Related Deaths Database; see Chapters 3 and 5 for full details of the variables and parameters that they collect. The main factors explored in this chapter include: demographic; social; economic, health (physical and mental); and substances.

This chapter provides an insight into how such information can provide not only granularity to some of the phenomena described in GMR publications but also understand other factors to which such sources do not have access.

The following analyses are a combination of *ad hoc* literature reviews on specific factors, secondary analyses of existing published GMR data, and reference to relevant studies, using SMRs and other resources, undertaken by the author and colleagues in the past and for the purposes of his programme of research.

Defining ‘at risk’ groups

Such groups can include both those with known health problems as well as those who are apparently healthy. Alternatively, the term ‘population-at-risk’ can be applied to groups of individuals prone or susceptible to the index event of interest (e.g., in this context, a drug-related death) at a specific point in time or occurring during a particular timeframe. It is important to be clear as to what case definitions are being used by the sources being used as these can differ, see, for example, Chapter 2 for the range of ways in which drug-related deaths can be construed.

Approaches to identifying ‘at risk’ groups

The basic aim is to try and determine what pre-disposing factors, or combinations thereof, influence the likelihood of an index event occurring. In other words, what characteristics (personal and/or situational) lead to a higher risk of an event occurring. Usually, from an epidemiological perspective this would mean looking at measures such as Standard Mortality Ratios, Years of Lives Lost, case fatality rates, and other types of statistical approaches.

However, whilst GMRs can do this at a higher level (see Chapter 6), they can only do so for a limited range of factors. Evaluation of (potential) causal relationships between certain socio-demographics, drug-types, mode of drug administration, *loci* of exposure and death, and death mechanisms is a more complex undertaking. Chapters 8 to 12 look at statistical relationships between high-level factors, but what follows here is a consideration of ‘profiling’ potential ‘at risk’ groups/populations.

Typically, the approach to identifying such groups has involved the use of retrospective cohort studies of those in treatment or known to treatment services, e.g., the Home Office Addicts Index (see Chapter 2) rather than the general population. Limitations of this approach include: loss to follow-up of initial recruits; what information was included on admission to the cohort; subjects are not representative of the general population, etc.. Other considerations include the length of time of reporting of cause of death to GMRs (e.g., following inquests, criminal cases, etc.), and what causes of death were screened for inclusion.

Variables typically looked at included: age, gender, length of opiate/opioid drug use, age of first drug use, injecting status, viral status, referral to treatment, etc. (for example, Ødergård et al., 2007; McDonald et al., 2021). Some studies have also used: length of injecting use, regular and problematic drug use, polydrug use, presence of clinically significant psychopathology, and suicide history (Ødergård et al., 2007; Darke et al., 2011; Stockings et al., 2019). Few studies,

such as Andersen et al., 2024), have looked at the setting of use, living arrangements, or the presence of others. Analyses have either focused on general characteristics of decedents or cause of death.

Methods used were either simple numbers/percentages, or crude and standard mortality rates. Models have looked at the risk of overdose as a function of age but have tended to use multivariate analysis or separated analyses without controlling for confounders, or they have explored how the crude mortality rate may vary as a function of age (Ødergård et al., 2007). To obviate the problems associated with reviewing such studies, Ødergård et al. (2007) used a Cox proportional hazard regression model employing a competing risk approach (Lunn et al., 1995). Deploying a similar approach, Darke et al. (2011) undertook a cohort study where bivariate Cox proportional hazard regressions examined baseline characteristics, such as socio-demographics, health, crime, drug usage, psychopathology, overdose and suicide. A multivariate approach was conducted to determine independent predictors of mortality.

GMRs report on information from death certificates typically only related to deaths from poisoning or overdose rather than all drug-related causes. This means that such statistics are weaker in this respect than cohort studies, where all types of death should be captured, including: road traffic accidents, drownings, etc.; the consequences of injecting drugs, acquisition of hepatitis C, HIV/AIDS; and age-related factors in cohorts of ageing drug users.

Although the use of information from autopsy and toxicological investigations can strengthen investigations into risk factors, a more comprehensive approach is required. This can be provided by using all the data available to SMRs, e.g., drug use, prescribing and treatment histories, etc. Researchers can lessen the likelihood reporting ‘ecological’ fallacies (i.e., drawing incorrect inferences about the nature of individuals based on inferences about the group to which those individuals belong) by looking at aggregated data from individual deaths.

The author has led on and/or contributed to a number of studies, both prior to registering for the PhD research programme and since his registration, which although having similarities to previous research studies (e.g., Parkinson et al., 2018; Lewer et al., 2022) has sought to broaden the range of factors looked at: socio-demographics; prescribing history; context of fatal incident; locus (place) of death; mechanism(s) as well as cause(s) of death; intent and manner of death; and drugs involved (combinations, toxicology levels, etc). The completed studies are examined below, together with an indication of the author’s current data collection activities and planned outputs, including updates to past studies conducted by him and colleagues and/or NPSAD collaborators.

Table 7.1: Substances/drug classes looked at by the author when profiling 'at risk' groups

Drug class	*Specific substances*	*Types of output and year(s)*
Stimulant	Ecstasy	Research article (2003); detailed analysis of NPSAD data for ACMD report (2009);
	Amphetamine-type	Research article (2010);
	Synthetic cathinones, khat & mephedrone	Oral presentations (2012); published abstract (2012);
	Synthetic cathinones	Detailed analysis of NPSAD data for ACMD report (2010); book chapter (2018); oral presentation (2017, 2019); published abstract (2017, 2019); Member of ACMD working group (2023 onwards);
	Mephedrone	Book chapter (2012); research article (2012, 2014); poster and abstract (2013, 2017);
	Mephedrone & MDPV	Oral presentation to EMCDDA (2010);
	'Traditional' and 'New'	Oral presentations (2012, 2013); published abstract (2013);
	Stimulants	Oral presentation (2011);
	Cocaine	Oral presentation to EMCDDA (2010);
	Cocaine vs other stimulants	Oral presentation to EMCDDA (2011);
Dissociative	Ketamine	Contributions to ACMD Working Group (2003-4, 2013); Letter to Editor (2008); presentation and data to ACMD (2013); research article (2021);
	Methoxetamine (special 'M')	Presentation and data to ACMD (2012-2013); research article (2015);
	Ketamine & Methoxetamine	Data, oral presentation & report to ACMD (2012-2013);
	Diphenidine & Methoxphenidine	Provided data, led on deaths for ACMD Working Group (2022-2023); (paper to be written);
Opiate/Opioid	Heroin	Oral presentation to EMCDDA (2014);
	Dihydrocodeine	Research article (2011);
	Nitazenes	Data contributed to ACMD report (2022-2023);
Benzodiazepine	Phenazepam	Rapid Response (Letter to editor) (2011); research article (2012);
	Alprazolam	Posters (2021, 2022); research article (2022);
Natural product	Khat	Abstract and presentation to WHO (2007); oral presentations (2009, 2011, 2011); presentation to ACMD (2012); research articles (2011, 2011, 2020);
	Kratom	Published abstract (2016); oral presentations (2016, 2018); poster (2019); research article (2019);
	Ibogaine	Book chapter (2018);
Hypnotic/Sedative	'Z' drugs	NPSAD data analyses and contribution to ACMD report (2013);
CNS depressant	GHB and analogues	Member of ACMD working group (2002-3, 2009); provided NPSAD data for ACMD report (2008); oral presentation and published abstract (2014);
	GHB, GBL & 1,4-BD; BDO	Research articles (2015, 2018);
Polysubstance	Polysubstance	Presentation to ACMD (2012);
	Recreational	Oral presentation to EMCDDA (2013);
Novel psychoactive substances	New substances of abuse	Invited lecture (2012);
	Novel Psychoactive Substances	Oral presentations (2013);
	SCRAs	Contributed on deaths to ACMD NPS Committee (2020, 2022);
Volatile Substances	Nitrous oxide	Provision of data and led on deaths for ACMD Working Group (2022-2023); (paper to be written)
	Alkyl nitrites ('Poppers')	Contributed on deaths to ACMD Working Group (2016); contributed to and led of deaths for ACMD Working Group (2023 onwards); papers to be written;
Notes: ACMD = Advisory Council on the Misuse of Drugs; GHB = Gamma hydroxybutyrate; GBL = Gamma butyrolactone; 1,4-BD, BDO = 1,4 butanediol; MDPV = Methylenedioxypyrovalerone; NPS = New/ Novel Psychoactive Substances; SCRA = Synthetic cannabinoid receptor agonists; 'Z' drugs = Zopiclone, Zolpidem & Zaleplon		

Types of study providing profiles of 'at risk' groups/populations

The author and colleagues have principally looked at profiling the characteristics of decedents and/or deaths involving specific substances or drug classes. The findings of these studies have been presented orally or as posters at conferences, published as peer-reviewed journal articles and book chapters, or submitted as contributions to advice published by the Advisory Council on the Misuse of Drugs (ACMD). In some cases, all three modes of dissemination have been used or are planned. The substances/drug classes covered are summarised in Table 7.1 (further details are provided in the "Future work" section below and in Appendices C and D). A reminder that the author started his PhD programme in mid-2018, so some of these outputs were produced during this timeframe.

Some other studies have looked at specific type of death circumstances or scenarios: fatal injuries under the influence of psychoactive drugs, using NPSAD data (Oyefeso et al., 2006); suicide in substance misusers (Vento et al., 2011; drownings, using National Records of Scotland (NRS) data (Corkery et al., 2023); or amongst specific sentinel sub-groups (Corkery et al., 2018).

Profiling decedents' socio-demographic characteristics

The variables or parameters that have typically been explored by studies using NPSAD data are: age, gender, ethnicity, marital status, living arrangements, employment status, occupation, area deprivation level, substance use history, prescription drug history. In respect of certain substances (GHB, GBL, nitrous oxide, alkyl nitrites or 'poppers'), sexual orientation and/or gender identity have been explored (e.g., Corkery et al., 2018). Looking at different combinations of age and gender in association with the type(s) of substances used (for example, medicines vs. recreational drugs) can help identify and define particular sub-groups on whom prevention initiatives and interventions should be focused.

Profiling deaths

The key elements focused on here, looking at deaths themselves, include: events leading up to death, scenarios (e.g., driving, drowning, sexual activity); scene and setting, e.g., *locus* and circumstances of a fatal event; place of death, if different to locus of fatal event, e.g., hospital; mode or route of administration of implicated substances; the motivation(s) or purpose(s) of use (Corkery et al., 2018); intent or mode of death (accidental, intentional, undetermined intent); substances involved, including combinations and toxicological levels; cause(s) of death, including contributory factors such as underlying health issues (known and unknown); mechanism(s) of death.

Examining mono-substance deaths enables researchers to calculate and provide information on fatal levels more easily than if in combination with other substances; in the latter case, the relative contributions of individual substances may be difficult or even impossible to reckon. Looking at the ratio of sole to polysubstance deaths has enabled the former head of the Forensic Science Service's Drugs Intelligence Unit and the author to further develop their Fatal Lethality Index (King and Corkery, 2010, 2018). This has facilitated an approach to comparing the relative lethality of a range of index substances and drug classes, including NPS. The author plans to publish a systematic literature review of other lethality indices following completion of this thesis (see "Future work" section below).

At a higher level of abstraction, the author developed a taxonomy for khat-related deaths (Corkery et al., 2011a, 2011b). Although rather than concentrating on purely physiological aspects of death (Klein, 2011; Singleton, 2011) this used a very broad-based approach, the author strongly believes in and advocates its application to other substances. This he has done in respect of preparing contributions to the recently published ACMD advice on nitrous oxide (ACMD, 2023a), the dissociative drugs diphenidine and methoxphenidine (ACMD, 2023b), and alkyl nitrites or 'poppers' (ACMD, 2024); the author plans to publish these as research articles following completion of this thesis (see "Future work" section below).

Selected examples of profiles already undertaken

Extracts of abstracts from 15 selected studies providing profiles of 'at risk' groups involving the author are presented below. The studies represent research conducted primarily over the past couple of decades, rather than just since the author started his PhD programme of research in 2018. These are presented in chronological order so as to demonstrate: how the approach of the author and his colleagues has evolved; the variety of groups examined; and the variables/parameters covered. It is believed that their inclusion is in line with the principle of 'fair dealing' in respect of UK copyright law (British Library, 2023; Intellectual Property Office, 2014). In addition, only abstracts of studies which the author has led on and/or contributed and thus has intellectual and copyright rights are presented. Copyright information is presented, where known. The abstracts have been reformatted to be consistent with the style adopted for this thesis. Original spellings have been retained.

Fatal accidents (Oyefeso et al., 2006)

“Background: Studies of drug-related mortality rarely describe fatal injuries due to psychoactive drug intoxication (FIUI). The main aim of this study was to determine the nature, extent and pattern of FIUI.

Methods: This observational study covered the period January 1999 to December 2001. Data were provided by members of a study panel of coroners in England using a standard protocol. Sources of data for this study included autopsy protocols, death certificates, hospital records, police reports, toxicology reports and inquest transcripts. Inclusion criteria for this were (i) the mention of one or more psychoactive substances as contributing to fatality; and (ii) the presence of a Controlled Drug at post mortem.

Results: A total of 3,803 drug-related deaths of persons aged 16-64 years were reported by the study panel during the three-year period. The study panel accounted for 86% of drug-related deaths in England in this period. There were 147 FIUI cases (119 males, 28 females), giving a proportionate mortality ratio of approximately 4%. The majority of FIUI cases (84%) were aged 16-44 years, with a median age at death of 33 years (Quartile deviation = 7). Fifty-six percent of FIUI occurred in urban areas of England. The population of the study jurisdictions aged 16-64 years contributed 49,545,766 person-years (py) to the study, giving an annual crude rate of 3/1,000,000 person-years (py). Rates for male and females were 4.9 and 1.1/1,000,000 py respectively, giving a male/female rate ratio of 4.5 (95%CI = 2.9-6.8). The rates of intentional and unintentional FIUI were 2 and 1/1,000,000 py respectively. The leading mechanism for intentional FIUI was suffocation while the predominant mechanisms in unintentional FIUI were road traffic accidents and falls. There is a significant difference in the pattern of drug-specific risk between FIUI and fatal poisoning. Risks of intentional FIUI are elevated among Black and Minority Ethnic groups.

Conclusion: There are differences in the nature, extent and pattern of intentional and unintentional FIUI that should necessitate targeted prevention strategies. Also, there is an opportunity for cross-discipline collaboration between injury prevention specialists and substance abuse/mental health specialists.”

Amphetamine-type substances (Schifano et al., 2010)

“Background/aims: Despite being amphetamine derivatives, MDMA and its analogues show a number of clinical pharmacological differences with respect to both amphetamine (AMP) and methylamphetamine (METH). We aimed here at reporting and analysing information relating to the socio-demographics and clinical circumstances of the AMP-type stimulant-related deaths for the whole of the UK.

Methods: Data (1997-2007) were taken from the National Programme on Substance Abuse Deaths (np-SAD) database, collecting information from UK coroners/procurators fiscal. To calculate rates of fatalities per 100,000 users, appropriate AMP/METH and ecstasy users' numbers were taken from the 2001-2007 British Crime Survey.

Results: Overall, 832 AMP/METH- and 605 ecstasy (mostly MDMA and methylenedioxyamphetamine/MDA)-related deaths were respectively identified. In comparison with AMP/METH victims, the ecstasy ones were more likely to be younger (28.3 vs. 32.7 years; $p < 0.0001$) and less likely to be known as drug users (PR = 1.9; CI 1.5-2.6). Ecstasy was more likely to be identified on its own than AMP/METH ($p = 0.0192$). Contributory factors were more frequently mentioned by coroners in the 'AMP/METH-only' (106 cases) group than in the 'ecstasy-only' (104 cases) one ($p = 0.0043$). Both poly- and monodrug AMP/METH fatalities per 100,000 16- to 59-year-old users were significantly more represented than ecstasy fatalities (respectively 17.87 +/- 4.77 deaths vs. 10.89 +/- 1.27; $p = 0.000$; 2.09 +/- 0.88 vs.

1.75 +/- 0.56; p = 0.0096). However, mono-intoxication ecstasy fatalities per 100,000 16- to 24-year-old users were significantly more represented than AMP/METH fatalities (1.67 +/- 0.52 vs. 0.8 +/- 0.65; p = 0.0007).

Conclusion: With respect to AMP/METH, ecstasy was here more typically identified in victims who were young, healthy, and less likely to be known as drug users. AMP/METH high mortality rates may be explained by users' high levels of physical co-morbidity; excess ecstasy-related fatality rates in young users may be a reason for concern. Although the coroners' response rate was of 90-95%, study limitations include both reporting inconsistency over time and lack of routine information on drug intake levels prior to death."

Khat (Corkery et al., 2011b)

"Twenty million people worldwide use khat (*Catha edulis).* Previously confined to Eastern Africa and Arabia, consumption is spreading to other regions. Chewing khat leaves releases the stimulants cathinone and cathine. Khat consumption has adverse health consequences including myocardial infarction, liver failure, depression, psychoses and dependence. Literature regarding khat-related mortality is scant: only one death (in 1945) due to physiological complications, and a small number of fatalities due to psychological problems associated with long-term khat use have been reported. However, deaths associated with khat do occur. Thirteen deaths in the UK occurring in 2004–2009 associated with khat consumption are described. All decedents were males (mean age 35). Four deaths resulted from the physiopathological consequences of long-term khat use; liver failure (3), left ventricular failure and pulmonary oedema (1). In a further case, the deceased died of a cardiovascular event precipitated by khat use causing either an infarction or electrical instability (arrhythmia) leading to death. Three confirmed and one possible suicide occurred of individuals with psychoses caused and/or exacerbated by long-term khat consumption. An accidental overdose of an anti-psychotic occurred where schizophrenia was exacerbated by khat use. Impaired judgment due to khat and alcohol led to two fatalities in road accidents. One fatality resulted from heroin intoxication, but khat was also present. Khat-consuming communities and health professionals need to be aware of the physiological and psychological effects of khat, together with the risks for mortality associated with its use."

Dihydrocodeine (Zamparutti et al., 2011)

"Aims: Although its effectiveness is somewhat controversial, it appears that dihydrocodeine (DHC) is still prescribed in the UK as an alternative to both methadone and buprenorphine for the treatment of opiate addiction.

Methods: Data covering the period 1997-2007 voluntarily supplied by coroners were analysed. All cases pertaining to victims with a clear history of opiate/opioid misuse and in which DHC, either on its own or in combination, was identified at post-mortem toxicology and/or implicated in death, were extracted from the database.

Results: Dihydrocodeine, either alone or in combination, was identified in 584 fatalities meeting the selection criteria. In 44% of cases it was directly implicated in the cause of death. These cases represented about 6.8% of all opiate/opioid-related deaths during this period. Typical DHC cases identified were White males in their early thirties. Accidental deaths (96%) were likely to involve DHC in combination with other psychoactives, mainly heroin/morphine, hypnotics/sedatives and methadone. Both paracetamol and antidepressants were found in proportionately more suicide cases than in accidental overdoses. DHC had been prescribed to the decedent in at least 45% of cases.

Conclusions: Opiate/opioid misusers should be educated about risks associated with polydrug intake. More in particular, co-administration of DHC with heroin, methadone and benzodiazepines may increase the risk of accidental fatal

overdose. Prescribers should carefully consider pharmacological intervention alternative to DHC (e.g., methadone, buprenorphine) when managing and treating opiate addiction. More resources are required to do prospective research in this area."

Suicides (Vento et al., 2011)

"Background: Substance-related deaths account for a great number of suicides.

Aim: To investigate levels and characteristics of suicide verdicts, as opposed to accidental deaths, in substance misusers.

Methods: Psychological autopsy study of cases from the UK National Programme on Substance Abuse Deaths (np-SAD) during the period 2001-2007.

Results: Between January 2001 and December 2007, 2108 suicides were reported to the np-SAD. Typical suicide victims were White and older than 50 (respectively 95% and 41% of cases). Medications, especially antidepressants (44%), were prescribed to 87% of victims. Significantly fewer suicide victims than controls presented positive blood toxicological results for illicit drugs (namely: cocaine, heroin, amphetamines, ecstasy-type drugs, cannabis, and GHB/GBL) and alcohol.

Conclusions: Suicide prevention programmes should devote specific attention to deaths among substance misusers who are at high risk of fatal intentional self-harm. Specific characteristics distinguish those at risk; caregivers should be better educated as to what these factors are. Limitations of the current study included lack of provision of comprehensive information relating to the victims' psychosocial variables. Furthermore, no differentiation between different classes of antidepressants in terms of involvement in suicide was here provided."

Mephedrone (Schifano et al., 2012)

"Background: International media have been reporting about fatalities allegedly related to mephedrone, a popular recreational stimulant, but now a proportion of them have been confirmed. We aimed here at analyzing information relating to the circumstances of mephedrone-related deaths in the United Kingdom.

Methods: Descriptive analysis of information was mainly extracted from the UK National Programme on Substance Abuse Deaths database. With an average annual response rate of 95%, UK National Programme on Substance Abuse Deaths receives information from coroners on drug-related deaths among both addicts and nonaddicts in the United Kingdom, the Channel Islands, and the Isle of Man.

Results: So far, 128 alleged mephedrone-associated fatalities have been reported; mephedrone was identified at postmortem in 90 cases; inquests have been concluded in 69 cases, 62 of which are analyzed here. Typical mephedrone victims were young (mean age, 28.8 years), male, and with a previous history of drug misuse. There was a notable number (18 cases [29%], 11 being from hanging) of deaths involving self-harm. Mephedrone alone was identified at postmortem on 8 occasions (13% of the inquests' sample).

Conclusions: Present mortality data may suggest a significant level of caution when ingesting mephedrone. Limitations include an inability to determine the exact extent of risks associated with mephedrone consumption."

GHB/GBL (Corkery et al., 2015)

“Misuse of gamma hydroxybutyrate (GHB) and gamma butyrolactone (GBL) has increased greatly since the early 1990s, being implicated in a rising number of deaths. This paper reviews knowledge on GHB and derivatives, and explores the largest series of deaths associated with their non-medical use. Descriptive analyses of cases associated with GHB/GBL and 1,4-butanediol (1,4-BD) use extracted from the UK's National Programme on Substance Abuse Deaths database. From 1995 to September 2013, 159 GHB/GBL-associated fatalities were reported. Typical victims: White (92%); young (mean age 32 years); male (82%); with a drug misuse history (70%). Most deaths (79%) were accidental or related to drug use, the remainder (potential) suicides. GHB/GBL alone was implicated in 37%; alcohol 14%; other drugs 28%; other drugs and alcohol 15%. Its endogenous nature and rapid elimination limit toxicological detection. Post-mortem blood levels: mean 482 (range 0-6500; SD 758)mg/L. Results suggest significant caution is needed when ingesting GHB/GBL, particularly with alcohol, benzodiazepines, opiates, stimulants, and ketamine. More awareness is needed about risks associated with consumption.”

Mephedrone (Loi et al., 2015)

“Objective: Mephedrone is a stimulant drug chemically related to amphetamine, with effects similar to those of amphetamine and cocaine. This study aims to analyse fatalities following ingestion of mephedrone in the UK amongst 16- to 24-year-olds in 2009-2013, providing an update on data presented at the 2nd International Conference on Novel Psychoactive Substances.

Methods: A literature search was undertaken to identify published information on pharmacology, toxicity and fatalities associated with mephedrone. Fatalities involving mephedrone were extracted from the National Programme on Substance Abuse Deaths database, which receives information on drug-related deaths from coroners in the UK and Islands and other data suppliers. Selection criteria are as follows: deceased aged 16-24 years at time of death and mephedrone directly implicated in the cause of death and/or mentioned in the coroner's verdict.

Results: Thirty cases met the study criteria, and when known, all were of White ethnicity, most (85%) had a history of drug use and 73% were male. Two-thirds (63%) were accidental poisonings. Mephedrone was used with other substances in most cases (87%); other substances were implicated in 60% of deaths.

Conclusions: Mephedrone use can have potentially fatal consequences, especially in combination with other substances. Deaths from its use in the 16-24 years' age group continue to occur in the UK, despite it being a controlled drug. Health professionals and potential consumers should be alert to this risk.”

Methoxetamine (Chiappini et al., 2015)

“Objective: The goal of this study is to provide an update on the data given on methoxetamine (MXE)-related fatalities that occurred in 2011-2013, presented at the Second International Conference on Novel Psychoactive Substances.

Methods: Fatalities involving MXE were extracted from the database of the National Programme on Substance Abuse Deaths, which receives information on drug-related deaths from Coroners in the UK and Islands (Isle of Man, Jersey, Guernsey) and other data suppliers.

Results: Eight cases, received by 3 September 2013, in which MXE was found at post-mortem and/or directly implicated in the death and/or mentioned in the Coroner's verdict are described. The median age at death was 27 years, with the majority of White ethnicity (6/8) and male (7/8). MXE was used together with other substances in 7/8 cases. MXE was found at post-mortem in all cases, directly implicated in the deaths of four and likely to have had an influence in two.

Conclusions: More research needs to be conducted into its health effects and toxicity potential. Health care professionals should be made aware of the potential health harms of MXE, in order to develop early intervention measures and minimise the number of MXE-related poisonings and fatalities.”

Cocaine (Corkery et al., 2017)

“Cocaine-related deaths have increased since the early 1990s in Europe, including the UK. Being multi-factorial, they are difficult to define, detect and record. The European Monitoring Centre for Drugs and Drug Addiction commissioned research to: describe trends reported to Special Mortality Registries and General Mortality Registers; provide demographic and drug-use characteristic information of cases; and establish how deaths are identified and classified. A questionnaire was developed and piloted amongst all European Monitoring Centre for Drugs and Drug Addiction Focal Point experts/Special Mortality Registries: 19 (63%) responded; nine countries provided aggregated data. UK General Mortality Registers use cause of death and toxicology to identify cocaine-related deaths. Categorisation is based on International Classification of Diseases codes. Special Mortality Registries use toxicology, autopsy, evidence and cause of death. The cocaine metabolites commonly screened for are: benzoylecgonine, ecgonine methyl ester, cocaethylene and ecgonine. The 2000s saw a generally accelerating upward trend in cases, followed by a decline in 2009. The UK recorded 2700-2900 deaths during 1998-2012. UK Special Mortality Registry data (2005-2009) indicate: 25-44 year-olds account for 74% of deaths; mean age=34 (range 15-81) years; 84% male. Cocaine overdoses account for two-thirds of cases; cocaine alone being mentioned/implicated in 23% in the UK. Opioids are involved in most (58%) cocaine overdose cases.”

GHB/GBL (Corkery et al., 2018)

“Background: Misuse of gammahydroxybutyrate (GHB) and its prodrugs gammabutyrolactone (GBL) and 1,4 butanediol (1,4-BD) has increased greatly since the early 1990s, particularly amongst lesbian, gay, bisexual and transgender (LGBT) individuals in recreational and sexual settings, e.g., 'chemsex'.

Objective and method: This paper presents an overview of GHB pharmacotoxicology and provides analyses of cases in the LGBT population associated with the use of these substances extracted from the UK's National Programme on Substance Abuse Deaths database, to which notification is voluntary.

Results: From 1995 to September 2013, 21 GHB/GBL-associated fatalities were reported. None involved 1,4-BD. Typical victims were: Male (100%); White (67%), young (mean age 34 years); employed (90%); with a drug misuse history (81%). Most deaths were accidental (67%) or related to recreational drug use (19%), the remaining (potential) suicides. The majority of fatalities (83%) occurred in private residences, typically following recreational use; others occurred in specific 'gay'-oriented locales including clubs and saunas. Three London boroughs accounted for 62% of all notified deaths, reflecting the concentration of both resident and visiting 'gay' individuals. However, this may be an artefact of the voluntary nature of the data submission procedure in particular areas. GHB/GBL alone was implicated in 10% of fatalities. The following substances were implicated either alone or in combination in the remaining cases (percentages may add to more than 100%): cocaine (38%); alcohol (33%); amphetamines (29%); ecstasy (29%); diazepam (24%); ketamine (24%); mephedrone (24%). Post-mortem blood levels: mean 660 (range 22 - 2335; S.D. 726) mg/L.

Conclusion: Significant caution is needed when ingesting GHB/GBL, particularly with alcohol, benzodiazepines, stimulants, and ketamine. Risk of death is increased due to their CNS-depressant properties. Of these, 'chemsex' drugs such as cocaine, mephedrone and ketamine are of note. More awareness is needed in the 'gay' community about risks associated with the consumption of such substances."

Ibogaine (Corkery, 2018)

Chapter abstract: "Ibogaine is an indole alkaloid found in the root bark of the Iboga shrub native to west Africa possessing hallucinogenic properties. For centuries it has been used in religious ceremonies and to gain spiritual enlightenment. However, since the early 1960s, its apparent ability to reduce craving for psychoactive substances including alcohol, cocaine, methamphetamine, opiates, and nicotine has led to its use in detoxification treatments. In many instances, clients receive treatment in non-medical settings, with little by way of robust scientific clinical trials. This chapter provides an overview of the potential benefits that could arise from such research. This is balanced against the serious adverse effects that can occur due to undiagnosed health conditions and/or concomitant use of other drugs. A detailed update is provided of the 33 deaths known to have occurred, including 5 in the UK. Looking forward, there is a need to develop better opiate detoxification treatment against a background of increasing opioid-related fatalities. A congener of ibogaine, 18-MC, appears to be safer and is to undergo clinical trials. In the meantime, would-be consumers and treatment providers must make more careful, detailed risk-assessments before using ibogaine. Treatment outcomes, including deaths, need to be accurately recorded and published."

Excerpt from page 241: "The profiles of these additional cases are in broad keeping with those reported by Alper et al. (2012). To summarize briefly these 33 cases: 25 males, 8 females; mean age = 39.5 (range 24–60) years; purpose of use—religious/spiritual 3, opioid detoxification 26, treat alcoholism 5, treat addiction to methamphetamine 2; form of ibogaine taken —HCl 15, alkaloid extract 5, root bark 3, brown powder 1; unknown 9; ibogaine blood concentrations (N = 16) mean 2.11 (range 0.24–9.3) mg/L; commonly used drugs of abuse or medications were found in at least 12 cases; medical co-morbidities were present in at least 18 cases; where ethnicity was known (N = 11), 10 were White/Caucasian and one was Black; country of death—Mexico 8, USA 7, UK 5, France 4, Netherlands 2, Cameroon, Costa Rica, Germany, Greece, New Zealand, South Africa, and Thailand 1. The range of countries where deaths have occurred has grown, probably in line with the increasing number of countries where ibogaine treatments are offered."

Kratom (Corkery et al., 2019)

“Background: Kratom (*Mitragyna speciosa* Korth) use has increased in Western countries, with a rising number of associated deaths. There is growing debate about the involvement of kratom in these events.

Aims: This study details the characteristics of such fatalities and provides a 'state-of-the-art' review.

Methods: UK cases were identified from mortality registers by searching with the terms 'kratom', 'mitragynine', etc. Databases and online media were searched using these terms and 'death', 'fatal*', 'overdose', 'poisoning', etc. to identify additional cases; details were obtained from relevant officials. Case characteristics were extracted into an Excel spreadsheet, and analysed employing descriptive statistics and thematic analysis.

Results: Typical case characteristics (*n* = 156): male (80%), mean age 32.3 years, White (100%), drug abuse history (95%); reasons for use included self-medication, recreation, relaxation, bodybuilding, and avoiding positive drug tests. Mitragynine alone was identified/implicated in 23% of cases. Poly substance use was common (87%), typically controlled/recreational drugs, therapeutic drugs, and alcohol. Death cause(s) included toxic effects of kratom ± other substances; underlying health issues.

Conclusions: These findings add substantially to the knowledge base on kratom-associated deaths; these need systematic, accurate recording. Kratom's safety profile remains only partially understood; toxic and fatal levels require quantification.”

Recreational ketamine (Corkery et al., 2021)

“Background: Ketamine is a phencyclidine derivative with dissociative anaesthetic properties. Increasing numbers of individuals in England take ketamine recreationally. Information on deaths arising from such use in England is presented.

Methods: Cases were extracted on 31 January 2020 from the National Programme on Substance Abuse Deaths database, based on text searches of the cause of death, coroner's verdict and positive toxicology results for the terms 'ketamine' or 'norketamine'.

Findings: During 1997-2005, there were <5 deaths p.a. in which ketamine was implicated. Numbers increased until 2009 (21), plateauing until 2016; thereafter, deaths have risen to about 30 p.a. Decedents' characteristics (*N* = 283): male 84.1%, mean age 31.2 (SD 10.0) years, employed 56.5%, drug use history 79.6% and living with others 60.3%. Ketamine was detected with other substances in most cases. Main (74.6%) underlying cause of death was accidental poisoning. Ketamine may have impaired judgement in other cases.

Conclusions: Although controlled, recreational ketamine use and related fatalities continue to increase. Consumers need to be more aware of the potentially fatal risks they face.”

Diphenidine and Methoxphenidine (ACMD, 2023b: 18-20).

"A detailed review was undertaken in late August 2022 by members of the ACMD NPS Committee and the ACMD Secretariat in preparation of this ACMD report. The review included information from a systematic literature review of published scientific papers and other information in the public domain; anonymised data provided by the National Records of Scotland, the National Programme on Substance Abuse Deaths, and EU-MADNESS project; and information from the ONS and the Northern Ireland Statistics and Research Agency. …

More detailed demographic information was available for analysis for 35 of these identified deaths: - The majority (32, 91.4%) were males - The overall mean (range) age was 37.2 (19-65) years old; the mean age differed between countries: Wales 34.7 years; England 36.3 years; Scotland 41.4 years - Ethnicity was available for 19 deaths, of which 18 were white and 1 was black. - Employment status was available for 24, and 13 were currently employed at the time of the death … Previous/current drug use status was known in 25, and 18 (72%) had a history of drug use … The majority (65.7%) of deaths had one or more other drug and/or alcohol detected or implicated in the death. The most common substances detected were morphine (11 deaths), codeine (7 deaths), alcohol (6 deaths) and methiopropamine (6 deaths). … The place of death was known in 24 deaths, and 20 died at home, in university accommodation or in another private residential property, 3 died in hospital and 1 died on the street… The underlying cause of death was i) acute drug toxicity: 33 deaths; ii) cardiac causes: 2 deaths; iii) trauma: 1 death; iv) unascertained: 1 death. Of the 33 deaths due to acute drug toxicity, 14 were due to diphenidine or methoxyphenidine alone, 15 due to diphenidine or methoxyphenidine in combination with other drugs/alcohol and 4 were due to other drugs (where diphenidine or methoxyphenidine were noted to have been used but were not listed as the underlying cause of the death)."

Purposes of profiling 'at risk' groups

"Any drug-related death is a tragedy, and everyone agrees more needs to be done… review processes can make a vital contribution to this effort" (NTA, 2011:3). As mentioned in passing above, profiling specific groups at risk of a drug-related death can assist in trying to understand and mitigate such events.

A commentary by Hjorthøj et al. (2022) on research undertaken by Formánek et al. (2022) using a retrospective cohort study approach underlines the wide range of factors that can contribute to substance-induced or substance-related deaths, but not as extensive as that proposed by the author (Corkery et al., 2011a). Many of the factors listed can be identified through examination of information collected by SMRs such as NPSAD (see, for example, the abstracts above).

The benefits of looking at deaths to profile 'at risk' groups include: predicting the needs of those using newly created molecules and/or new modes of administration (e.g., vaping); informing decisions about funding and provision of services; informing educational needs for (potential) substance users and those who deal with them; identifying and informing interventions that have regard to potential decedents' socio-economic determinants and characteristics, such as employment status, marital status, living arrangements, set and setting of drug consumption, mode of substance administration, type of death *locus*, etc.

Existing provision and intervention strategies can be examined with a view to considering what improvements could be made and benefits arising for different types of stake-holders.

The guidance issued by the National Treatment Agency for Substance Misuse (NTA, 2011) was based on the data collection form developed and used by the author and colleagues at NPSAD (see Chapter 3). Data collected using this form enabled NPSAD to conduct 17 local confidential inquiries between 2003 and 2007 for specific geographical areas in England, and to tailor the approach in accordance with commissioners' needs, typically local authorities or NHS (National Health Service) Trusts.

Collective Voice from the voluntary sector collaborated with the NHS Substance Misuse Provider Alliance to "pool and share … [their] expertise to maximise the treatment sector's contribution to minimise early and avoidable deaths" (Collective Voice, 2017). They focused on five key areas of clinical practice:

- Identifying risk of drug-related death;
- Delivering safe, recovery-orientated drug treatment;
- Preventing overdose in people who use drugs;
- Meeting physical and mental health needs; and
- Reducing the risk of drug-related death for people outside drug treatment.

There is a plethora of risk factors that need to be considered when profiling (potential) decedents and deaths. The author has tried to categorise these in Table 7.2; it is not an exhaustive list.

Table 7.2: Types of risk factors that can be used in profiling 'at risk' groups

Type of risk factor	*Example*
Demographic	Age
	Gender
	Ethnicity
Social	Religion/Spirituality
	Sexual orientation
	Educational level (including about substance use)
	Marital/relationship status
Economic	Occupation
	Employment status
	Deprivation
	Housing/living arrangements
Health	Physical health conditions (known & unknown)
	Mental health conditions (especially psychiatric comorbidity/dual diagnosis, psychoses, suicidality)
	Prescription history
	Substance use history, including dosages, age at first use, length of use, route(s) of administration
	Diseases/infections acquired through/ caused by injecting use (e.g., botulism, hepatitis C, HIV/AIDS)
Substances	Combinations & interactions (prescription, OTC, 'street', NPS, etc.)
	Purity/potency, contamination/ cutting agents
	Drug identification, screening, testing
	Medical interventions, e.g., naloxone

In the author's opinion, it would take several PhD theses to examine and (perhaps) establish which of these factors may be more amenable to change or influence than others, and how that might be done. However, it is clear that few, if any, of these aspects can be tackled alone. There can be various inter-relationships at play in any given scenario, so a multi-disciplinary, multi-agency holistic approach is required. Some of these inter-connections can be very complex and difficult to tease out. Chapters 8 to 12 attempt to look at some of the 'higher level' influences that have been at work in the UK and national contexts. The national and, indeed, international factors do have a bearing on what happens at a local level. Earlier chapters (3 to 5) have described the present situation, what improvements have occurred and suggested areas for future consideration.

Future work - on-going data collection and proposed outputs

The author had an on-going strategy over the past decades of identifying, obtaining and curating statistical data, case-studies, etc. concerning issues on which he has previously written and on emerging topics that interest him. Sometimes, it is necessary to be very patient in order to assemble sufficient material on which to base a paper or project.

The author's current thoughts to classifying possible future outputs based around substance-related deaths are presented below.

ACMD-related activities

Material gathered for several recently published or imminent reports by the ACMD, along with additional cases being identified on a pro-active basis, will form the basis of several papers. These will be drafted by the author, and involve collaborators as indicated.

- Deaths related to use of Diphenidine and Methoxphenidine - J.M. Corkery (UH), C.J. Copeland (NPSAD), F. Schifano (UH)

- Deaths in the UK related to use of Nitrous Oxide – J.M. Corkery (UH), C.J. Copeland (NPSAD), S. Ream (Re-Solv), F. Schifano (UH)

- Deaths in the UK related to use of Alkyl Nitrites (‘poppers’) - J.M. Corkery (UH), C.J. Copeland (NPSAD), S. Ream (Re-Solv), F. Schifano (UH)

- UK deaths from swallowing ‘poppers’ - J.M. Corkery (UH), C.J. Copeland (NPSAD), S. Ream (Re-Solv), F. Schifano (UH)

Amphibian secretions

The author presented an oral presentation at the IX International Conference on Novel Psychoactive Substances Panama City on “ ‘Croaking on Kambô’: intoxications and fatalities associated with use of secretions from phyllomedusa bicolor (giant leaf frog, giant monkey frog)”. It is intended to work this presentation (Corkery, 2022) up into a paper and submit for publication as there is no ‘academic’ literature looking at such fatalities. The author is currently following two key inquests that have been going on in Australia over past year or two; these are ongoing (May 2024). The proposed paper and contributors are:

- ‘Croaking on Kambô’: fatalities associated with use of secretions from *Phyllomedusa bicolor* (giant leaf frog, giant monkey frog – J.M. Corkery (UH), F. Schifano (UH), L. Orsolini (Università Politecnica delle Marche, Ancona), G. Martinotti (UH).

Bufotenine (5-HO-DMT) is an alkaloid secretion made by the *Bufo* toad genus. It is a DMT analogue of the tryptamine chemical class, and possesses psychoactive (hallucinogenic) properties. The author intends to prepare a case-series paper of bufotenine-related fatalities based on netnographic sources.

Plants with psychoactive constituents

More than a decade has passed since the author published the first papers (Corkery et al., 2011a, 2011b) establishing the basis of a still poorly populated literature on fatalities related to the khat shrub *Catha edulis*. The author has been monitoring academic papers and 'grey literature' on such events and curating relevant material. He is of the opinion that an up-to-date review of khat-related fatalities would be a feasible activity.

As part of a book chapter published several years ago (Corkery, 2018), the author provided an overview of UK deaths related to derivatives from the *Tabernanthe iboga* tree as well as an update on such deaths globally. As with khat, the author has been monitoring academic papers and 'grey literature' on similar events and collecting relevant material. An update of iboga-related fatalities would be appropriate given the increased interest in ibogaine in a range of treatments (Mosca et al., 2023).

Drug-related deaths (DRDs) and other drug indicators

The series of correlational studies looking at DRDs and other drug indicators presented in Chapters 9 to 11 could not only provide the basis for a several papers that could update previous studies by the author and his collaborators on stimulants, but also new papers on the following drug classes: opiates/opioids; benzodiazepines; cannabis; NPS, GHB, ketamine, etc.

The use of DRD statistics in combination with prevalence and drug seizure/prescription data formed the basis of papers developing a Fatal Lethality Index (King and Corkery, 2010, 2018). As noted above, the author aims to finish a systematic literature review of other lethality indices; part of this endeavour could include an attempt to provide a comprehensive mapping of the respective lethality of a range of drug classes and index substances covered by the literature. The working title and collaborators are:

- The past, present and future uses of fatal toxicity and lethality indices – J.M. Corkery, F. Schifano, G. Martinotti

Possible updates and extensions of existing studies using NPSAD data in conjunction with other data sources could be suggested to our NPSAD collaborators. For example, the paper by Kalk et al. (2022) on gabapentinoids could be extended geographically to include Scottish drug-related deaths data via the existing EU-MADNESS arrangement with the National Records of Scotland, as well as using prescription data, and bringing the datasets up to date.

Another prescription drug that is overdue an update is buprenorphine. It is almost two decades since the author and colleagues last looked at UK fatalities related to use and availability (Schifano et al., 2005). Although the Home Office has ceased to publish data on seizures (confiscations, interdictions, etc.) of buprenorphine, looking at the relationship between deaths and prescription data would merit consideration.

Chapter overview

This chapter has outlined how 'at risk' groups and populations can be defined, and approaches that can be employed to identify such groups. It then briefly discussed the types of study that can be used to provide profiles of 'at risk' groups/populations, using a combination of profiling (a) decedents' socio-demographic characteristics and (b) characteristics of deaths. These were illustrated by way of 15 selected studies, across a range of substances and scenarios, with which the author was directly involved. His on-going data collection activities and planned outputs are also outlined.

Finally, the purposes of profiling 'at risk' groups were considered. A range of factors important at the local level were identified here. 'Higher level' or macro factors influencing drug-related deaths at the national (and international) level are considered in Chapters 8 to 12. These external factors provide the backdrop against which local scenarios occur.

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PART 4 - RELATIONSHIP(S) BETWEEN DRUG DRUG-RELATED DEATHS AND OTHER DRUG INDICATORS

Drug-related deaths (DRDs) do not occur in a vacuum. A range of factors can lead to a death, influence how it occurs, how it is identified, reported, recorded and analysed. Identifying such factors is the subject of Part 3 (Chapters 6 and 7). In particular, Chapter 7 illustrates/explores how the interplay between some of these factors and others can be understood in the context of specific *ad hoc* studies undertaken using data on deceased individuals from Special Mortality Registers (SMRs).

In this Part (Part 4), an investigation is undertaken of the statistical inter-relationship(s) between DRDs, using data either published or provided by the United Kingdom (UK) General Mortality Registers (GMRs), and other relevant key 'drug indicators' at a population level. This descriptive and correlational study covers the period 1990 to 2022, where data availability allows.

Chapter 8 provides a brief section on context-setting, a definition of 'drug indicator' and outlines of the drug classes and substances examined, the indicators, measures and sources used. The statistical approach for investigating the relationships between indicators is then presented. The essence of this Part comprises the results for each of the drug classes and index substances covered, accompanied by brief commentaries and comparisons with other studies (where they exist) using the same approach. Chapter 9 looks at the commonest drug groups implicated in UK DRDs: opiates/opioids and hypnotics/sedatives. Stimulants (cocaine, 'crack', amphetamines, 'ecstasy' (MDMA), and mephedrone) are the focus of Chapter 10. Chapter 11 looks at the remaining drug classes and index substances: cannabinoids; anaesthetics/dissociatives; Central Nervous System (CNS) depressants, and Novel Psychoactive Substances (NPS). Chapter 12 presents a brief discussion and summary of the main findings of Part 4, together with a section on the strengths and limitations of this study.

CHAPTER 8: CONTEXT-SETTING FOR EXAMINING ASSOCIATIONS BETWEEN DRUG INDICATORS

"Failing the possibility of your measuring that which you desire, the lust for measurement may, for example, merely result in your measuring something else – and perhaps forgetting the difference – or in your ignoring some things merely because they cannot be measured."
Yule (1921:108)

"If ... we choose a group of social phenomena with no antecedent knowledge of the causation or absence of causation among them, then the calculation of correlation coefficients, total or partial, will not advance us a step toward evaluating the importance of the causes at work."
Fisher (1970:192)

“Regression analysis is the hydrogen bomb of the statistics arsenal.”
Wheelan (2013:213)

"In statistics, what disappears behind rows of numbers is death."
Grass (2002)

Introduction

This chapter comprises a brief section on context-setting for Part 4 of this thesis. A definition of ‘drug indicator’ is presented. This is followed by outlines of the drug classes and substances examined, the indicators, measures and sources used. The statistical approach for investigating the relationships between these drug indicators is then explained.

Previous United Kingdom studies looking at Drug-Related Deaths and other drug indicators

The analyses reported on and presented here use an ‘ecological’ approach, i.e., looking at a specific outcome (drug-related deaths) in relation to different ‘exposures’ (e.g., factors, influences, etc.) at a population level. In the present context, the author is using the term ‘drug indicator’ to mean an objective quantitative epidemiological measure that defines a dimension of drug-related phenomena. It is used here to convey the notion of statistical information relating to the different elements describing the drugs phenomenon: (a) cultivation, production and manufacture; (b) demand and use; (c) availability, supply, price, purity and potency; (d) harms, including hospital admissions and deaths; and (e) treatment.

Several of these robust national indicators have been used in previous studies conducted by the author and colleagues: amphetamine-type stimulants (Schifano et al., 2007); buprenorphine (Schifano et al., 2005); cocaine/crack (Schifano and Corkery, 2006; Schifano and Corkery, 2008); ecstasy (MDMA/MDA) (Schifano et al., 2006); ketamine (Corkery et al., 2021a). The aims of these studies were to see if such indicators were inter-related across a number of drugs, and to ascertain if they were appropriate to contribute to descriptive overviews of trends for specific drugs, i.e., to provide a narrative or context for drug deaths associated with a number of index drugs (Schifano and Corkery, 2008). The author and colleagues believe that these seminal works provide a solid foundation for both (a) extending this approach to other drugs but also (b) to repeat, extend and update the studies already conducted, including that on ketamine. These were the aims of Part 4 of this thesis.

Materials for new analyses undertaken as part of this doctoral research programme

The range of drug classes and index drugs examined are detailed in Table 8.1. It will be noted that the range of classes has been widened considerably, and thus the substances they cover.

Table 8.1: Drug classes and specific drugs selected for analysis

Drug class	*Specific drug(s)*
Opiates/opioids	Heroin/morphine, methadone
Benzodiazepines	Any benzodiazepine, diazepam, temazepam
Stimulants	Cocaine (including 'crack'), amphetamines, 'ecstasy' (MDA, MDMA), mephedrone
Cannabinoids	Cannabis
Anaesthetics/Dissociative	Ketamine
Antidepressants	Barbiturates
Central nervous system depressants	GHB/GBL
Novel Psychoactive Substances (NPS)	Any molecule classified as an NPS
Notes: GBL = gamma-Butyrolactone; GHB = gamma-Hydroxybutyric acid ; MDA = 3,4-Methylenedioxyamphetamine; MDMA = 3,4-Methylenedioxymethamphetamine	

Based on his previous extensive knowledge of and familiarity with sources for UK information on drug indicators (especially deaths, treatment, drug seizures, drug offenders/offences, price and purity), their 'gatekeepers', geographical and temporal coverage, etc., the author devised the schema below (Table 8.2) to map the indicators, the measures used and data sources. There are no robust indicators to cover: (a) cultivation, production and manufacture; and (b) demand across the period reviewed. However, information is available for: (c) prevalence of use; (d) availability, supply, price, purity and potency; (e) harms, including hospital admissions and deaths; and (f) treatment. The nine main drug indicators cover the following facets: death numbers; price; purity, drug offenders/offences; prevalence of use; availability; treatment for dependence; hospital admissions; and accesses to poison information.

Table 8.2: Indicators, measures and sources used in analyses

Indicator	*High level measures*	*Sources*
Death	Number of deaths registered in year: UK and constituent countries	Office for National Statistics; National Records of Scotland; Northern Ireland Statistics & Research Agency
Price	UK street level (£) per unit (gram, pill, etc.)	UK Focal Point reports to EMCDDA; National Criminal Intelligence Service/National Crime Agency; Home Office Statistical Bulletins; UNODC World Drug Report
Purity	UK percentage purity (police, Customs/Border Force), weighted mean street purity, cannabis potency, content of ecstasy tablets	Forensic Science Service Drugs Intelligence Unit; Home Office Statistical Bulletins; UK Focal Point reports to EMCDDA; National Crime Agency; UNODC World Drug Report;, LGC/Eurofins
Drug offenders and offences	Number of offenders found guilty, cautioned, etc.; drug possession, drug trafficking offences: UK, England & Wales, Scotland, Northern Ireland	Home Office Statistical Bulletins; Police Scotland; Police Service of Northern Ireland
Prevalence	Lifetime & last year use, broken down by age-group and by country; estimated number of users – lifetime and last year for England & Wales	British Crime Survey/Crime Survey for England & Wales (Home Office/Office for National Statistics); Scottish Criminal Justice Survey (Scottish Government): Drug Prevalence Survey (Department of Health, Northern Ireland)
Availability	Number and quantity of seizures (UK/England & Wales/Northern Ireland); number of seizures and amount seized for possession & supply offences (Scotland); Number of prescription items (specific drugs) by country and UK	UK police forces; Customs/Border Force; Police Scotland; Police Service Northern Ireland; Prescription Cost Analysis (NHS Business Services Authority – England; NHS Wales Shared Services Partnership; ISD Scotland; HSC Business Services Organisation – Northern Ireland)
Treatment	Number starting agency episodes, primary (drug) presentation, any (drug) presentation, never previously treated, all in treatment; adults, young people; opiate/heroin – breakdowns vary by country	Home Office Statistical Bulletins; Regional DMDs; NTA (England); Welsh DMD; Scottish DMD; Northern Ireland DMD; EMCDDA Statistical Bulletins
Hospital admissions	Admissions/stays (definition varies by country) broken down by ICD-10 codes (only available for limited number of drug classes/ index substances)	NHS digital (England); Public Health Wales; Public Health Scotland; Public Health Agency Northern Ireland
Accesses to poison information	Telephone calls to the National Poisons Information Service; online accesses to Toxbase	National Poisons Information Service (UK)

Notes: EMCDDA = DMD = Drug Misuse database; European Monitoring Centre for Drugs & Drug Addiction; HSC = Health & Social Care; ISD = Information Services Division; LGC = Local Government Chemist; NHS = National Health Service; NTA = National Treatment Agency for Substance Misuse; UK = United Kingdom; UNODC = United Nations Office on Drugs & Crime

Materials and methods

Data and data sources

Deaths

Information on deaths resulting from drug poisoning were derived from statistics published by the three UK GMRs (Office for National Statistics; National Records for Scotland; Northern Ireland Statistics & Research Agency), supplemented by information from data requests made by the author. Detailed information on definitions, death investigations, data collection, coding, etc. can be found in Chapters 2 to 4.

Price

Prices are given in pounds sterling without any adjustment for inflation. They relate to average UK street-level prices per gram for most substances but to tablet/dose for ecstasy as reported by police forces to the National Crime Intelligence Service/National Crime Agency. Historically, these prices were based on police officers asking dealers how much they charged, users how much they paid for the amount found in their possession, and in some areas from test purchases. This information was then reported centrally on a voluntary basis. There are, therefore, concerns about consistency and representativeness (Sutton and Maynard, 1992). However, this is the only long term source of information available. This source was used by the author in the Home Office statistical bulletins he was responsible for compiling, e.g., Corkery (2002). This information was also provided to the EMCDDA and UNODC for their annual statistical publications. Price data are not available for all the drugs considered here.

Purity

Information on the purity levels of drugs interdicted (seized) in the UK are only available over time for powdered drugs, i.e., heroin, cocaine, 'crack' cocaine and amphetamine. Information was available on both average MDMA dosage levels per tablet and ecstasy content in terms of MDMA, MDA, MDEA, MBDB based upon analyses conducted by the Forensic Science Service (FSS). This information was collated by the FSS Drugs Intelligence Unit and provided to the Home Office for inclusion in their statistical bulletins (see, for example, Corkery, 2002). Following the closure of the FSS, information on these issues was provided by the Local Government Chemist (LGC) and subsequently Eurofins in their restricted circulation quarterly bulletin "Class A". The author has had access to these sources since 1994. Data from these sources were provided for the EMCDDA and UNODC annual statistical outputs.

Information on the potency of cannabis is somewhat patchy and inconsistent. The data used for this investigation were taken from four *ad hoc* studies (Bone and Waldron, 1997; Hardwick and King, 2008; Potter et al., 2008; Potter et al., 2016), supplemented by returns made by the UK Focal Point to the EMCDDA (EMCDDA, 2022).

Drug offenders and offences

Information on convictions is derived from the respective legal systems in the different parts of the UK. The police provide information on the disposals (sanctions) which they can apply, such as cautions, cannabis and khat warnings, etc.

The Home Office collated this information and published Statistical Bulletins on a UK-wide basis on the number of persons dealt with (convicted, cautioned, etc.) for any drug offences, as well as breakdowns for specific drugs and disposals (such imprisonment, fines, etc.), for the period up to and including 2002 (Ahmad and Mwenda 2004). Statistics for England and Wales were only published for a further two years (Mwenda, 2005).

Since then, other measures of police activities in respect of drug offences, i.e., offences recorded by the police (recorded crime) have had to be used for England and Wales, but these do not provide the same continuity of approach, measurement, and level of detail as the historic Home Office Statistics. What information is available for England and Wales covers the period from 2006 to 2016 and has been taken from UK Focal Point reports.

The Home Office was split in May 2007 with the new Ministry of Justice taking over responsibility for statistics on convictions, although the Courts Proceedings statistics section of the Home Office used to provide the detailed output for the Drug Seizures and Offenders Statistical Bulletin (Corkery, 2002). Devolution has resulted in different definitions and approaches to reporting statistics. It is difficult, therefore, to derive detailed UK-wide statistics on a consistent basis across the last 20 years of the time-period examined here.

Some information on drug possession and trafficking offences is available for Scotland, derived from crimes associated with drug seizures (Scottish Government, 2023). However, these are very different to the data collated by the Home Office, limited to the age characteristics of drug possession offenders in a statistical publication which looks primarily at drug seizures.

No information has been available for convictions and cautions relating to specific drug offences in Northern Ireland since 1996 (Corkery, 2002). Information on Drug Arrests is included in the annual statistical publications from the Police Service of Northern Ireland (PSNI), see PSNI (2023). There is information available for possession offences (cannabis) from the recorded crime system from 2007 (see PSNI, 2022).

Prevalence

The Crime Survey for England and Wales (CSEW) has been conducted by ONS since 2020. Previously, this survey and its predecessor, the British Crime Survey (BCS), was run by the Home Office. The survey has included a drug misuse component since its inception in 1992. In the early years of its existence, the drugs component took place every two or three years before becoming an annual occurrence. The Covid-19 pandemic meant the 2021/22 sweep did not take place. The most recent figures are for the year ending June 2022 (ONS, 2022).

The drug misuse self-completion component of the BCS/CSEW asks about drug use (i.e., heroin, methadone, cocaine, crack cocaine, ecstasy, heroin, LSD, magic mushrooms, etc.) over the respondent's lifetime, in the last year and in the last month. Occasionally, other substances, such as khat, mephedrone and ketamine have been included.

Figures relate to general household surveys of 16-59 year-olds conducted in England and Wales only. The results for young people were for respondents aged 16-29 for the 1992, 1994, 1996 and 1998 sweeps, but for 16-24-year olds from 2000/01. Figures for intermediate years e.g., 1995 were the mid-point between the rates for the year preceding and year following e.g., 1994 and 1996. Estimated numbers of individuals using index drugs during respondents' lifetime, last year and last month are derived by multiplying the prevalence rate by the relevant mid-year population estimates in the age-groups covered. Such estimates have been typically available from about 2002/3.

The fact that the survey only covers individuals aged 16 to 59 years living in households means it has several limitations. It does not cover all ages. It does not cover those individuals who live alone, are homeless or roofless, and those who live in residential institutions, e.g., boarding schools, university accommodation, penal establishment, hospitals, care homes, rehab centres, etc. Therefore, many 'at risk' and drug misusing populations are missed. Given that use of some drugs, e.g., heroin and methadone, may be relatively low in households, the prevalence figures for such substances may well be under-estimated.

There are much more limited survey data available for other parts of the UK. In Scotland, the Crime and Justice Survey has a section on 'illicit substance use'. It uses a similar approach to the CSEW, in that it is a household survey of individuals aged 16 to over 60 years. However, the focus is on use in the last 12 months prior to the survey. The survey has been running every few years since 1993. The latest survey covers 2019/20 (Scottish Government, 2021). The same limitations as those for the CSEW apply here; perhaps even more so because of the vastly lower number of respondents in Scotland (e.g., 4,880 vs. 20,903 for the 2017/18 sweeps).

Information for Northern Ireland is derived from two sources: (a) the Northern Ireland Crime Survey (Toner and Freel, 2010) for 1998-2009; and (b) the All Ireland Drug Prevalence Survey (NACDA & Department of Health, Northern Ireland, 2017) for 2002/03-2014/15. Data on the prevalence of drug misuse is less well covered than the other parts of the United Kingdom in terms of the time-period examined in this chapter. The age-range and periods of use employed by Crime Survey were the same as for the CSEW; however, the Drug Prevalence Survey used the EMCDDA definition of 15-64 year-olds. The 2009 sweep of the Crime survey had 2,224

respondents and the latest sweep of the Drug Prevalence Survey had 2,500 respondents in Northern Ireland. The limitations noted for the CSEW also apply in Northern Ireland.

Availability

There are two separate sources of information on the availability of drugs. Due to the clandestine nature of the phenomenon, there is no accurate information available on the quantities of illicit drugs manufactured or supplied in the UK. The only measure of availability of illicit drugs is the quantities 'seized' by law enforcement agencies (police forces, National Crime Agency (formerly National Crime Squad), Border Force, and historically Her Majesty's Customs & Excise). In this context, drug 'seizures' mean confiscation, interdictions, interceptions, etc. As far as the author is aware, there is no published information on the number of cannabis plants grown in the UK, although the number seized is known. The data used for this chapter are the number of seizures and quantities seized.

As noted earlier, the Home Office published UK drug seizure statistics in the same statistical bulletin as the drug offender statistics for the period up to 2002. Statistics for seizures and offenders continued at UK level for the next two years. However, data published for the period from 2005 to date have only covered England and Wales (Home Office, 2023). The Scottish Government (2023) have published data on a range of drugs; however, there was a gap between 2007 and 2009. The information provided is on a similar basis to that used by the Home Office. The Police Service of Northern Ireland (PSNI) publish information on most of the main drugs traditionally covered by the Home Office Statistical Bulletins (PSNI, 2023). Where necessary, the author has made successful data requests to PSNI's statistical branch.

The second way of considering availability relate to prescription drugs. The key measures considered by this thesis in this respect are the number and quantity of prescriptions dispensed on the National Health Service. Information on private prescriptions is not collated at national levels. However, each part of the UK publishes information from its Prescription Cost Analysis databases. Information is currently available online for prescriptions dispensed in the community for the period since 2001, although the author has managed to collect and track down data for earlier years, especially England. For the present analyses reported here, the author has only included information on the number of items dispensed so as to lessen the time taken to prepare data for this chapter; quantities dispensed are omitted. It important to note that such information does not cover: illicit purchases, importations, etc. of prescription drugs; illicit manufacture of counterfeit drugs; the diversion of legitimately dispensed drugs; or thefts of prescription drugs, etc.

Treatment

The Home Office Addicts Index provided information on 'notified addicts' for Great Britain for the period up to 1996 (Corkery, 1997). The Index only covered notifications about individuals seeking treatment for addiction to (dependence on) 13 opiates/opioids (including diamorphine/heroin and methadone) and cocaine. Similarly, the Northern Ireland Addicts Index monitored 'registered addicts' to the same list of drugs. Published data are available for the period 1992-2012 (PHIRB, 2013).

Devolution led to the different parts of the UK either continuing with their own national drug misuse databases or setting up a new one (e.g., Northern Ireland). Regional Drug Misuse Databases were introduced in Great Britain in 1993; collated data was published for the period 1994-1999); the focus was on England, but some statistics were also presented for Great Britain (Department of Health, 2000). The statistics covered individuals presenting with drug dependence on a number of substances, including the following: heroin; methadone; barbiturates; benzodiazepines; amphetamines; cocaine; cannabis; antidepressants; and ecstasy.

Treatment data for England are derived from the National Drug Treatment Monitoring System (NDTMS) which was set up in 2003 (NDEC, 2023). Although the NDEC website hosts an interactive dashboard, there is no provision for drilling down into information for specific substances. However, the annual NDTMS statistics are published online by the Office for Health Improvement and Disparities (OHID). OHID presents statistics separately for adults and young people (< 18 years), thus there can be some overlap as young people become adults during the year being reported on. Data available online on the OHID website (https://www.gov.uk/government/collections/alcohol-and-drug-misuse-and-treatment-statistics) cover the period from 2016/17, but previous statistics back to 2005/06 for adults and 2009/10 for young people are available from the archived National Treatment Agency (NTA) website (https://webarchive.nationalarchives.gov.uk/ukgwa/20170807160711/http://www.nta.nhs.uk/statistics.aspx). The statistics published by OHID include the following substances: cannabis; cocaine; 'crack'; benzodiazepine; amphetamine (other than ecstasy); ecstasy; antidepressant; barbiturate. There is no separate breakdown for heroin or methadone; they are subsumed within the 'opiate (not crack cocaine)' category. A separate classification for 'club drugs' includes: ecstasy, mephedrone; ketamine; GHB/GBL; methamphetamine; and NPS.

Annual reports on substance misuse in Wales are published by the Welsh Government. The most recent annual report provides statistics, for 2016/17 – 2020/21, on the main problematic drug use of individuals starting treatment, broken down by gender, median age and age-group;

these include the following substances – heroin, cannabis, cocaine, methadone, amphetamines, crack cocaine (Welsh Government, 2022). Time series are also available for treatments by main problematic substance; however, the range of substances also includes: cocaine; benzodiazepines; and ecstasy. Other reports are available for 2019 and 2020 (https://www.gov.wales/substance-misuse-annual-reports), and also 2018 (https://www.gov.wales/substance-misuse-wales-2018-2019-treatment-data) covering the period back to 2014/15. Public Health Wales also presents some limited information in its "Data mining Wales: The annual profile for substance misuse" series; these cover the period from 2011/11 to 2021/22 (https://phw.nhs.wales/publications/). However, as not all issues are available online, the author obtained earlier reports from one of the co-authors of the most recent one.

The Scottish Drug Misuse Database was set up in 1990 to "collect information about people in Scotland with drug problems" (ISD, 2015). Information on treatment presentations in 1997/98 was first included in the first issue of the Drug Misuse Statistics Scotland series published by the newly formed Information & Statistics Division (ISD) of the Scottish Government (ISD, 1999). The full series of statistical publications bearing on this database are available on the Public Health Scotland website: here for 1998-2010 annual reports https://www.isdscotland.org/Health-Topics/Drugs-and-Alcohol-Misuse/Drugs-Misuse/Historic-Publications/ and here for the period up to 2020 https://www.isdscotland.org/health-topics/drugs-and-alcohol-misuse/publications/. The most recent statistics cover 2020/21 (Public Health Scotland, 2023). The information provided covers all drugs and main drugs used; the former include: heroin; methadone; dihydrocodeine; diazepam; amphetamines; cocaine/crack cocaine; ecstasy; cannabis; and gabapentinoids. The Scottish Drugs Misuse Database (SDMD) was closed in March 2021 due to the introduction of the Drug and Alcohol Information System (DAISy). Open data for financial years 2021/22 onward are available at: https://www.opendata.nhs.scot/dataset/initial-assessments-for-specialist-drug-and-alcohol-treatment.

The Northern Ireland Substance Misuse Database includes information on the following substances: cannabis; benzodiazepines; cocaine; 'crack'; ecstasy; amphetamines; heroin; tramadol; fentanyl; oxycodone; pregabalin; 'Z' drugs; ketamine; and NPS (Foster et al., 2022). The latest statistics provide breakdowns by drug for gender, age-groups and Health & Social Care Trusts. Previous publications had less detail and presented data in a different way (see, for example, Foster et al., 2018). Information is available online for the periods 2001/02 - 2016/17 (https://www.health-ni.gov.uk/publications/statistics-northern-ireland-substance-misuse-database-200102-202021) and 2020/21 - 2021/22, although the accompanying datasets are only available for 2016/17, 2020/21, and 2021/22.

From the above descriptions it is possible see how difficult it is to compile statistics at a UK level. This is primarily due to differences (lack of consistency) in case definition, substances listed, gaps in time-period covered, and a lack in the continuity of sources. The only study of which the author is aware that has tackled the last aspect looked at the relationship between the Home Office Addicts Index and the Regional Drug Misuse Databases (Hickman et al., 2004). To try and mitigate these challenges, the annual returns from the UK Focal Point to the EMCDDA have been used, where available.

Hospital admissions

NHS Digital published Statistics on Drug Misuse for England for the period ending 2020. These statistics were integrated into the new Statistics on Public Health publication, issued by ONS, following a consultation in early 2022. The earlier publications are still available on the new website (https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-public-health/). The latest figures are for 2020, and include: "the number of NHS hospital admissions for drug-related mental and behavioural disorders (primary diagnosis of a drug-related mental and behavioural disorder), the number of NHS hospital admissions where drug-related mental and behavioural disorders were a factor (primary or secondary diagnosis of drug related mental and behavioural disorders), and the number of NHS hospital admissions for poisoning by drug misuse (primary diagnosis of poisoning by drug misuse involving a controlled substance)" (NHS Digital, 2021).

The first category covers ICD-10 codes (WHO, 1992) F11-F19. As can be seen from Table 8.3 the only index substance identified is cocaine (F14); other substances are grouped together, some based on their chemical structure e.g., opioids (F11)), others on their effects e.g., hallucinogens (F16). The breakdowns for poisonings are more specific for opiates/opioids, i.e., opium, heroin and methadone have their own T codes (see Table 8.4). Although there are additional T codes available for other substances, e.g., T423 (barbiturates) and T424 (benzodiazepines), they are not routinely used for data collection in hospitals. Thus, there is a distinct lack of granularity.

Table 8.3: F codes used for completed hospital admissions with a primary diagnosis of drug related mental and behavioural disorders

F11	Mental and behavioural disorders due to use of opioids
F12	Mental and behavioural disorders due to use of cannabinoids
F13	Mental and behavioural disorders due to use of sedatives or hypnotics
F14	Mental and behavioural disorders due to use of cocaine
F15	Mental and behavioural disorders due to use of other stimulants, including caffeine
F16	Mental and behavioural disorders due to use of hallucinogens
F18	Mental and behavioural disorders due to use of volatile solvents
F19	Mental and behavioural disorders due to multiple drug use and use of other psychoactive substances

An analysis of admissions during 2008 to the Guys & St Thomas Emergency Department (ED), London, found that "only 13.2% of all acute recreational drug toxicity presentations would have been identified based their primary ICD-10 diagnostic code" (Wood et al., 2011). The authors concluded that such presentations were not being appropriately coded. As noted above, there are often no specific ICD-10 codes available for the drugs involved in acute recreational drug ED admissions.

Table 8.4: T codes used for finished admission episodes with a primary diagnosis of poisoning by drug misuse

T400	Poisoning: Opium
T401	Poisoning: Heroin
T402	Poisoning: Other opioids[5]
T403	Poisoning: Methadone
T404	Poisoning: Other synthetic narcotics
T405	Poisoning: Cocaine
T406	Poisoning: Other and unspecified narcotics
T407	Poisoning: Cannabis (derivatives)
T408	Poisoning: Lysergide [LSD]
T409	Poisoning: Other and unspecified psychodysleptics [hallucinogens]
T436	Poisoning: Psychostimulants with abuse potential

A survey of 176 Clinical Coding Departments of acute hospital trusts in England and Wales, undertaken by the same research team, looking at this issue found that such admissions for drug toxicity are either assigned a wide range of primary codes or recreational drug use remains uncoded (Shah et al., 2011).

An earlier study compared results from published studies with Hospital Episode Statistics (HES) for England and concluded that the latter “grossly underestimate the burden of drug-induced disorders as a cause of hospital admission” (Waller et al., 2005). The researchers concluded that underlying reasons for this may include: “under-recognition, under-recording and limitations of the coding system”. The unavailability of detailed data on individual cases limits the potential of such information for identifying previously unrecognised serious adverse drug reactions (ADRs).

These issues are not unique to the UK. For example, an Australian study found that the Australian Modification to ICD-10 (ICD-10-AM), when used in coding surveillance, is an effective and efficient method of improving ADR reporting when employing data collected for administrative purposes (Nair et al., 2018). Similar studies have been conducted on other continents (e.g., Hohl et al., 2014; Martins et al., 2018; Cheng et al., 2021).

On a more constructive note, although the range of hospital admissions for specific drugs is limited they can be used to examine the impact of certain drugs on ED workloads. The author contributed information on Hospital Episode Statistics in England to an EMCCDA study which looked at cocaine-related emergencies in Europe (Mena et al., 2013; EMCDDA, 2014).

Information on drug-related hospital admissions in Wales is included in the annual profile for substance misuse published by Public Health Wales (Whelan and Smith, 2022). The main drug groups/index substances reported on are: opioids; cannabinoids; cocaine; and benzodiazepines. The latest profile, for 2021/22, notes that “no distinction is possible in hospital admission data for differentiation between cannabinoid products: cannabis resin, stronger strains of herbal cannabis ‘skunk;’ or newer forms of synthetic cannabinoid receptor agonists (SCRAs), sometimes referred to as ‘Spice’ “ (Whelan and Smith, 2022:22). Although Chart 5 (page 23) in this publication provides numbers for each group/drug from 2012/13 to 2021/22 for drug poisoning admissions, there is no legend to inform the reader as to which coloured lines represents specific substances! Fortunately, the previous annual profile does contain such a legend; the assumption is that the colours are consistent year on year.

Other Welsh data are available, using the ICD-10 F and/or T codes for an earlier period (1999/2000 - 2012/13) for a wider range of substances, including heroin, benzodiazepines, cocaine, cannabinoids, and barbiturates, from the Patient Episode Database for Wales (PEDW). Information was published on primary diagnosis by 3 and 4 character ICD-10 codes by the NHS Wales Informatics Service. The author had downloaded the historic datasets about a decade ago. These are now archived but available online back to 2014/15 (https://dhcw.nhs.wales/information-services/information-delivery/archived-pedw-data-online/).

However, bespoke data requests can be made to Digital Health and Care Wales; the author was also given access to download datasets.

Information on drug-related hospital admissions was included in the Drug Misuse Statistics Scotland published by ISD from their first publication in covering 1997/8 (ISD, 1999). Historic reports and data are available here (https://www.isdscotland.org/Health-Topics/Drugs-and-Alcohol-Misuse/Drugs-Misuse/Historic-Publications/) and here (https://www.isdscotland.org/Health-Topics/Drugs-and-Alcohol-Misuse/Publications/).

Information on drug-related hospital statistics from 2018/19 onwards are available as online reports and datasets on the Public Health Scotland website (https://publichealthscotland.scot/publications/show-all-releases?id=32315). The latest information (2021/22) for drug-related hospital statistics is now available in a published report (Public Health Scotland, 2022) and trend data back to 1996/97 are available via a Public Health Scotland dashboard (https://publichealthscotland.scot/publications/drug-related-hospital-statistics/drug-related-hospital-statistics-scotland-2021-to-2022/summary/).

The breakdown for admissions and overdoses (poisonings) by drug class/index substance (because of the ICD-10 F and T codes used) is as noted above for other parts of the UK. Thus, the same observations and limitations apply here.

In Northern Ireland, the Department of Health publishes annual updates on episode based activity. The latest figures (2021/22) and those back to 2011/12 are available here (https://www.health-ni.gov.uk/articles/episode-based-activity). Earlier information is available using the search facility on https://www.health-ni.gov.uk/publications.

The latest publication comprises four volumes which detail key information on all activity and provides breakdowns of activity by specialty, diagnosis, procedure/intervention and healthcare resource group. The relevant volume for the purposes of the analyses covered by this chapter is volume 2 (Hillen and Morgan, 2022). As noted above, breakdowns by drug class/index substance are restricted by the ICD-10 F and T codes available. The author has been able to locate and extract information for the period back to 1996/7.

Accesses to poison information

The main source of information in the UK on inquiries about poisons, including psychoactive drugs, is the National Poisons Information Service (NPIS). NPIS is commissioned by the UK Health Security Agency on behalf of all four national health departments. The agency has a

24/7 telephone advice service and an internet database “TOXBASE” (www.toxbase.org) which is only accessible to registered healthcare departments, etc. TOXBASE is also available on Apple and Android smart phones. The two measures considered appropriate to look at by this agency are: (a) calls to the Helpline and (b) TOXBASE accesses. Some information on these functions is available in the NPIS annual reports (see, for example, NPIS, 2022). However, the information is not provided on a consistent basis. The data on individual drug classes/index substances used for analyses in this chapter are based, in part, on information extracted from NPIS annual reports. In addition, data on telephone calls and online accesses to TOXBASE for the years 2016/7 to 2022/3 have been provided to the author by Professor Simon Thomas, NPIS Newcastle. Some of the latter information is not in the public domain.

Data entry and analyses

Data from the sources outlined above were first extracted from the individual sources into a series of Excel datasheets (one for each substance) contained within a single Excel for Microsoft 365 workbook. Each datasheet had the same structure to provide consistency and facilitate data entry; rows represented the year and columns the specific variables/parameters. All data items were entered, double-checked, and amended (if necessary) by the author. The latest version of data were entered (as at August 2023) so that they are consistent with any revisions made by data suppliers. It may be that retrospective changes may be made to data published subsequently by data suppliers.

Data entry for these time series was very time-consuming, since several tens of thousands of data items had to be input across 9 indicators for 15 drug classes/substances; covering to 33 years; with up to 130 measures/parameters for a single drug (i.e., cannabis). The values in the Microsoft Excel datasets were then imported into IBM® SPSS® (version 28) datafiles. Some data cleaning was necessary, e.g., to convert ‘string’ variables to numeric ones, standardise the number of decimal points for specific variables, and convert ranges to a single (mean) number.

Although other approaches, such as Time Series Analysis and Partial Regressions, could have been conducted to examine relationships between the nine Indicators and their specific measures/parameters, the author opted for continuity of approach. The earlier studies which he had conducted with colleagues had used the Pearson correlation coefficient to identify possible correlations between different indicators. Two-tailed tests were employed due to the possibility of both positive and negative relationships; the latter are designated by a minus sign preceding the coefficient values in the tables. Therefore, the same method was used for the investigations reported in this Part of the thesis.

A negative correlation exists where one variable (indicator) decreases as another variable (indicator) increases or *vice versa*, e.g., prevalence of drug use increases as drug prices fall. A positive correlation exists where one variable (indicator) increases as another variable (indicator increases) - but not necessarily at the same rate, e.g., drug prices rising as drug purity increases.

There is no commonly agreed or standard interpretation of how the strength of correlation coefficients should be described. There are differences as to what ranges of values are grouped together, let alone what labels (descriptions) are attached to them. Furthermore, the cutoff points between these ranges "are arbitrary and inconsistent" (Schober et al., 2018). Schober et al. (2018) argue that instead of "using oversimplified rules, … a specific coefficient should be interpreted as a measure of the strength of the relationship in the context of the posed scientific question. Note that the range of the assessed values should be considered in the interpretation, as a wider range of values tends to show a higher correlation than a smaller range…". It should also be remembered that a "statistically significant correlation does not necessarily mean that the strength of the correlation is strong" (Akoglu, 2018).

Table 8.5: Examples of interpreting the strength of correlation coefficients

Correlation coefficient (+ or -)	Dancey & Reidy (2007) (Psychology)	Duffy et al. (2011) (Politics)	Chan (2003) (Medicine)	Schober et al. (2018) (Anaesthesiology)	Calkins (2005) Andrews University
1.0	Perfect	Perfect	Perfect	Very strong	Very high
0.9	Strong	Very strong	Very strong	Very strong	Very high
0.8	Strong	Very strong	Very strong	Strong	High
0.7	Strong	Very strong	Moderate	Strong	High
0.6	Moderate	Strong	Moderate	Moderate	Moderate
0.5	Moderate	Strong	Fair	Moderate	Moderate
0.4	Moderate	Strong	Fair	Moderate	Low
0.3	Weak	Moderate	Fair	Weak	Low
0.2	Weak	Weak	Poor	Weak	Little if any
0.1	Weak	Negligible	Poor	Weak	Little if any
0.0	Zero	None	None	Negligible	Littke if any

Table 8.5 provides some examples of correlation coefficient interpretations from a range of disciplines. The author has applied his own rules to the interpretation of the results presented below: p values of 0.000 are considered very highly statistically significant, those below 0.01 are considered highly statistically significant, those above 0.01 are not presented in the main text. However, in reality, $p<0.05$ is acceptable universally.

Where data allowed, analyses were undertaken at country levels as well as at the UK level. For some indicators this meant using UK level data (such as price, purity, potency, and NPIS accesses) as proxy measures at the national level. On the other hand, in some cases it was not

possible to collate UK-level data due to different ways of categorising data, e.g., age-group for prevalence, or different offence definitions (across the whole of the period examined).

Since reading of SPSS output files requires access to SPSS or an SPSS file reader, the output files were exported as Excel spreadsheets. Some of these are small enough to be captured as graphic files and presented as figures in the text. However, many of them are very extensive and not easy to follow when converted into pdf format. For consistency and ease of access, the Excel spreadsheets are embedded in Appendix F so that readers may view them.

Results

The key results from the Pearson correlation coefficient analyses (using two-tailed tests) are presented as tables in the relevant drug class/substance section below. The number of data points refers to the number of years for which data were available for the relevant variable. Fifteen drug classes/index substances are considered at five geographical levels (UK, England, Wales, Scotland and Northern Ireland); a theoretical total of 75 sets of correlational analyses. However, due to a lack of data for some countries for three index substances (GHB, ketamine, mephedrone), the results covered here relate to a lower total of correlational sets.

Table 8.6: Abbreviations and symbols used in Results

£	Pound sterling
CJS	Criminal Justice System
DMD	Drug Misuse Database
DTI	Drug Treatment Indicator
E	England
E&W	England and Wales
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
Est no	Estimated number
FG	Found Guilty
FG/Caut	Found Guilty/Cautioned
FP	Focal Point
FSS DIU	Forensic Science Service Drugs Intelligence Unit
GB	Great Britain
HOSB	Home Office Statistical Bulletin
JC	John Corkery (author's calculation)
Kg	Kilogram
LGC	Local Government Chemist
MDMA	3,4-Methylenedioxymethamphetamine
mg	Milligram
MoJ	Ministry of Justice
NCA	National Crime Agency
NI	Northern Ireland
No	Number
NPIS	National Poisons Information Service
RDMD	Regional Drug Misuse Database
S	Scotland
SCJS	Scottish Crime and Justice Survey
TabPres	Tablets prescribed
UK	United Kingdom
UK FP	United Kingdom Focal Point
W	Wales

The abbreviations and symbols listed in Table 8.6 are used in Chapters 9 to 11. The detailed correlation matrices are presented in Appendix B. The results for each drug class/substance are discussed in the light of previous studies of a similar nature, if any, by the author and colleagues as well as other researchers.

Chapter overview

This chapter has outlined the potential sources of data for the statistical analyses presented in Part 4 of this thesis. Information regarding their availability is provided. A description of the index drugs and drug classes examined are provided, along with the ICD-10 codes used for categorising DRDs. Detailed information is provided on the statistical approach and the associated statistical test applied. The contents of this chapter provide the context for the other chapters in this Part.

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CHAPTER 9: DRUG INDICATOR ASSOCIATIONS FOR OPIATES/OPIOIDS AND HYPNOTICS/SEDATIVES

"We found that regardless of the type of opioid-related death, a large number involved polysubstance use, as observed previously…
Of particular concern was the high amount of benzodiazepine use regardless of the type of death, known to have high-risk when co-prescribed with opioids….
Results regarding benzodiazepine involvement in opioid-related deaths, regardless of type, as well as the high proportions of patients on opioid analgesics receiving prescriptions for benzodiazepines highlight that more work is needed to address risky prescribing practices contributing to opioid deaths."
Nechuta et al. (2018)

Introduction

This chapter presents the results for opiates/opioids and hypnotics/sedatives, accompanied by brief commentaries and comparisons with other studies (where they exist) using the same approach.

Opiates/opioids (heroin/morphine and methadone)

These groups of substances make the greatest contribution of any class of drugs to United Kingdom (UK) drug-related deaths. It is, therefore, crucial to take a close look at how they relate to other drug indicators.

Heroin/morphine

At the UK level, there were 9 parameters that had a statistically significant relationship with heroin/morphine deaths, the most significant being: year, number of offenders found guilty or cautioned, new notifications to the Home Office Addicts Index, and price of street level heroin – all $p < 0.000$ (Table 9.1). As deaths increased over time, so did the number of addicts notified to the Home Office as seeking treatment for heroin and the number of individuals found guilty or cautioned for heroin offences (i.e., positive correlations), but the street price of heroin fell (i.e., a negative correlation). At a slightly less significant level, there were also increases in the overall number of heroin addicts reported to the Home Office, new notifications to regional drug misuse databases in Great Britain, and online NPIS queries.

Table 9.1: Selected statistically significant correlations between numbers of death and other parameters for heroin/morphine, United Kingdom

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	0.883	0.000
Price (£) (UK) street level (gram) UK FP report 2019 & 2017: source NCA &; HOSBs	26	- 0.696	0.000
Weighted mean purity (street level) E&;W UK FP report 2019, 2017, 2015, 2003: source NCA	22	0.434	0.044
No of offenders (UK) (00s) Found Guilty or Cautioned	23	0.770	0.000
Addict Index - New notifications	7	0.955	0.000
Addict Index - all notifications	4	0.976	0.024
RDMDs GB starting agency episodes (6 month reports summed)	6	0.978	0.001
EMCDDA Stats Bulletin 2019 (UK) Never previously treated	13	- 0.626	0.022
NPIS - online queries (heroin/diamorphine)	12	0.680	0.015

Table 9.2: Selected statistically significant correlations between numbers of death and other parameters for heroin/morphine, England

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	0.833	0.000
Price (£) (UK) street level (gram) UK FP report 2019 & 2017: source NCA & HOSBs	26	- 0.643	0.000
Weighted mean purity (street level) E&W UK FP report 2019, 2017, 2015, 2003: source NCA	22	0.535	0.010
No of offenders (E&W) (00s) Found Guilty or Cautioned	12	0.936	0.000
Prevalence (%) 16-24 ever use (E&W)	22	- 0.563	0.006
Prevalence (%) 16-24 last year use (E&W)	22	- 0.480	0.024
Prevalence (%) 16-59 last year use (E&W)	22	- 0.619	0.002
Est no (thousands) 16-24 last year use (E&W)	19	- 0.680	0.001
Est no (thousands) 16-59 ever use (E&W)	19	- 0.486	0.035
Est no (thousands) 16-59 last year use (E&W)	20	- 0.726	0.000
No of prescription items (E) (000s)	24	- 0.473	0.020
RDMD E starting agency episodes (6 month reports summed)	7	0.984	0.000
Adults - New presentations to treatment (E) - opiate (not crack)	17	- 0.744	0.001
Adults - All referrals to treatment (E) - opiate (not crack)	17	- 0.860	0.000
Young people in treatment new presentations (E) All referrals: primary drug - heroin	17	- 0.529	0.529
Young people in all in treatment (E) All referrals: primary drug - heroin	17	- 0.546	0.023
Hospital admissions (E) finished admission episodes Mental & Behavioural disorders F11 (opioids) primary diagnosis	12	- 0.699	0.011
Historic data hospital admissions (E) T401	13	0.628	0.022
Historic data hospital admissions (E) F11	13	0.580	0.038
NPIS - online queries (heroin/diamorphine)	12	0.749	0.005

For England there was a total of 20 parameters with a statistically significant correlation with the number of heroin/morphine deaths (Table 9.2). The most important relationships ($p < 0.000$) were similar to those at for the UK: year, number of offenders found guilty or cautioned for heroin offences, number of individuals referred to the English Drug Misuse Database, adults referred for opiate treatment, and price of street level heroin price - all in the same directions as for the UK overall. In addition, there was a positive correlation for the estimated number of those aged 16-59 using heroin in the last year. Echoing the UK picture, there were also less statistically significant

relations between heroin/morphine death numbers and the estimated number of individuals aged 16-24 using heroin in the last year and lifetime prevalence use amongst those aged 16-59 (both negative), with positive correlations for new presentations for opiate dependence to the English Drug Misuse Database, and NPIS online queries about heroin/morphine.

In Wales, there were only 8 parameters that shared a high statistically significant relationship with the number of heroin/morphine deaths (Table 9.3). Those with a positive correlation of $p < 0.000$ were year and the number of offenders found guilty or cautioned for heroin offences; the estimated number of last year users of heroin and the street level price of heroin had negative correlations. At a lower level of significance, there was a negative association between heroin/morphine deaths and prevalence rates for 16-24 year-olds' lifetime and last year use, and 16-59 year-olds' last year use.

Table 9.3: Selected statistically significant correlations between numbers of death and other parameters for heroin/morphine, Wales

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	0.883	0.000
Price (£) (UK) street level (gram) UK FP report 2019 & 2017: source NCA &; HOSBs	26	- 0.783	0.000
No of offenders (E&W UK) Found Guilty or Cautioned	12	0.900	0.000
Prevalence (%) 16-24 ever use (E&W)	22	- 0.641	0.001
Prevalence (%) 16-24 last year use (E&W)	22	- 0.604	0.003
Prevalence (%) 16-59 last year use (E&W)	22	- 0.633	0.002
Est no (thousands) 16-24 last year use (E&W)	19	- 0.595	0.007
Est no (thousands) 16-59 last year use (E&W)	20	- 0.707	0.000

There were six parameters for Scotland with high statistically significant correlations with the number of heroin/morphine deaths (Table 9.4). Four of these were significant at the $p < 0.000$ level: year, amount seized in supply and possession offences, and hospital admissions for opioid-related mental and behavioural disorders had positive correlations, whereas the street level price of heroin had a negative relationship - in line with the rest of the UK. It is also worth noting that there was a slightly less statistically significant finding for the number of diamorphine prescription items dispensed; this had a negative correlation.

Table 9.4: Selected statistically significant correlations between numbers of death and other parameters for heroin/morphine, Scotland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	33	0.915	0.000
Price (£) (UK) street level (gram) UK FP report 2019 2017: source NCA & HOSBs	29	- 0.795	0.000
Amount seized (kg) (Scotland) supply & possession offences	29	0.662	0.000
No of prescription items (S) (000s)	22	- 0.661	0.001
Hospital admissions (S) stays (opioids) Mental & behavioural disorders	26	0.865	0.000
Hospital admissions (S) stays (heroin) overdoses	26	0.482	0.013

Only five parameters were highly statistically significant for Northern Ireland (Table 9.5). Three of these were significant at the $p < 0.000$ level, all with positive correlations: year, number of heroin seizures, and number of finished admission episodes for opioid-related mental and behavioural disorders. There were also statistically significant negative correlations for the street level price of heroin and the number of diamorphine prescription items dispensed - as was the case in Scotland.

Table 9.5: Selected statistically significant correlations between numbers of death and other parameters for heroin/morphine, Northern Ireland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	25	0.875	0.000
Price (£) (UK) street level (gram) UK FP report 2019 & 2017: source NCA & HOSBs	22	- 0.560	0.007
Number of seizures (NI)	18	0.774	0.000
No of prescription items (NI) (000s)	22	- 0.590	0.004
Hospital admissions (NI) finished admission episodes Mental & Behavioural disorders F11 (opioids) primary diagnosis	22	0.709	0.000

Methadone

There are far fewer parameters generally available for methadone than heroin/morphine. At the UK level, there were six parameters that showed a statistically significant correlation with the number of methadone deaths (Table 9.6). The strongest positive relationships ($p < 0.000$) were with year, and new and all notifications to the Home Office Addicts Index. There were slightly less significant but negative correlations for new and all entrants to treatment for methadone dependence, but a positive correlation for the number of offenders found guilty or cautioned for methadone drug offences. It is of interest that the relationships for the treatment figures are in opposite directions: positive for Addict Index notifications but negative for later treatment figures. The reason(s) for this divergence remain unknown. By contrast there are clear positive relationships for the other parameters: the number of methadone drug offenders and number of

deaths over time.

Table 9.6: Selected statistically significant correlations between numbers of death and other parameters for methadone, United Kingdom

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	33	0.839	0.000
No of offenders (UK) Found Guilty or Cautioned	15	0.663	0.007
Addict Index - New notifications	7	0.986	0.000
Addict Index - All notifications	7	0.983	0.000
EMCDDA Stats Bulletin 2019 (UK) Never previously treated	13	- 0.771	0.002
EMCDDA Stats Bulletin 2019 (UK) All treatment entrants	13	- 0.796	0.001

There are six parameters available for England (Table 9.7). The strongest correlation ($p < 0.000$) is between the number of methadone deaths and year. Less statistically significant positive correlations are apparent for the number of methadone tablets and overall number of methadone prescription items dispensed and hospital admissions for methadone poisoning; there are negative correlations for primary presentations for methadone dependence treatment and NPIS telephone queries. The positive relationships suggest that both methadone-related overdoses and fatalities increased over time as the availability – as measured by the number of items dispensed - of methadone, especially tablets, grew.

Table 9.7: Selected statistically significant correlations between numbers of death and other parameters for methadone, England

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	0.669	0.000
TabPres E 00s items	16	0.575	0.020
No of prescription items (E) (000s)	29	0.483	0.008
DTI England (main drug of use) Primary presentation	12	- 0.647	0.023
Historic data hospital admissions (E) T403	13	0.781	0.002
NPIS - telephone queries	12	- 0.645	0.024

Only five parameters reached very high statistical significance ($p < 0.000$) for Wales (Table 9.8): year and the number of methadone prescription items dispensed. These and the less significant correlations for prevalence of lifetime use of methadone by 16-59 year-olds and their estimated numbers, together with online NPIS queries were all positive relationships. Overall, as the number of methadone deaths increased in Wales do did all of these five parameters.

Table 9.8: Selected statistically significant correlations between numbers of death and other parameters for methadone, Wales

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	0.632	0.000
Prevalence (%) 16-59 ever use (E&W)	22	0.488	0.021
Est no (thousands) 16-59 ever use (E&W)	19	0.542	0.017
No of prescription items (W) (000s)	22	0.781	0.000
NPIS - online queries	12	0.607	0.036

Seven parameters reached very high statistical significance ($p < 0.000$) for Scotland (Table 9.9): year (positive relationship) and individuals starting new agency episodes with methadone as primary or any drug dependence (negative relationship). There were slightly less positive statistically significant relationships between the number of methadone deaths and hospital methadone overdose admissions, together with number of offenders, but negative relationships for individuals starting new agency episodes for methadone dependence and number of offenders. It would appear that as the number of methadone deaths has increased in Scotland, so have overdoses and the number of methadone drug offenders. Yet, at the same time, the number of individuals entering treatment for the first time has gone in the opposite direction; the number of NPIS telephone queries has also fallen. One needs to recall that the NPIS figures used here are for the UK as a whole.

Table 9.9: Selected statistically significant correlations between numbers of death and other parameters for methadone, Scotland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	33	0.876	0.000
No of offenders (S)	13	0.640	0.019
Number of seizures (Scotland)	29	- 0.371	0.048
Individuals starting new agency episodes recorded by Scottish DMD - main drug	27	- 0.664	0.000
Individuals starting new agency episodes recorded by Scottish DMD - any drug	27	- 0.682	0.000
Hospital admissions (S) stays overdoses	26	0.593	0.001
NPIS - telephone queries	13	- 0.617	0.025

For Northern Ireland, there were only four parameters that yielded important statistically significant relationships (Table 9.10). Of these, year and the number of methadone prescription items dispensed were significant at the $p < 0.000$ level, both positively. The lifetime prevalence of methadone use in 15-64 year-olds was also positive, whereas NPIS telephone queries fell. As for Scotland, one needs to recall that the NPIS figures used here are for the UK as a whole.

Table 9.10: Selected statistically significant correlations between numbers of death and other parameters for methadone, Northern Ireland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	25	0.849	0.000
Prevalence (%) 15-64 ever use NI	4	0.963	0.037
No of prescription items (NI) (000s)	22	0.888	0.000
NPIS - telephone queries	12	- 0.782	0.003

The negative correlations between methadone deaths in Northern Ireland and NPIS telephone queries may reflect the fact that methadone is well known and recognised as a factor in drug-related deaths.

Morgan et al. (2006) also used the approach employed in this chapter to look at the relationships between heroin and methadone deaths with methadone prescribing and seizures of heroin and methadone in England and Wales between 1993 and 2004. Their main finding was that, for male decedents, deaths were strongly associated with both heroin ($p = 0.001$) and methadone ($p = 0.0013$) seizures. They concluded their study "suggests the 'British System' can deliver substantial expansion of treatment without increased mortality risk" (Morgan et al., 2006). The researchers worded their conclusions in a suitably cautious way: "The fall in heroin/morphine deaths since 2000 may also be an indication of success of increasing methadone treatment. Data on mortality risk is needed to determine whether increased methadone treatment has reduced drug-related deaths." They were wise to do; in the period since that covered by their study, patterns in both heroin and methadone deaths in England and Wales have continued to evolve. Indeed, the author and colleagues have consistently made the point over the decades in annual reports from the National Programme on Substance Abuse Deaths (NPSAD) that up to two-thirds of methadone deaths involved individuals who had not been prescribed the drug (e.g., Corkery et al., 2014); this finding is echoed in other UK research, including Scotland (e.g., Seymour et al., 2003).

At a local level in the USA, the correlation between seizure data and fatalities was examined for fentanyl and carfentanil deaths (Noriega et al., 2023). The main finding was a strong positive correlation (0.92, $p < 0.001$) between seizures of carfentanil and fatalities involving the drug in Cuyahoga County, Ohio, between 2016 and 2020. Cano et al. (2024) conducted a scoping review of the association between law enforcement drug seizures and overdose mortality in the USA. They found that most (86%) of the 14 studies examined demonstrated "at least one statistically significant positive association between a law enforcement drug seizure measure and an overdose mortality outcome, most consistently for fentanyl-related seizures."

In Norway, opioid prescribing policies were liberalised during the 2010s with consequent increases in pharmaceutical opioid dispensing which was accompanied by increases in accidental overdose deaths (Gersing and Amundsen, 2022). These findings were in line with those observed in a number of other countries where similar shifts in prescribing policies had occurred, e.g., Australia, the USA, and parts of Canada; by contrast that does not appear to have happened in England and Scotland (Kimber et al., 2019).

Using a descriptive/narrative approach, the ACMD Working Group on Reducing Opioid-related Deaths in the UK discussed a number of potential causes which may have led to substantial changes in opioid-related deaths:

"They include:

- The ageing of the heroin-using population; this combines with their wide variety of risk behaviours and their increasingly complex health problems and substance use patterns.
- Changes in the availability and purity of heroin at street level.
- Socio-economic changes, including increasing deprivation and cuts to support services in deprived areas.
- Changes in the commissioning and provision of drug treatment.

It should be noted that research has not definitively established the causal contribution of each of these factors to changing trends in DRDs."
ACMD (2016:23)

The Working Group, which included the author and his Principal Supervisor, concluded that:

"we can assert with a good degree of confidence that the increasing vulnerability of the UK's ageing cohort of heroin or opioid users with increasingly complex health needs (including long-term conditions and poly-substance use), social care needs, and continuing multiple risk behaviours is highly likely to have contributed to recent increases in DRDs. …
Other factors, including changes in the availability of street heroin, socio-economic changes (including cuts to health and social care, welfare benefits and local authority services) and changes in treatment services and commissioning practices may also have contributed to these increases."
ACMD (2016:28)

The arguments underpinning these conclusions are available on pages 22-28 of the ACMD report.

Hypnotics/sedatives (barbiturates and benzodiazepines)

Barbiturates

There were only a few parameters for barbiturates available during the period examined by this thesis.

At the UK level, the number of seizures achieved the $p < 0.000$ level of significance, with a positive correlation (Table 9.11). At a lower significance level, year had a negative association but the number starting GB agency records generated a positive correlation.

Table 9.11: Selected statistically significant correlations between numbers of death and other parameters for barbiturates, United Kingdom

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	33	- 0.400	0.021
Number of seizures (UK)	23	0.715	0.000
RDMDs GB starting agency episodes (6 month reports summed)	6	0.878	0.021

No parameters for England reached the $p < 0.000$ level of significance, although at lower significance levels there were positive correlations for the number starting GB agency records, and adults referred to treatment in the subsequent period (Table 9.12).

Table 9.12: Selected statistically significant correlations between numbers of death and other parameters for barbiturates, England

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
RDMD England starting agency episodes (6 month reports summed)	7	0.899	0.006
Adults - All referrals to treatment (E)	8	0.787	0.021

There were no statistically significant findings recorded for Wales and Northern Ireland. In Scotland, both year and number of seizures achieved the $p < 0.000$ level of significance (Table 9.13).

Table 9.13: Selected statistically significant correlations between numbers of death and other parameters for barbiturates, Scotland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	33	- 0.613	0.000
Number of seizures (Scotland)	29	0.671	0.000

Most of the UK research on deaths involving barbiturates was undertaken several decades ago, e.g., Johns (1977) who looked at the relationship between deaths and hospital overdose admissions and prescription numbers, or even earlier, e.g., Brooke and Glatt (1964), Glatt (1962). A slightly more recent study, but still two decades old, by Buckley and McManus (2004) found that whilst the ratio of barbiturate deaths to the number of prescriptions dispensed showed no substantial change over the period covered by the study (1983-1999), the observed fall in such fatalities occurred subsequent to reduced prescribing of barbiturates.

The ACMD has not published any research or reports on barbiturates.

Benzodiazepines

There are relatively few parameters consistently available for 'any benzodiazepine' as well as for diazepam and diazepam individually, as this section demonstrates. However, since these are one of the commonest classes contributing to polysubstance deaths, it is important to see what insights can be gained.

Any benzodiazepine

At the UK level, the only very highly statistically significant ($p < 0.000$) correlations with deaths related to any benzodiazepine were year and the number of seizures and amount seized, all with positive correlations. (Table 9.14).

Table 9.14: Selected statistically significant correlations between numbers of death and other parameters for any benzodiazepine, United Kingdom

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	33	0.737	0.000
Number of seizures (UK)	21	0.876	0.000
Amount seized (UK)	21	0.942	0.000

At the England level, however, there are seven parameters to consider that reach statistically significant levels (Table 9.15). Only two of these, year and new adult presentations to treatment reach the $p < 0.000$ significance level; the former has a positive relationship, the latter a negative one. There were positive correlations, at a lower level of significance, between benzodiazepine deaths and number of benzodiazepine seizures, individuals starting treatment notified to English Drug Misuse Database, young people's new presentations for treatments with benzodiazepines as primary substance of dependence. The negative correlation between deaths and NPIS telephone queries may reflect the fact that benzodiazepines are well known and recognised as a factor in drug-related deaths.

Table 9.15: Selected statistically significant correlations between numbers of death and other parameters for any benzodiazepine, England

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	0.716	0.000
Number of seizures (E&W)	28	0.400	0.035
RDMD England starting agency episodes (6 month reports summed)	7	0.799	0.031
Adults - New presentations to treatment (E)	17	- 0.923	0.000
Young people in treatment new presentations (E) All referrals: primary drug	17	0.562	0.019
Young people in all in treatment (E) All referrals: primary drug	17	0.541	0.025
NPIS - telephone queries	6	- 0.834	0.039

Only two parameters reached the p < 0.000 level of significance for deaths in Wales related to benzodiazepines: year and number of seizures, both positive relationships (Table 9.16). There was a negative correlation between deaths and hospital admissions for benzodiazepine overdoses.

Table 9.16: Selected statistically significant correlations between numbers of death and other parameters for any benzodiazepine, Wales

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	0.828	0.000
Number of seizures (E&W)	28	0.721	0.000
Historic data hospital admissions (W) T424	14	- 0.576	0.031

For Scotland, there were positive correlations at the p <0.000 significance level for year and the total amount seized in benzodiazepine supply and possession offences (Table 9.17). In addition, the individual breakdowns for these offences were statistically significant but at a lower level.

Table 9.17: Selected statistically significant correlations between numbers of death and other parameters for any benzodiazepine, Scotland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	33	0.749	0.000
Amount seized (kg) (Scotland) supply offences	8	0.733	0.038
Amount seized (kg) (Scotland) possession offences	8	0.713	0.047
Total amount seized (kg) (Scotland) supply & possession offences	23	0.897	0.000

The range of parameters that were statistically significant for Northern Ireland numbered four (Table 9.18). Two of these were significant at the p < 0.000 level: year and number of seizures; whilst the total amount seized and number of people in treatment for the first time with

benzodiazepines as the main drug of misuse also had positive correlations with death, but at a lower level of significance.

Table 9.18: Selected statistically significant correlations between numbers of death and other parameters for any benzodiazepine, Northern Ireland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	25	0.938	0.000
Number of seizures (NI)	16	0.978	0.000
Total amount seized (kg) (NI)	12	0.653	0.021
People in treatment (NI) - main drug of misuse - not treated before	11	0.826	0.002

Diazepam

As with benzodiazepines generally, there were very few parameters displaying statistically significant relationships with diazepam deaths.

At the UK level, only year had a statistically significant positive relationship with diazepam deaths at the $p < 0.000$ level of significance (Table 9.19). There was also a positive relationship with the number of diazepam prescription items dispensed and a negative one with the street level price of diazepam tablets – both at a lower significance level.

Table 9.19: Selected statistically significant correlations between numbers of death and other parameters for diazepam, United Kingdom

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	30	0.801	0.000
Price (£) (UK) (10 mg)	5	- 0.905	0.035
No of prescription items (UK) (000s)	23	0.439	0.036

Both year and the number of diazepam prescription items dispensed had positive correlations at the $p < 0.000$ level in England (Table 9.20). Surprisingly, there was a negative correlation with NPIS telephone queries, but at a lower level of significance.

Table 9.20: Selected statistically significant correlations between numbers of death and other parameters for diazepam, England

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	0.917	0.000
No of prescription items (E) (000s)	29	0.648	0.000
NPIS - telephone queries	6	- 0.834	0.039

For Wales, the only statistically significant relationship was a positive correlation ($p < 0.000$) with

year (Table 9.21).

Table 9.21: Selected statistically significant correlations between numbers of death and other parameters for diazepam, Wales

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	0.766	0.000

The most diazepam parameters available (n = 5) were for Scotland (Table 9.22). Both year and new agency episodes reported to the Scottish Drug Misuse Database with diazepam as the main drug had positive correlations that were statistically significant at the $p < 0.000$ level. New agency episodes with diazepam as a drug of dependence also had a positive correlation but at a lower significance level. There were negative correlations at this lower level between diazepam deaths and the estimated number of diazepam drug possession crime and prevalence of last year diazepam use among 16 to 60+ individuals.

Table 9.22: Selected statistically significant correlations between numbers of death and other parameters for diazepam, Scotland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	33	0.739	0.000
Estimated no of drug possession crimes (S)	4	- 0.999	0.001
SCJS 16-60+ Last year use (%)	7	- 0.821	0.023
Individuals starting new agency episodes recorded by Scottish DMD - main drug	27	0.640	0.000
Individuals starting new agency episodes recorded by Scottish DMD - any drug	27	0.521	0.005

In Northern Ireland, both year and the number of diazepam prescription items dispensed had positive correlations that were statistically significant at the $p < 0.000$ level (Table 9.23).

Table 9.23: Selected statistically significant correlations between numbers of death and other parameters for diazepam, Northern Ireland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	25	0.945	0.000
No of prescription items (NI) (000s)	22	0.863	0.000

Temazepam

The number of parameters available for temazepam was similar to that for diazepam. However, some of the patterns were in the opposite direction - notably that for year.

At the UK level, year had a very high negative correlation with temazepam deaths ($p < 0.000$), whereas the number of temazepam prescription items dispensed at a positive correlation at the same significance level (Table 9.24). The same patterns were evident for England (Table 9.25) and Wales (Table 9.26).

Table 9.24: Selected statistically significant correlations between numbers of death and other parameters for temazepam, United Kingdom

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	30	- 0.903	0.000
No of prescription items (UK) (000s)	23	0.865	0.000

Table 9.25: Selected statistically significant correlations between numbers of death and other parameters for temazepam, England

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	- 0.903	0.000
No of prescription items (E) (000s)	29	0.929	0.000

Table 9.26: Selected statistically significant correlations between numbers of death and other parameters for temazepam, Wales

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	- 0.667	0.000
No of prescription items (W) (000s)	22	0.691	0.000

Whilst there was also a negative correlation between temazepam deaths and year in Scotland (Table 9.27), there were positive correlations for the number of temazepam seizures, number of temazepam prescription items dispensed, and new agency episodes reported to the Scottish Drug Misuse Database with temazepam as the main or any drug; the last listed parameter was the only one - apart from year - to be statistically significant at the $p < 0.000$ level.

Table 9.27: Selected statistically significant correlations between numbers of death and other parameters for temazepam, Scotland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	33	- 0.743	0.000
Number of seizures (Scotland)	25	0.525	0.007
No of prescription items (S) (000s)	22	0.483	0.023
Individuals starting new agency episodes recorded by Scottish DMD - main drug	15	0.736	0.002
Individuals starting new agency episodes recorded by Scottish DMD - any drug	15	0.828	0.000

No relevant results for Northern Ireland were statistically significant.

Temazepam became very popular on the UK 'recreational' drug scene in the 1980s, especially in Scotland; but a number of deaths ensued, often because of injecting the gel from the capsules (Jenkinson and Pusey, 1994). A ban on the prescription of this formulation was introduced in January 1996 (Dyer, 1996). This action probably made a major contribution to the overall decline in deaths involving this drug.

The author is unaware of any studies which have looked at possible relationships between deaths involving benzodiazepines as a group or for diazepam and temazepam separately and other drug indicators using the approach employed in this chapter. However, Buckley and McManus (2004), using the number of fatalities in Great Britain in conjunction with the number of prescriptions in England and Scotland, derived a fatal toxicity index of deaths per million prescriptions. This was applied to anxiolytic and sedative drugs during the period 1983-1999. This process revealed that a major reduction in temazepam deaths had coincided with the above-noted withdrawal of gelatin capsule formulations.

Chapter overview

This chapter has presented the correlation results for some of the key substances involved in UK drug-related deaths.

Deaths involving heroin/morphine deaths continue to increase against a background of increasing availability, prevalence of use, purity and lower prices. Methadone deaths continue to increase against a background of increased prescribing; however, it should be noted that most such deaths occur in individuals that were not in receipt of a methadone prescription.

Benzodiazepines have made a large contribution to deaths across the UK, especially in the 'Celtic' regions such as Scotland, Northern Ireland, and (to a lesser extent) Wales. Whilst tighter prescribing has led to a decline in temazepam-related deaths, the legal supply of diazepam shows

a positive correlation with deaths involving this medication. At a higher level, the availability and prevalence of ‘novel benzos’ in recent years has impacted deaths across the UK, especially Scotland where they made a highly important contribution to the increase of drug-related death rates.

Combined with the emergence of very potent synthetic opioids such as fentanyl analogues and ‘nitazenes’ (see Chapters 13 and 14), polysubstance use involving the opiates/opioids and benzodiazepines (both classes are CNS depressants) does not augur well for the future. They are part of a polysubstance phenomenon including stimulants.

Some clear narratives have been presented for the substances examined in this chapter. The information for barbiturates is less clear, but this drug class is a disappearing concern.

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CHAPTER 10: ASSOCIATIONS BETWEEN STIMULANT DRUG INDICATORS

"Six key indicator data sources (i.e. number of mentions on death certificates, last year's use, number of drug offenders, seizures, price, average MDMA dosage levels per tablet) were here deemed appropriate for contribution to a descriptive overview of ecstasy trends … Furthermore, we aimed at testing the hypothesis that these indicators were inter-related to each other."
Schifano et al. (2006)

Introduction

This chapter presents the results for five stimulants (cocaine, 'crack', amphetamines, MDMA/'ecstasy', and mephedrone/synthetic cathinones), all of which have similar properties. Although the effects of individual substances overlap to some extent there are differences between them, and also in their mode/route of administration. As with the previous chapter, the results are given with brief commentaries and comparisons with other studies (where they exist) using the same approach.

Cocaine

There is a considerable range of parameters available, both at the UK and country levels, to consider the relationships between cocaine deaths and other drug indicators.

At the UK level, there are nine parameters yielding positive correlations with death which are statistically significant at the $p < 0.000$ level: year; street level purity; number of individuals found guilty of or cautioned for cocaine offences; number of seizures and quantity of cocaine seized; treatment episodes - three measures covering much of the last two decades; and online NPIS queries (Table 10.1). There are also very strong positive correlations for new and all notifications to the Home Office Addicts Index, in line with the later treatment figures. There are negative correlations for purity levels, both at import and street levels.

Table 10.1: Selected statistically significant correlations between numbers of death and other parameters for cocaine, United Kingdom

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	33	0.785	0.000
Purity/Potency (police) FSS DIU UK	19	- 0-569	0.011
Purity/Potency (Customs/ Border Force) FSS DIU UK	17	- 0.654	0.004
Purity/Potency (Customs/ Border Force) HOSB E&W	8	- 0.726	0.041
Purity/Potency (LGC/Eurofins) E Police (street level)	14	0.812	0.000
No of offenders (UK) (00s) Found Guilty or Cautioned	26	0.829	0.000
Number of seizures (UK) JC	29	0.618	0.000
Amount seized (UK)	29	0.762	0.000
Addict Index - New notifications	7	0.933	0.002
Addict Index - all notifications	7	0.931	0.002
RDMDs GB starting agency episodes (6 month reports summed)	6	0.984	0.000
EMCDDA Stats Bulletin 2019 (UK) Never previously treated	14	0.812	0.000
EMCDDA Stats Bulletin 2019 (UK) All treatment entrants	14	0.909	0.000
NPIS - online queries	13	0.851	0.000

There are even more parameters available for England (Table 10.2). Indeed, 11 of these are statistically significant at the $p < 0.000$ level, most of these are positive relationships: year; street level purity (Eurofins data); number of individuals found guilty of or cautioned for cocaine offences; lifetime prevalence and estimated numbers of lifetime cocaine users aged 16-59 years; amount of cocaine seized; new presentations to treatment, especially adults, over the last couple of decades; hospital admissions, including poisonings; and online NPIS queries. Purity at import level (FSS data) shows a negative correlation at this level. There are also eight other positive relationships between cocaine deaths and other parameters at a slightly lower statistically significant level, mostly for prevalence and estimated numbers of cocaine users; adults in treatment, and number of seizures. As well, there are five negative correlations, principally for purity levels and young people in treatment.

Table 10.2: Selected statistically significant correlations between numbers of death and other parameters for cocaine, England

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	0.847	0.000
Purity/Potency (police) FSS DIU UK	16	- 0.663	0.005
Purity/Potency (Customs/ Border Force) FSS DIU UK	15	- 0.798	0.000
Purity/Potency (police) HOSB E&W	8	- 0.714	0.047
Purity/Potency (Customs/ Border Force) HOSB E&W	8	- 0.791	0.019
Purity/Potency (LGC/Eurofins) E Police (street level)	13	0.886	0.000
No of offenders/FG (E&W)	12	0.975	0.000
FG/Caut FP report (E&W) dealing etc	11	0.670	0.024
Prevalence (%) 16-24 last year use (E&W)	22	0.433	0.044
Prevalence (%) 16-59 ever use (E&W)	22	0.740	0.000
Prevalence (%) 16-59 last year use (E&W)	22	0.596	0.003
Est no (thousands) 16-59 ever use (E&W)	19	0.728	0.000
Est no (thousands) 16-59 last year use (E&W)	20	0.654	0.002
Number of seizures (E&W)	28	0.565	0.002
Amount seized (kg) (E&W)	28	0.717	0.000
RDMD England starting agency episodes (6 month reports summed)	7	0.975	0.000
Adults - New presentations to treatment (E)	17	0.909	0.000
Adults - All referrals to treatment (E)	17	0.650	0.005
Young people in treatment new presentations (E) All referrals: primary drug	17	- 0.452	0.069
Young people in treatment (E) All referrals: primary drug	17	- 0.561	0.019
Historic data hospital admissions (E) F14	13	0.774	0.002
Hospital admissions (E) finished admission episodes Mental & Behavioural disorders F14 primary diagnosis	12	0.914	0.000
Historic data hospital admissions (E) T405	13	0.809	0.001
Hospital admissions (E) finished admission episodes with a primary diagnosis of (cocaine T405) poisoning by drug misuse	8	0.953	0.000
NPIS - online queries	12	0.938	0.000

For Wales, there are only four parameters that are statistically significant at the $p < 0.000$ level: year; street level purity (Eurofins data); amount of cocaine seized; and online NPIS queries; all are positive correlations (Table 10.3). At the lower levels of significance reported in this chapter, there are seven positive relationships: number of individuals found guilty of any cocaine offences; lifetime and last year use prevalence and estimated numbers of those aged 16-59; number of seizures; and hospital poisoning admissions. In addition, there are three negative ones: import and street level purity (FSS data) and individuals found guilty of or cautioned for cocaine possession offences.

Table 10.3: Selected statistically significant correlations between numbers of death and other parameters for cocaine, Wales

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	0.778	0.000
Purity/Potency (police) FSS DIU UK	16	- 0.513	0.042
Purity/Potency (Customs/ Border Force) FSS DIU UK	15	- 0.650	0.009
Purity/Potency (LGC/Eurofins) E Police (street level)	13	0.833	0.000
No of offenders/FG (E&W)	12	0.772	0.003
FG/Caut FP report (E&W) possession	11	- 0.608	0.047
Prevalence (%) 16-59 ever use (E&W)	22	0.648	0.001
Prevalence (%) 16-59 last year use (E&W)	22	0.483	0.023
Est no (thousands) 16-59 ever use (E&W)	19	0.644	0.003
Est no (thousands) 16-59 last year use (E&W)	20	0.551	0.012
Number of seizures (E&W)	28	0.472	0.011
Amount seized (kg) (E&W)	28	0.694	0.000
Hospital admissions for (cocaine) poisonings (W)	14	0.728	0.003
NPIS - online queries	12	0.912	0.000

The picture for Scotland is somewhat more straightforward (Table 10.4). Eight of the eleven parameters exhibit results that are statistically significant at the $p < 0.000$ level; they are all positive relationships: year; street level purity (Eurofins data); number of cocaine offenders; new episode treatments (main and any mention) reported to the Scottish Drug Misuse Database; hospital admissions, including overdoses; and online NPIS queries. In addition, negative correlations were indicated, at a lower level of significance, for import and street level purity (FSS data); and a positive correlation for the amount seized in possession and supply offences.

Table 10.4: Selected statistically significant correlations between numbers of death and other parameters for cocaine, Scotland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	33	0.763	0.000
Purity/Potency (police) FSS DIU UK	19	- 0.600	0.007
Purity/Potency (Customs/ Border Force) FSS DIU UK	17	- 0.556	0.021
Purity/Potency (LGC/Eurofins) E Police (street level)	14	0.828	0.000
No of offenders (S)	13	0.882	0.000
Amount seized (kg) (Scotland) supply & possession offences	29	0.433	0.019
Individuals starting new agency episodes recorded by Scottish DMD - main drug	20	0.898	0.000
Individuals starting new agency episodes recorded by Scottish DMD - any drug	20	0.924	0.000
Hospital admissions (S) stays (cocaine) Mental & behavioural disorders	26	0.942	0.000
Hospital admissions (S) stays (cocaine) overdoses	26	0.919	0.000
NPIS - online queries	13	0.920	0.000

As for other substances, the information on cocaine in Northern Ireland (Table 10.5) is somewhat limited compared to other parts of the UK. Three of the eight parameters reach statistical significance at the $p < 0.000$ level: year, number of seizures, and online NPIS queries - all positive correlations. There are also positive relationships, at lower levels of significance for treatment presentations and street level purity (Eurofins data). By contrast, there are negative relationships for import (both FSS and Eurofins data) and street level (FSS data) purity.

Table 10.5: Selected statistically significant correlations between numbers of death and other parameters for cocaine, Northern Ireland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	25	0.762	0.000
Purity/Potency (police) FSS DIU UK	12	- 0.700	0.011
Purity/Potency (Customs/ Border Force) FSS DIU UK	12	- 0.730	0.007
Purity/Potency (Customs/ Border Force) HOSB EW	8	- 0.812	0.014
Purity/Potency (LGC/Eurofins) E Police (street level)	13	0.769	0.002
Number of seizures (NI)	25	0.902	0.000
People in treatment (NI) - main drug of misuse - all presentations	19	0.711	0.001
NPIS - online queries	12	0.856	0.000

Crack cocaine

The parameters available for looking at relationships between crack indicators are relatively good in number. The main limitation is accurate information on the number of deaths involving crack (Schifano and Corkery, 2008; Fryer et al., 2005); cocaine deaths are, therefore, used as a proxy measure.

At the UK level, the crack-related parameters with correlations with cocaine deaths at the $p < 0.000$ significance level are: year; number of individuals found guilty of or cautioned for crack offences; number of seizures and amount seized; and street level purity (FSS data). The latter is a negative correlation, along with import level purity (FSS data) at a lower level of statistical significance. On the other hand, street level purity from Eurofins indicated a positive correlation for the most recent period covered by the data (Table 10.6). At the UK level, as cocaine deaths increased over time, there were positive relationships with law enforcement activities targeting crack whilst purity levels showed the reverse relationship.

Table 10.6: Selected statistically significant correlations between numbers of death and other parameters for crack, United Kingdom

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	33	0.723	0.000
Purity/Potency (police) FSS DIU UK	18	- 0.948	0.000
Purity/Potency (Customs/ Border Force) FSS DIU UK	11	- 0.691	0.019
Purity/Potency (LGC/Eurofins) E Police (street level)	14	0.645	0.013
No of offenders (UK) (00s) Found Guilty or cautioned	22	0.826	0.000
Number of seizures (UK) JC	18	0.989	0.000
Amount seized (UK)	18	0.620	0.006

The picture for England (Table 10.7) presents seven parameters with correlations statistically significant at the $p < 0.000$ level: year; street level purity (albeit in different directions, as at the UK level); number of individuals found guilty of or cautioned for crack offences; number of seizures; lifetime use rates amongst 16-24 year-olds; and estimated numbers of users of crack in the last year aged 16-59 years. The law enforcement parameters had positive associations, whereas the prevalence ones showed negative associations. There were also eight crack parameters with lower levels of statistical significance in terms of their relationship to the number of cocaine deaths. Of these, the prevalence ones, import level purity (FSS data); and young people referred for treatment were all negative correlations; the positive correlations were for the number of individuals found guilty of or cautioned for crack dealing offences, and online NPIS queries.

Table 10.7: Selected statistically significant correlations between numbers of death and other parameters for crack, England

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	0.847	0.000
Purity/Potency (police) FSS DIU UK	16	- 0.945	0.000
Purity/Potency (Customs/ Border Force) FSS DIU UK	11	- 0.715	0.013
Purity/Potency (LGC/Eurofins) E Police (street level)	13	0.843	0.000
No of offenders/FG (E&W)	11	0.973	0.000
FG/Caut FP report (E&W) dealing etc	11	0.627	0.039
Prevalence (%) 16-24 ever use (E&W)	22	- 0.763	0.000
Prevalence (%) 16-24 last year use (E&W)	22	- 0.601	0.003
Prevalence (%) 16-59 last year use (E&W)	22	- 0.518	0.014
Est no (thousands) 16-24 ever use (E&W)	14	- 0.734	0.003
Est no (thousands) 16-24 last year use (E&W)	19	- 0.704	0.001
Est no (thousands) 16-59 last year use (E&W)	19	- 0.799	0.000
Number of seizures (E&W)	28	0.665	0.000
Young people in all in treatment (E) All referrals: primary drug	17	- 0.515	0.035
NPIS - online queries	6	0.872	0.023

Turning to Wales (Table 10.8), many of the patterns exhibited are in line with those in England, especially the prevalence ones. The key positive relationships that achieved statistical significance at the $p < 0.000$ level were year and treatment for main problematic drug; the two negative relationships at this level were both prevalence ones. At a lower level, there were positive correlations for: (mean) street level purity; number of individuals found guilty of or cautioned for crack offences; number of seizures; and online NPIS queries.

Table 10.8: Selected statistically significant correlations between numbers of death and other parameters for crack, Wales

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	0.778	0.000
Purity/Potency (police) FSS DIU UK	16	- 0.771	0.000
Weighted mean purity (street level) E&W UK FP report 2019: source NCA	19	0.471	0.042
Purity/Potency (LGC/Eurofins) E Police (street level)	13	0.791	0.001
No of offenders/FG (E&W)	11	0.812	0.002
Prevalence (%) 16-24 ever use (E&W)	22	- 0.685	0.000
Prevalence (%) 16-24 last year use (E&W)	22	- 0.554	0.007
Prevalence (%) 16-59 last year use (E&W)	22	- 0.547	0.008
Est no (thousands) 16-24 ever use (E&W)	14	- 0.650	0.012
Est no (thousands) 16-24 last year use (E&W)	19	- 0.630	0.004
Est no (thousands) 16-59 last year use (E&W)	19	- 0.794	0.000
Number of seizures (E&W)	28	0.608	0.001
Wales: Treatments by main problematic substance	15	0.932	0.000
NPIS - online queries	6	0.816	0.048

At the Scottish level, only year demonstrated a statistically significant correlation (a positive one) with the number of cocaine deaths at the $p < 0.000$ level (Table 10.9). At lower significance levels, there was only one negative correlation - FSS street level purity, whereas all the rest exhibited positive relationships: Eurofins street level purity; number of crack offenders; last year use by 16-24 year-olds; amount of crack seized; number of new agency episodes for crack (as main or any drug) recorded by the Scottish Drug Misuse Database; and online NPIS queries.

Table 10.9: Selected statistically significant correlations between numbers of death and other parameters for crack, Scotland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	26	0.766	0.000
Purity/Potency (police) FSS DIU UK	13	- 0.795	0.001
Purity/Potency (LGC/Eurofins) E Police (street level)	13	0.779	0.002
No of offenders (S)	7	0.839	0.018
SCJS 16-24 Last year use (%)	5	0.887	0.045
Amount seized (kg) (Scotland)	21	0.532	0.013
Individuals starting new agency episodes recorded by Scottish DMD - main drug	10	0.805	0.005
Individuals starting new agency episodes recorded by Scottish DMD - any drug	10	0.732	0.016
NPIS - online queries	6	0.957	0.003

There were two parameters with positive correlations, at the $p < 0.000$ level, with the number of cocaine deaths in Northern Ireland: year and number of telephone queries to the NPIS (Table 10.10). At lower levels of significance, there were positive correlations for: presentations for treatment with crack as the main drug of misuse; online NPIS queries; Eurofins street level purity; and FSS import level purity. By contrast, FSS street level purity had a negative relationship.

Table 10.10: Selected statistically significant correlations between numbers of death and other parameters for crack, Northern Ireland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	25	0.762	0.000
Purity/Potency (police) FSS DIU UK	12	- 0.738	0.006
Purity/Potency (Customs/ Border Force) FSS DIU UK	11	- 0.761	0.007
Purity/Potency (LGC/Eurofins) E Police (street level)	13	0.717	0.006
People in treatment (NI) - main drug of misuse - all presentations	10	0.884	0.001
NPIS - telephone queries	3	1.000	0.000
NPIS - online queries	6	0.952	0.003

Seven cocaine and crack indicators, including deaths, over the time-frame 1990-2004 were looked at by an earlier paper (Schifano and Corkery, 2008). Using a two-tailed approach, most Pearson correlation coefficients for deaths related to cocaine were highly significant at the $p < 0.001$ level. There were positive relationships with: last year use of cocaine (powder); number of cocaine offenders; number of cocaine seizures; and number of cocaine RDMD episodes. However, there was a negative association with the street price of cocaine. The number of cocaine/crack cocaine death mentions was positively correlated with both the number of crack cocaine offenders and seizures ($p < 0.001$), but negatively with both street level crack cocaine purity ($p < 0.001$), and crack street level price (p 0.05).

In the earlier study, Schifano and Corkery (2008) postulated several possible explanations, not necessarily contradicting each other, for the overall increase in number of cocaine/crack related deaths noted over this 15-year period. These included:

"[an] increase in cocaine/crack cocaine consumption in a polydrug, including opiates/opioids … misuse context, and higher reporting rates of cocaine/crack cocaine on death certificates.

Alternatively, since only a minority of fatalities involved a cocaine/crack cocaine mono-intoxication, [the] increase in death mentions … observed might reflect increase[s] in fatalities related to other drugs, such as ecstasy (Schifano et al., 2006). Huge media interest surrounded some of the high profile cases of cocaine-related incidents occurring in the last decade or so in the UK and this may have increased awareness of the possible consequences of drug consumption. In turn, this may have led to improved surveillance, monitoring and recording of the substance in investigations of sudden and/or unexpected deaths.

The increase in cocaine/crack cocaine-related death figures was positively correlated with levels of cocaine powder availability indicators. Conversely, the price of cocaine powder was correlated negatively both with availability indicators and death figures. One could hypothesize [sic] that, with conditions of increasing drug availability having been met here, decrease over time in cocaine powder price facilitated easier access to the drug and hence an increase in its consumption levels. This, in turn, has contributed to an increase in [the] number of cocaine-related fatalities.
Schifano and Corkery (2008)

The author argues that these explanations are still pertinent in the context of looking at what has happened during a period double the length of that examined in the earlier study. As was already noted in Chapter 6, the number of deaths related to poisoning by cocaine/crack has reached record levels (2021 registrations), standing at least four times higher than when the previous study was published. Over the same time-scale the numbers of deaths of the other main stimulants have also risen, albeit slightly less spectacularly: amphetamines and ecstasy both doubling by 2020. This is against a continuing background of polysubstance use and deaths. The last decade or so has seen a developing recognition of the challenge posed by cocaine-related deaths in the European and UK contexts, as well as improvements in approaches to their identification and recording (Corkery, 2012; Corkery et al., 2017). For most of the period examined in this chapter, the price of cocaine fell whilst purity increased whereas crack prices remained very stable, but purity increased in recent years.

A narrative examination of cocaine-related deaths (n=18) in Northern Ireland recorded by the State Pathologist's Department between 1999 and 2007 noted an increased incidence of such events (Lyness, 2009). This pattern echoed similar upward movements in statistics (drug seizures and from other agencies that suggested both increased availability (as measured by policer seizures) and use (number in treatment with cocaine as their main problem drug) of cocaine.

An ACMD review of cocaine powder noted a possible link during 2000-2008 between use of cocaine (prevalence of last year use) and “an increase in mortality risk associated with cocaine use” (ACMD, 2015:31).

Amphetamines

There are only a few parameters available at the UK level to examine relationships between amphetamine deaths and other indicators (Table 10.11). At the $p < 0.000$ significance level, year demonstrates a positive correlation whilst new and all treatment entries show negative ones. At lower levels of statistical significance, both street level purity and the number of prescription items show a positive relationship whilst street level price shows a negative one.

Table 10.11: Selected statistically significant correlations between numbers of death and other parameters for amphetamine, United Kingdom

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	33	0.812	0.000
Price (£) (UK) street level (gram) UK FP report 2019: source NCA	29	- 0.451	0.014
Purity/Potency (police) FSS DIU UK	18	0.617	0.006
No of prescription items (UK) (000s)	23	0.652	0.001
EMCDDA Stats Bulletin 2019 (UK) Never previously treated	14	- 0.841	0.000
EMCDDA Stats Bulletin 2019 (UK) All treatment entrants	14	- 0.853	0.000

There are far more parameters available for England (Table 10.12). There are 10 parameters which attain the $p < 0.000$ level of statistical significance, only year and number of prescription items dispensed with positive relationships; the rest have negative relationships - four prevalence ones, number of adult (new and any) presentations to treatment, number of overall young people treatment presentations, and NPIS telephone queries. At lower levels of significance, there is only one positive association (street level purity), whereas the remainder are negative - number of individuals found guilty of or cautioned for amphetamine drug offences, prevalence parameters, number of seizures and amount seized, overall amphetamine treatment presentations, as well as new presentations of young people to treatment.

Table 10.12: Selected statistically significant correlations between numbers of death and other parameters for amphetamine, England

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	0.846	0.000
Purity/Potency (police) FSS DIU UK	16	0.506	0.046
FG/Caut FP report (E&W) possession	11	- 0.826	0.002
Prevalence (%) 16-24 ever use (E&W)	22	- 0.659	0.001
Prevalence (%) 16-24 last year use (E&W)	22	- 0.578	0.005
Prevalence (%) 16-59 ever use (E&W)	22	- 0.682	0.000
Prevalence (%) 16-59 last year use (E&W)	22	- 0.662	0.001
Est no (thousands) 16-24 ever use (E&W)	14	- 0.865	0.000
Est no (thousands) 16-24 last year use (E&W)	19	- 0.797	0.000
Est no (thousands) 16-59 ever use (E&W)	20	- 0.476	0.034
Est no (thousands) 16-59 last year use (E&W)	20	- 0.796	0.000
Number of seizures (E&W)	28	- 0.591	0.001
Amount seized (kg) (E&W)	28	- 0.414	0.028
No of prescription items (E) (000s)	24	0.868	0.000
DTI England (main drug of use) Primary presentation	12	- 0.608	0.036
DTI England (main drug of use) Any presentation	12	- 0.660	0.019
Adults - New presentations to treatment (E)	17	- 0.851	0.000
Adults - All referrals to treatment (E)	17	- 0.799	0.000
Young people in treatment new presentations (E) All referrals: primary drug	17	- 0.740	0.001
Young people in all in treatment (E) All referrals: primary drug	17	- 0.798	0.000
NPIS - telephone queries	12	- 0.849	0.000

In Wales, there are only two parameters statistically significant at the $p < 0.000$ level (both positively): year and number of prescription items (Table 10.13). As with England, at lower levels of significance there are a number of prevalence indicators all with negative correlations, along with number of seizures, treatment by main problematic drug, and NPIS telephone queries.

Table 10.13: Selected statistically significant correlations between numbers of death and other parameters for amphetamine, Wales

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	0.742	0.000
FG/Caut FP report (E&W) possession	11	- 0.860	0.001
FG/Caut FP report (E&W) dealing etc	11	- 0.666	0.025
Prevalence (%) 16-24 ever use (E&W)	22	- 0.492	0.020
Prevalence (%) 16-24 last year use (E&W)	22	- 0.524	0.012
Prevalence (%) 16-59 last year use (E&W)	22	- 0.533	0.011
Est no (thousands) 16-24 ever use (E&W)	14	- 0.586	0.028
Est no (thousands) 16-24 last year use (E&W)	19	- 0.657	0.002
Est no (thousands) 16-59 last year use (E&W)	20	- 0.665	0.001
Number of seizures (E&W)	28	- 0.597	0.001
No of prescription items (W) (000s)	22	0.735	0.000
Wales: Treatments by main problematic substance	15	- 0.610	0.016
NPIS - telephone queries	12	- 0.734	0.007

Scotland has fewer parameters available for investigation (Table 10.14). Three are statistically significant at the $p < 0.000$ level: year with a positive correlation, and both number of seizures and prescription items dispensed having negative correlations. At lower significance levels, there are positive correlations for import and street level purity but negative relationships for individuals starting new agency episodes for amphetamines (main or any drug), and both telephone and online NPIS queries.

Table 10.14: Selected statistically significant correlations between numbers of death and other parameters for amphetamine, Scotland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	33	0.846	0.000
Purity/Potency (police) FSS DIU UK	18	0.486	0.041
Purity/Potency (Customs/ Border Force) FSS DIU UK	12	0.585	0.046
Number of seizures (Scotland)	29	- 0.687	0.000
No of prescription items (S) (000s)	22	- 0.795	0.000
Individuals starting new agency episodes recorded by Scottish DMD - main drug	27	- 0.414	0.032
Individuals starting new agency episodes recorded by Scottish DMD - any drug	27	- 0.569	0.002
NPIS - telephone queries	13	- 0.641	0.018
NPIS - online queries	13	- 0.676	0.011

For Northern Ireland, none of the three available parameters are statistically significant at the higher level of statistical significance used in the present exercise (Table 10.15). However, positive correlations are exhibited for year, number of prescription items dispensed, and presentations to treatment services.

Table 10.15: Selected statistically significant correlations between numbers of death and other parameters for amphetamine, Northern Ireland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	25	0.570	0.003
No of prescription items (NI) (000s)	22	0.561	0.007
People in treatment (NI) - main drug of misuse - all presentations	12	0.581	0.048

Whilst an earlier study (Schifano et al., 2007) did look at the relationships between amphetamine indicators, including deaths in England and Wales between 1990 and 2002, it only provided a narrative description of these associations. In passing, the authors noted that

"The only indicator which seems not to show any declining rates is the number of deaths. … this increase may be related to a more general increase in stimulant death rates. Reasons behind this increase may include: increase in ATS [Amphetamine-type stimulant) drugs use in a polydrug, including opiates/opioids, misuse context, and higher reporting rates of ATS drugs on death certificates. Alternatively, since only a minority of fatalities involved an ATS drugs mono-intoxication, [the] increase in death mentions here observed might reflect [an] increase in fatalities related to other drugs, such as

ecstasy."
Schifano et al. (2007)

In retrospect, it would have been worth investigating these relationships via Pearson correlation coefficients, as was done for cocaine, crack and ecstasy - also referenced in this chapter. However, this omission has now been rectified through the present exercise.

The ACMD review of methylamphetamine in 2005, at least in its Executive Summary, did not directly refer to deaths involving this substance, other than suggesting improvements to the way that both ONS and NPSAD identified and recorded them so that they were differentiated from d-amphetamine cases (ACMD, 2005:47).

Ecstasy (MDMA, MDA)

Compared to cocaine, crack and amphetamine, there are fewer parameters available across the board to investigate relationships between the number of ecstasy deaths with other indicators.

At the UK level, there are three parameters significant at the $p < 0.000$ level: year and number of individuals found guilty of or cautioned for ecstasy drug offences both have positive correlations, but the amount of MDMA content in tablets has a negative relationship (Table 10.16). In addition, there are positive correlations, but at lower significance levels for street level purity, referrals to British Drug Misuse Databases and online NPIS queries whereas there is a negative correlation for street level tablet prices.

Table 10.16: Selected statistically significant correlations between numbers of death and other parameters for ecstasy, United Kingdom

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	33	0.705	0.000
Price (£) (UK) street level UK (tablet) FP report 2019: source NCA	29	- 0.426	0.021
MDMA content (mg) FSS DIU UK	18	- 0.845	0.000
Purity/Potency (LGC/Eurofins) E Police (street level)	9	0.823	0.006
No of offenders (UK) (00s) Found Guilty or Cautioned	26	0.775	0.000
RDMDs GB (100s)	9	0.679	0.045
NPIS - online queries	13	0.661	0.014

Even at the England level, there are only two parameters that reach the $P < 0.000$ significance level: year and number of individuals found guilty of or cautioned for ecstasy offences, both with positive correlations (Table 10.17). Other parameters with lower significance levels but with positive relationships are: number of individuals found guilty of or cautioned for dealing and related

offences, lifetime use by 16-59 year-olds, numbers of young people newly referred to treatment with ecstasy as their primary drug of concern, and online NPIS queries; MDMA content of ecstasy tablets has a negative correlation in the context of FSS reports. However, data since then suggests an almost equal but opposite correlation; this would be in line with the increasing levels of MDMA content in 'ecstasy' tablets reported across Europe (including the UK) in the last decade or more To be more precise, the content ratio has remained level while the size/weight of tablets has increased, thereby increasing the volume of MDMA (Vrolijk et al., 2022).

Table 10.17: Selected statistically significant correlations between numbers of death and other parameters for ecstasy, England

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	0.728	0.000
MDMA content (mg) FSS DIU UK	15	- 0.783	0.001
No of offenders/FG (E&W)	12	0.850	0.000
FG/Caut FP report (E&W) dealing etc	11	0.624	0.040
Prevalence (%) 16-59 ever use (E&W)	22	0.591	0.004
Est no (thousands) 16-59 ever use (E&W)	20	0.497	0.026
Young people in treatment new presentations (E) All referrals: primary drug	17	0.659	0.004
NPIS - online queries	12	0.620	0.031

In Wales, no parameter reached the $p < 0.000$ level of statistical significance, not even year (Table 10.18). At lower significance levels, there were positive correlations for: the overall number of individuals found guilty of or cautioned for any ecstasy offence, as well as for possession offences and dealing, etc. offences; amount of ecstasy seized; lifetime use by 16-24 year olds, as well as estimated numbers of 16-24 year-olds ever using or using in the last year, and 16-59 year-olds using in the last year.

Table 10.18: Selected statistically significant correlations between numbers of death and other parameters for ecstasy, Wales

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
No of offenders/FG (E&W)	12	0.600	0.039
FG/Caut FP report (E&W) possession	11	0.737	0.010
FG/Caut FP report (E&W) dealing etc	11	0.724	0.012
Prevalence (%) 16-24 ever use (E&W)	22	0.536	0.010
Est no (thousands) 16-24 ever use (E&W)	14	0.669	0.009
Est no (thousands) 16-24 last year use (E&W)	19	0.521	0.022
Est no (thousands) 16-59 last year use (E&W)	20	0.522	0.018
Amount seized (kg) (E&W)	28	0.516	0.005

In Scotland, only three parameters reached the cut-off for statistical significance applied in this Part (Table 10.19): year, number of ecstasy offenders, and MDMA content of ecstasy tablets; the first two were positive correlations at the $p < 0.000$ level, the third was a negative relationship at a lower significance level.

Table 10.19: Selected statistically significant correlations between numbers of death and other parameters for ecstasy, Scotland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	33	0.732	0.000
MDMA content (mg) FSS DIU UK	18	- 0.697	0.001
No of offenders (S)	12	0.933	0.000

Year was the only parameter that reached the $p < 0.000$ threshold for statistical significance in Northern Ireland (Table 10.20), with a positive correlation. At a lower level of significance, purity and online NPIS queries have positive associations with ecstasy deaths whereas the MDMA content of ecstasy tablets has a negative one.

Table 10.20: Selected statistically significant correlations between numbers of death and other parameters for ecstasy, Northern Ireland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	25	0.687	0.000
MDMA content (mg) FSS DIU UK	11	- 0.685	0.020
Purity (%) from UNODC WDR 2022 data tables	5	0.915	0.030
NPIS - online queries	12	0.590	0.044

An earlier study which plotted a time series for ecstasy looking at a narrower range of indicators at the UK level and over a far shorter time-period (1994-2003) found that the number of death mentions for ecstasy was positively correlated with: prevalence of last year's use ($p< 0.01$); number of offenders ($p< 0.01$); number of seizures ($p< 0.01$) and number of doses seized ($p< 0.05$) but negatively correlated with ecstasy price ($p< 0.05$) over the years (Schifano et al., 2006). Whilst these relationships were measured using a lower level of statistical significance they are in line with the results of the present study.

Statistics on amphetamines as a class and separately for MDMA/ecstasy from ONS, NRS and NPSAD are presented in the review of MDMA undertaken by the ACMD (2009). Some estimates were undertaken, accompanied by appropriate 'health warnings', of the risk of suffering an ecstasy-related death for different age-groups using BCS estimates of numbers of users. Indices of fatal toxicity for a range of substances are also presented, using BCS prevalence data, Home Office drug seizure data and estimates of the market size for each substance. Although the source

of this methodology is not stated (ACMD, 2009:18), it was written by Dr Les King - a full Council member at the time. It drew on data that was then used by him and the author in their paper published the following year (King and Corkery, 2010).

A study of MDMA-related deaths in Norway from 2000 to 2019 revealed an increase in the number of such deaths from 2014; this was in line with increasing numbers of seizures and amounts seized made by law enforcement agencies, despite falls in the MDMA content of ecstasy tablets. On the other hand, the average post-mortem MDMA concentrations were higher at the end of the study than at the beginning. The authors note that these deaths were against a background of polysubstance use (Jamt et al., 2022).

Mephedrone/synthetic cathinones

There are very limited data available for mephedrone/synthetic cathinones at both the UK and individual country levels. At the UK level, there are no statistically significant relationships at the $p < 0.000$ level with mephedrone deaths (Table 10.21). However, at lower significance levels there are positive correlations for: year; number of seizures and amount of mephedrone seized; and for new and all treatment entrants for synthetic cathinones.

Table 10.21: Selected statistically significant correlations between numbers of death and other parameters for mephedrone/synthetic cathinones, United Kingdom

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	30	0.571	0.001
Number of seizures (UK)	12	0.588	0.044
Amount seized (UK)	8	0.869	0.005
EMCDDA Stats Bulletin 2019 (UK) Never previously treated - synthetic cathinones	7	0.798	0.031
EMCDDA Stats Bulletin 2019 (UK) All treatment entrants - synthetic cathinones	7	0.837	0.019

As no breakdowns of mephedrone deaths have been published separately for England and Wales (only combined), it is not possible to generate Pearson correlation coefficients for these countries.

In Scotland, telephone and online NPIS queries reached the $p < 0.000$ significance level, both with positive relationships (Table 10.22). At a lower significance level, year and number of seizures also had positive correlations with the number of mephedrone deaths.

Table 10.22: Selected statistically significant correlations between numbers of death and other parameters for mephedrone/synthetic cathinones, Scotland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	27	0.382	0.049
Number of seizures (Scotland)	12	0.622	0.031
NPIS - telephone queries	13	0.912	0.000
NPIS - online queries	13	0.853	0.000

There were no statistically significant results for Northern Ireland.

The ACMD report on cathinones contained limited information on deaths (compiled by the author on behalf of NPSAD using a range of sources including the GMRs) as the use of synthetic cathinones was a newly-emerging phenomenon, and there was only sparse information on its prevalence; thus, no statistical or correlational investigations were undertaken (ACMD, 2010). A further update on mephedrone deaths was provided to the ACMD (2011) when it considered NPS more broadly - see Chapter 11.

Chapter overview

Correlation results for five of the key stimulants involved in UK drug-related deaths have been detailed in this chapter. Again, it should be noted that these drugs are often taken together with those examined in Chapter 9, i.e., opiates/opioids and benzodiazepines. Stimulants are part of the polysubstance nature of UK drug-related deaths. Some clear narratives have been presented for some of these substances i.e., cocaine/crack and amphetamine, whilst others warrant further investigation i.e., amphetamines, ecstasy, and mephedrone/synthetic cathinones. For the latter group, the unavailability of sufficient data points across time and a restricted range of indicators (and associated parameters) limited what analyses could be undertaken.

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CHAPTER 11: DRUG INDICATOR ASSOCIATIONS FOR CANNABINOIDS, ANAESTHETICS/DISSOCIATIVES, CNS DEPRESSANTS AND NPS

"UK ketamine-related deaths have increased over time, especially in recent years, and show no signs of slowing down (1). Both availability and use in the general population have also increased over time. Consequently, there have been greater numbers seeking treatment for their dependence on the drug, as well as deaths. These relationships exist and need further exploration, especially in respect of how ketamine was acquired and used by decedents. This cannot simply be realised by an examination of coronial records …, it would also need to involve interviews with key informants/witnesses, i.e. conducting 'psychological autopsies."
Corkery et al. (2021b).

Introduction

This chapter presents the findings for the remaining drug classes/index drugs, i.e., cannabinoids (cannabis), anaesthetics/dissociatives (ketamine), Central Nervous System depressants (GHB/GBL), and Novel Psychoactive substances (NPS). As with Chapters 9 and 10, the results are accompanied by brief commentaries and comparisons with other studies (where they exist) that use the method adopted in this part.

Cannabinoids (cannabis)

Despite the fact that up to about 150 parameters were available for cannabis at some point over the past three decades, there were comparatively few that reached the levels of statistical significance applied in this part of the thesis.

At the UK level, no parameters achieved the $p < 0.000$ level of significance (Table 11.1). Four parameters reached lower significance levels; three positive correlations for year, number of individuals found guilty of or cautioned for dealing etc offences, and online NPIS queries. There was a negative correlation between the number of cannabis deaths and the number of individuals found guilty of and cautioned for cannabis possession offences.

Table 11.1: Selected statistically significant correlations between numbers of death and other parameters for cannabis, United Kingdom

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	32	0.444	0.011
No of offenders (UK) (000s) Found Guilty or Cautioned possession	10	- 0.855	0.002
No of offenders (UK) (000s) Found Guilty or Cautioned dealing etc	26	0.405	0.040
NPIS - online queries	12	0.799	0.002

Even for England, there were only three parameters that reached the $p < 0.000$ level of significance: year, online NPIS queries, and number of seizures of cannabis resin, the first two being positive correlations and the last one negative (Table 11.2). At lower significance levels, there were only two positive correlations: number of herbal seizures and NPIS telephone queries. The remaining correlations at these lower levels were negative: street level price; number of individuals found guilty of or cautioned/given penalty notices for cannabis offences, including possession, possession with intent to supply, and supply offences; lifetime use by 16-24 year-olds; young people with new or any referral to treatment with cannabis as their primary drug.

Table 11.2: Selected statistically significant correlations between numbers of death and other parameters for cannabis, England

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	0.677	0.000
UK street price (ounce) resin	16	- 0.563	0.023
Price (£) (UK) street level (resin) UK FP report 2019: source NCA	18	- 0.525	0.025
No of offenders/FG (E&W)	12	- 0.598	0.040
CJS FG/Caut (E&W) Possession	12	- 0.710	0.010
MoJ Outcomes by offence (E&W) FG possession	17	- 0.633	0.006
MoJ Out of Court disposals (E&W) Cautions possession	17	- 0.659	0.004
MoJ Out of Court disposals (E&W) PNDs Penalty Notices possession	13	- 0.771	0.002
CJS FG/Caut (E&W) Possession with intent	12	- 0.652	0.022
CJS FG/Caut (E&W) Supply	12	- 0.716	0.009
Prevalence (%) 16-24 ever use (E&W)	22	- 0.524	0.012
Number of seizures (E&W) herbal	27	0.409	0.034
Number of seizures (E&W) resin	27	- 0.632	0.000
Young people in treatment new presentations (E) All referrals: primary drug	17	- 0.569	0.017
Young people in all in treatment (E) All referrals: primary drug	17	- 0.680	0.003
NPIS - telephone queries	12	0.577	0.050
NPIS - online queries	12	0.853	0.000

In Wales, no parameters met the $p < 0.000$ threshold, but four had correlations at a lower significance level (Table 11.3). Three were negative: disposals (cautions, recorded crime) for cannabis possession); and the estimated number of 16-24 year-olds ever using cannabis. There

was a positive correlation for the number of individuals found guilty of or cautioned for cannabis possession offences.

Table 11.3: Selected statistically significant correlations between numbers of death and other parameters for cannabis, Wales

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
CJS FG/Caut (E&W) Possession	12	0.655	0.021
MoJ Out of Court disposals (E&W) Cautions possession	17	- 0.487	0.047
Recorded crime (E&W) cannabis possession	18	- 0.495	0.037
Est no (thousands) 16-24 ever use (E&W)	14	- 0.601	0.023

Similarly, in Scotland (Table 11.4), there were only statistically significant correlations at lower levels of statistical significance. Three were positive: street price for cannabis resin, number of offenders, and number of cannabis resin seizures; the relationship for the number of plants seized was a negative one.

Table 11.4: Selected statistically significant correlations between numbers of death and other parameters for cannabis, Scotland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Price (£) (UK) street level (resin) UK FP report 2019: source NCA	18	0.669	0.002
No of offenders (S)	13	0.709	0.007
Number of seizures (Scot) resin	29	0.536	0.003
Number of seizures (Scot) plants	29	- 0.438	0.017

In Northern Ireland, there were only two parameters statistically significant at lower levels: the amount of resin seized and online NPIS queries – both with positive correlations (Table 11.5).

Table 11.5: Selected statistically significant correlations between numbers of death and other parameters for cannabis, Northern Ireland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Amount seized (kg) (NI) resin	22	0.670	0.001
NPIS - online queries	12	0.692	0.013

There is a distinct lack of any statistically significant correlations between cannabis deaths and year for the three smaller countries.

Over the years there have been several reports by the ACMD or its predecessor – the Advisory Committee on Drug Dependence (ACDD) - looking at cannabis, mostly with regards to its classification or control under drugs legislation. The report from the ACDD, more commonly

known as the “Wootton Report”, only mentioned deaths in passing (ACDD, 1968, para 25), as was also the case with the first of the ACMD’s report (ACMD, 1982). Deaths and fatalities were not even mentioned in the following reports (ACMD, 2003, 2008a).

Anaesthetics/dissociatives (ketamine)

It is unknown if all ketamine deaths registered by GMRs were due to recreational use; some may have been medical accidents or suicides. There were very few parameters available for ketamine that reached statistically significant levels. At the UK level, only year achieved such a level ($p < 0.000$) - Table 11.6.

Table 11.6: Selected statistically significant correlations between numbers of death and other parameters for ketamine, United Kingdom

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	33	0.741	0.000

There were no data on ketamine deaths available separately for England and Wales; this precluded generating any Pearson correlation coefficients for these countries.

For Scotland, only year and online NPIS queries reached the $p < 0.000$ level of significance, both with positive correlations (Table 11.7). Last year use by 16-24 and 16-60+ year-olds, together with the number of prescription items dispensed also had positive correlations, albeit at lower significance levels.

Table 11.7: Selected statistically significant correlations between numbers of death and other parameters for ketamine, Scotland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	33	0.721	0.000
SCJS 16-24 Last year use (%)	5	0.990	0.001
SCJS 16-60+ Last year use (%)	8	0.860	0.006
No of prescription items (S) (000s)	22	0.477	0.025
NPIS - online queries	13	0.827	0.000

The sole parameter reaching a statistically significant level in Northern Ireland was year (Table 11.8).

Table 11.8: Selected statistically significant correlations between numbers of death and other parameters for ketamine, Northern Ireland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	25	0.605	0.001

So far as the author is aware, the only other examination of UK ketamine deaths and other drug indicators is his 2021 poster (Corkery et al., 2021b). In that study, there were 4 relationships significant at the $p < 0.01$ level, only 1 at $p \leq 0.001$. There were six relationships significant at $p < 0.01$ (one-tailed test), four of which were at the ≤ 0.001 level: ketamine as a sole mention in deaths with Northern Ireland treatment numbers; any ketamine mention in deaths with Northern Ireland treatment numbers, with year, and with the estimated number of life-time ketamine use in England & Wales.

The author's previous study found that UK ketamine-related deaths have increased over time, especially in recent years, and show no signs of slowing down (Corkery et al., 2021a). Both availability and use in the general population have also increased over time. Consequently, there have been greater numbers seeking treatment for their dependence on the drug, as well as deaths. The author and his PhD supervisors concluded that these relationships exist and need further exploration, especially in respect of how ketamine was acquired and used by decedents (Corkery et al., 2021b).

The ACMD looked at ketamine on several occasions. The author was a member of the ACMD Ketamine Sub-Committee which first looked at the drug (ACMD, 2004a). He reported that there were very few known deaths at that point in time, only 9 between 1993 and 2003 (ACMD, 2004b:17). The author also compiled an appendix (ACMD, 2004b: Appendix 3) relating to ketamine use in the recreational scene in the UK (ACMD, 2004b:42-54). There was no investigation of an association between deaths and other indicators.

Even when the author and colleagues published the first paper on such deaths, they were only able to identify a total of 27 cases up to 2006; they did not look at any other drug indicators (Schifano et al., 2008). However, by the time of the next consideration of ketamine by the ACMD (2013b), there was a section devoted to ketamine-related fatalities, including a summary of a presentation by the author on behalf of NPSAD concerning 93 deaths (ACMD, 2013b:30). Again, no investigation was undertaken to look for associations between deaths and other indicators.

Central Nervous System depressants (GHB/GBL)

There are extremely few statistically significant relationships identified between GHB/GBL deaths and other parameters.

At the UK Level, only year reached the $p < 0.000$ level of statistical significance, with a positive relationship (Table 11.9). The amount seized displayed a negative correlation at a lower significance level.

Table 11.9: Selected statistically significant correlations between numbers of death and other parameters for GHB/GBL, United Kingdom

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	33	0.793	0.000
Amount seized (UK)	8	- 0.771	0.025

A lack of published data available for GHB/GBL deaths in England and Wales separately meant that Pearson correlation coefficients could not be calculated for these countries.

In Scotland, the only parameter with a statistically significant relationship, albeit at a lower level than the $p < 0.000$ one, was year, with a positive association (Table 11.10).

Table 11.10: Selected statistically significant correlations between numbers of death and other parameters for GHB/GBL, Scotland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	33	0.356	0.042

There were no statistically significant findings for Northern Ireland.

The ACMD first looked at controls on GHB in 2002 following the approval in March 2001 by the United Nations Commission on Narcotic Drugs to add it to the UN Convention on Psychotropic Substances 1971 (Home Office, 2002). GHB subsequently became a Class C drug on 1 July 2003 by virtue of the Misuse of Drugs Act 1971 (Modification) Order 2003 (https://www.legislation.gov.uk/primary+secondary/2003/1243).

To assist with the ACMD's consideration of GBL and 1,4-BD in 2007, the author compiled a report on behalf of NPSAD on a total of 47 deaths involving GHB, GBL and 1,4-BD - see Annex 4: GHB/GBL deaths in the UK - some initial findings - of the Council's report (ACMD, 2008b:34-44). This report also included cases that were non-NPSAD in origin. No attempts were made by the

ACMD to seek statistical relationships between deaths and other indicators. Advice from the ACMD to the UK Government on scheduling of GHB, following the Commission on Narcotic Drugs' decision to reschedule the substance from Schedule IV to Schedule II of the Convention on Psychotropic Substances of 1971, included references to deaths recorded by ONS and NPSAD (ACMD, 2013a).

Data on GHB/GBL deaths from ONS and papers published by the author and colleagues (Corkery et al., 2015, 2018) were cited extensively in the ACMD's most recent report (ACMD, 2020), in particular the socio-demographic characteristics of decedents and the characteristics of the deaths on the NPSAD database. However, no correlational analyses were undertaken.

Novel Psychoactive Substances (NPS)

The final group examined in this chapter include any molecule classified by the GMRs as an NPS. Overall, this group had the lowest number of parameters with statistically significant correlations with NPS deaths. Indeed, only one parameter - year - met this criterion. It achieved the $p < 0.000$ level at the UK level (Table 11.11), in England (Table 11.12), and Scotland (Table 11.13), but at a lower significance level in Wales (Table 11.14) and Northern Ireland (Table 11.15). All these results were positive relationships.

Table 11.11: Selected statistically significant correlations between numbers of death and other parameters for NPS, United Kingdom

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	30	0.768	0.000

Table 11.12: Selected statistically significant correlations between numbers of death and other parameters for NPS, England

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	0.847	0.000

Table 11.13: Selected statistically significant correlations between numbers of death and other parameters for NPS, Wales

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	29	0.553	0.002

Table 11.14: Selected statistically significant correlations between numbers of death and other parameters for NPS, Scotland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	27	0.780	0.000

Table 11.15: Selected statistically significant correlations between numbers of death and other parameters for NPS, Northern Ireland

Parameters	*Number of data points*	*Pearson correlation coefficient value*	*Significance level*
Year	16	0.716	0.002

The ACMD included deaths in its remit when considering NPS. Fatalities involving a range of NPS classes were reported by the author on behalf of NPSAD, including a detailed update of mephedrone-related cases provided in Annex C of the report (ACMD, 2011:62-64). The latter information was an update to the data supplied to the ACMD for their consideration of synthetic cathinones (ACMD, 2010). Information on deaths has been used, together with information on other indicators, in many other reports on individual NPS index molecules and classes (see Chapter 13).

Chapter overview

This chapter has presented the correlation results for the remaining drug classes/index drugs examined by this study. However, there are no clear-cut narratives to present - even for cannabis. The other drug groups and index drugs (ketamine, GHB/GBL, NPS) merit additional further investigation. The unavailability of sufficient data points across time and a restricted range of indicators (and associated parameters) limited what could be done for NPS, and a lack of published figures for England and Wales separately prevented clearer narratives for ketamine and GHB/GBL. These issues are revisited in Chapter 12.

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CHAPTER 12: ASSOCIATIONS BETWEEN DRUG INDICATORS AND DRUG-RELATED DEATHS

"One could argue that most data sources in drug use prevalence, harm, and trends may be biased in some way, frequently by the resources devoted to the data-generating activity, be it treatment, police action, or investigation of cause of death. Thus it becomes essential to look for consistency in trends across data sources."
Schifano and Corkery (2008).

Introduction

The final chapter in this Part comprises a brief discussion and summary of the main findings detailed in Chapters 9 to 11. It concludes with a section on the strengths and limitations of this study.

Discussion

The analyses reported in Chapters 9 to 11 used the Pearson correlation coefficient approach to examine the statistical relationships between UK deaths involving a range of index drug and drug classes (n = 15) and eight other drug indicators (see Chapter 8 for details).

Thorough sweeps of the extant literature, including 'grey' literature, revealed that very few studies, other than those already undertaken by the author and his colleagues more than 15 years ago, have used this approach. Where such studies have been undertaken, they are referenced in the relevant chapters' sub-sections above.

Most other analyses have been narrative or descriptive accounts rather than statistical analyses. However, other approaches to looking at the relationships between deaths from index drugs and other drug indicators have been developed in recent years. For example, in the USA, Zibell and colleagues have used MGARCH (a multivariate generalized autoregressive conditional heteroskedasticity used to model autocorrelation in time series analysis) to look at the associations between law enforcement seizures of illicit drugs and drug overdose deaths involving cocaine and methamphetamine (Zibell et al., 2022) and heroin, fentanyl and carfentanil in Ohio (Zibell et al., 2019). Using similar data, but at a national level, Zibell et al. (2023) used Poisson regressions to look at opioid overdose deaths.

King and Corkery (2010) developed an index of fatal toxicity for drugs of misuse which was calculated for each of five drugs (heroin, cocaine/crack, ecstasy/MDMA, amphetamine and

cannabis) as the ratio of the number of deaths associated with that substance to its availability in the period 2003–2007. Three separate proxy measures of availability were used employing data for England and Wales (number of users as determined by household surveys, number of seizures by law enforcement agencies and estimates of the market size). A broad correlation was found between all three denominators of availability. Not unexpectedly, heroin and cannabis showed, respectively, the highest and lowest toxicities. The index of fatal toxicity of MDMA was close to that of amphetamine and cocaine/crack. The researchers, as part of a later study, extended the time period examined from 2000 to 2015/6 and broadened the range of drugs to include GHB, ketamine, piperazines and mephedrone. It was found that prevalence in the form of household surveys, as summarised in the BCS/CSEW, and law enforcement seizures were the best measures of availability. The findings of the 2010 study were validated by the later study (King and Corkery, 2018); the index of fatal toxicity of ketamine fell between those of amphetamine and MDMA, whilst that for mephedrone was lower than that for cocaine/crack (see Figure 12.1).

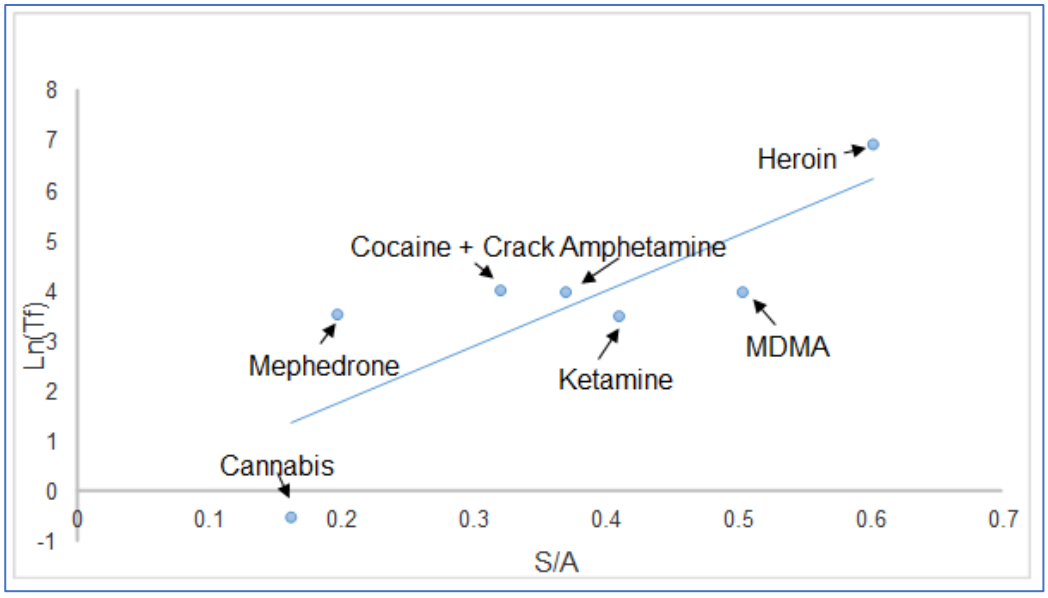

Figure 12.1: The relationship between the updated index LnT_f [based on a combination of prevalence and number of seizures] and values of S/A [Single/Any mention] (r = 0.923; P <0.01) for the seven reference compounds (amphetamine, cannabis, cocaine, heroin, ketamine, MDMA and mephedrone). The straight line is the least squares fit [LnT_f = 11.22(S/A) - 0.48].

Source: Figure 1, King and Corkery (2018). *Copyright © The Author(s) 2018*.

The 2018 study also differed from the 2010 one in that a new measure for deaths was developed as the ratio of single to any mention of the index drug on the death certificate. A systematic literature review is planned, following completion of this thesis, which will look at types of fatal toxicity indices which have been developed and how they have been used; it is now part of the author's planned future work.

Key patterns in main drug classes

The main back-drop to the drug-related deaths scene is the inexorable rise in such events over the period examined by this thesis. There are many factors at work and the nature of their relationships is complex, and further complicated by differences for individual index drugs/drug classes. As seen in Chapter 6, the primary driver in the overall upward trend are deaths involving opiates (heroin/morphine) and opioids (e.g., methadone), but other classes of drug such as stimulants, especially cocaine, have made significant contributions.

The main drivers for heroin/morphine deaths in the UK appear initially to have been increased use of heroin up to around 2000-2002 and plateauing until about 2015, as indicated by prevalence data. The number of law enforcement activities (seizures, individuals found guilty of or cautioned for heroin drug offences) peaked around 2007. This was accompanied by a fall and then levelling off in the price of illicit heroin, whilst purity levels also rose in this period, before tumbling around 2010-2011 because of a heroin 'drought'. It took several years for purity levels to recover. This period of increased availability saw a rise in the number of individuals seeking help to deal with their dependence, as evidenced by notifications to the Home Office Addicts Index and subsequently the drug misuse databases. However, the last decade has seen a fall in the number of new heroin users referred for treatment in England and Wales. The continuing increase in the number of heroin/morphine deaths in the UK would, therefore, suggest that more deaths are occurring amongst existing long-term heroin users. Several possible explanations have been posited by ONS (2022b): "there is an ageing cohort of drug users, likely to be suffering from the effects of long-term drug use and becoming increasingly susceptible to a fatal overdose; new trends in taking specific drugs, including gabapentinoids and benzodiazepines, alongside heroin or morphine, may increase the risk of an overdose; [and] there may have been an increase in disengagement or non-compliance with opiate substitute therapy (OST)." On the other hand, by pooling data from a Scottish study (Gao et al., 2016) and their own research, Pierce et al. (2018) demonstrated that the hazard ratio for methadone-specific death amongst opioid-dependent individuals' when compared with 25-34 year-olds nearly doubled for those aged 35-44 years and quadrupled for those aged over 44 years.

In the UK, methadone has been one of the main stays of OST and methadone maintenance treatment (MMT) for the last half century. However, despite its undoubted benefits, methadone, like any other drug, has the potential to be lethal (Corkery et al., 2004). As was noted in Chapter 6, deaths involving this drug fell towards the end of the twentieth century, but despite enjoying a period of stability they then started rising again. Availability of methadone has been facilitated by continued increasing of its prescribing. Although lower amounts of injectables are prescribed compared to several decades ago, and supervised consumption of methadone has been around since 1995 in Scotland and England from 1999, the number of fatalities continues to rise. This is despite the apparent success noted by Strang et al. (2010) of the latter initiative leading to "at least a fourfold reduction in deaths due to methadone related overdose per defined daily dose" during the 1993-2008 period in those two countries. Most (up to two-thirds) methadone-related deaths would appear to be due to diversion of prescribed methadone (Corkery et al., 2014). Other factors could also be at work e.g., the co-consumption of other substances especially Central Nervous System depressants such as heroin, other opioids, benzodiazepines and alcohol.

Availability, as primarily indicated by positive correlations with the number of seizures and amounts confiscated, seems to be the main driver behind deaths related to benzodiazepines in terms of prescribed drugs. Amongst prescribed benzodiazepines, diazepam and temazepam were historically the main contributors to overall patterns of mortality caused by this class of drug; at least until such time as initiatives were introduced to reduce their availability. Availability of illicit so-called 'designer benzos' has been a key factor in the overall rise in benzodiazepines deaths, especially in Scotland where these substances have been the major contributor to deaths in recent years (Corkery et al., 2020; 2022).

The main stimulant causing deaths in the UK is cocaine. ONS (2022) surmise, at least for England and Wales, that the rise in such deaths "is likely to be a direct consequence of the increasing prevalence in cocaine use … cocaine … [has] been reported to have high availability in recent years, with low prices and high purity levels." Lifetime prevalence of cocaine use has indeed been rising in recent years across the UK, but last year use has been falling. The overwhelming source of cocaine in the UK is imported supplies; none is prescribed on the NHS for use in drug treatment. There has been no information in the public domain about the estimated size of the demand for and supply of cocaine to UK for at least 20 years (Pudney et al., 2006). Price data show falling street prices for cocaine over the period to 2016, but since then (at least until 2020) prices doubled. Street purity levels fell from very high values in the early 2000s to an all-time low (in terms of the period considered here) in 2009 before rising again to record levels by 2019. These changes have been reflected in increasing numbers of individuals being admitted to hospital because of cocaine overdoses, or diagnoses of mental

and behavioural disorders due to its use, as well as in those seeking treatment for dependence. Convictions and cautions for cocaine drug offences peaked in 2011 and appear to have declined since then, although it is difficult to know what has happened in the last decade or so because of a lack of continuity in the provision of published statistics. By contrast, the number of cocaine seizures appears to be rising over time, whereas amounts seized fluctuate over time.

As one might expect, the drivers for 'crack' share similarities with those for cocaine powder, although there are some differences. Both prevalence of lifetime and last year crack use appears to have peaked about 2015. The overwhelming source of crack in the UK is probably imported supplies, although crack can be easily manufactured domestically; cocaine in smokeable form has only rarely been privately prescribed for use in drug treatment (Bean, 1993:7; Seddon, 2020) and probably not for two or three decades. [It may be the case that crack 'roaches' were prescribed on the NHS at that time (Nutt and Marks, 2024).] For most of the period covered by this thesis, the price of a 'rock' of crack remained extremely stable. Street purity levels of crack declined to their lowest level in 2009-11, since when they have climbed to record levels. The number of individuals seeking help for the crack use has been increasing over time. Numbers of crack seizures appear to have peaked in the last couple of years or so. However, due to gaps in published data, it is unclear whether the peak number of individuals convicted or cautioned for crack drug offences recorded in 2008, which was followed by a decline to 2015, was regained in subsequent years. Online queries made to the NPIS about crack peaked in 2020, as they did for cocaine, suggesting that there are still concerns about these drugs despite a, hopefully, greater awareness of their potential harms and lethality.

Most correlations for amphetamine are negative in direction, despite the fact that UK deaths involving amphetamine peaked around 2020. The factors demonstrating a positive relationship are: street purity levels (which can vary widely year to year) and number of prescribed items (now standing at record levels). Most indicators show negative associations with amphetamine deaths, especially lifetime and last year use which have seen falls in prevalence since 2007. The number of individuals found guilty of or cautioned for amphetamine drug offences has declined since 2011, as have the number of seizures and quantity of amphetamine confiscated. The price of amphetamine has been remarkably stable over the period examined by this thesis. These downward movements are echoed in treatment episodes, hospital admissions and NPIS queries. Yet, deaths are increasing. The author notes that the main parameter with a positive correlation is the number of prescription items dispensed and, therefore, the likelihood of increased amounts of drugs such as methylphenidate. There also appears to be increasing use of methylphenidate analogues, freely available via the Internet (Hockenhull et al., 2019), which may be contributing to the overall increase in deaths associated with this drug class (Corkery and Schifano, 2022).

Taken overall, the main ecstasy/MDMA indicators with positive associations with deaths are: street level purity, the number of individuals convicted or cautioned for ecstasy drug offences, lifetime use, new referrals of young people to treatment with ecstasy as their main drug of concern, and NPIS queries. On the other hand, there are negative associations with the MDMA content of ecstasy tablets and street level prices. UK ecstasy-related deaths peaked around 2018-2020, a period when the MDMA content of ecstasy tablets was at record levels although prices appear to have been stable in the preceding few years and during that time. By comparison, street prices were at their lowest between 2006 and 2012, but MDMA content was at its lowest point in 2007-2008. However, ecstasy-related deaths fell to their lowest level for some time between 2009 and 2011. This would suggest that availability *per se* was not a driving factor in causing deaths, neither was the prevalence of lifetime and last year use which were at relative low levels at this time. However, as noted in Chapter 10, the quantity of MDMA in ecstasy tablets did increase during the 2010s, as did deaths relating to MDMA use. Thus, the association between availability indicators and ecstasy-related deaths is not as clear-cut as the author and colleagues had previously understood (Schifano et al., 2006).

Mephedrone did not emerge in the UK as a recreational drug until the late 2000s. Unlike other synthetic cathinones that also emerged at around this time but were short-lived in their popularity, this one did become part of the stimulant scene. UK deaths peaked in 2015 (n = 62) but still remain at relatively high levels (n = 18 in 2021). There are positive associations between deaths and the number of seizures and amount of mephedrone seized; and for new and all treatment entrants for synthetic cathinones. Prevalence data for England and Wales suggests peak levels of last year use were reached in 2014. This ties in well with the peak number of deaths being registered in the following year, as the average time between a death being reported to a coroner and an inquest being completed is about six months. The number of seizures and quantity of mephedrone seized, as well as convictions and cautions, peaked several years before the peak number of deaths registered; availability (as measured by these law enforcement parameters) does not seem to have been a driver in fatality numbers.

The number of death certificates where cannabis is mentioned has varied over time, without any clear patterns being discernible. It is, therefore, unsurprising that at the UK level no parameters achieved achieved the $p < 0.000$ level of significance. Taken in the round, the UK figures and those for England, the key positive associations over time were: number of individuals found guilty of or cautioned for dealing etc offences, number of seizures of herbal cannabis and cannabis resin, and NPIS queries. There were far more negative relationships between the number of cannabis deaths and other parameters, including: the number of individuals found guilty of and cautioned for cannabis (possession, possession with intent to supply, and supply)

offences; street level price; lifetime use by 16-24 year-olds; and young people referred to treatment with cannabis as their primary drug. Street prices for both herbal cannabis and cannabis resin were fairly stable over the time-period examined here. There has also been a stable picture for the lifetime and last year prevalence rates for cannabis use. The number of individuals in the UK found guilty of or given a caution/warning for cannabis drug offences has varied across time; rising during the 1990s to a peak in 1998, before levelling out at lower level in the early 2000s before falling even lower in the mid-2000s before recovering to a new (but lower) peak in 2011, followed by a further decline. The number of UK cannabis seizures has also experienced a series of fluctuations over the past three decades, but not necessarily in step with those noted for individuals dealt with for cannabis offences. There are too few data points from a consistent source to make any comment on the relationship between cannabis potency and cannabis-related deaths. Taking the wide range of indicators and parameters as a whole, the author argues that there are no clear conclusions to be drawn as to the key drivers at work in relation to cannabis-related deaths. However, it should be noted that deaths caused by cannabis on its own are very rare events.

Key findings by type of factor

One of the clearest associations to emerge was a mainly positive one between the number of deaths and time (as indicated by the proxy measure of year of death). This is to be expected as typically deaths related to the use of the substances examined here have increased over the last three decades or so. At all geographical levels, the only exceptions were temazepam and barbiturates. Both of these groups of drugs have shown substantial declines in their involvement in deaths following the imposition of tighter controls on the prescribing of gelatin-filled temazepam capsules and on barbiturates as a class. These measures were introduced as a direct response to serious and well-founded concerns about deaths caused by these substances; they had very clear and positive results. The effects of prescribing methadone in OST and MMT remain hotly debated and can be argued either way.

By contrast, other initiatives to limit the adverse effects of other index drugs or drug classes have been unsuccessful. For example, the only indicator that had a very highly statistically significant association with NPS deaths was year. Such deaths have been increasing since these substances started being controlled under the Misuse of Drugs Act 1971 to be used in 2010. The available data for mephedrone, which also falls within the umbrella term of NPS, but which was analysed as a stimulant because of its high visibility, additionally indicate increases in the number of seizures and amount of mephedrone seizures as well as NPIS queries. Although the volume of these indicators has fallen in recent years, mephedrone has not disappeared, and it is now part of the repertoire of mainstream drugs available on the UK

recreational drug scene (Moore et al., 2013). In passing it is worth mentioning that the availability of mephedrone and other synthetic cathinones in the late 2000s - at a time when other stimulants, such as cocaine, amphetamine and ecstasy, were of much lower quality at street level (see above and Nutt (2011)) - may have actually reduced deaths from those drugs because of users seeking substitute substances (Bird and Mercer, 2011).

Interruptions to normal patterns of supply or associated problems may have a temporary impact on longer-term trends in drug-related deaths. There are three clear examples of such events, which lay outside the control of international bodies (e.g., UNODC, WHO, and EMCDDA), UK government departments and agencies, charities and voluntary organisations, civil society, etc. - heroin supplies contaminated with *Clostridium novyi*; heroin 'drought'; and the Covid-19 pandemic.

As was noted in Chapter 2, at least 40 deaths reported between April and August 2000 that occurred in Scotland and England were linked to the *Group A Streptococcus, Staphylococcus aureus, Clostridium* and *Bacillus* species (Jones et al., 2002; McGuigan et al., 2002). These fatalities occurred amongst groups of heroin users who injected into their muscles or skin ('popping'). McGuigan et al. (2002) surmised that the outbreak in Glasgow amongst those individuals whose heroin supply had come from a specific batch of contaminated heroin, which had probably originated in Afghanistan according to intelligence shared with the author by UK law enforcement agencies at the time of the outbreak. The indicators underpinning the conclusion that the proximal source of the bacteria was a contaminated heroin batch were: "the similarity of the clinical features and injecting methods of the cases, their temporal and geographical distribution, the high proportion that knew, and injected with, each other and the occurrence of similar contemporaneous outbreaks in Dublin and parts of England. According to police intelligence, the distribution of the clusters in Glasgow reflected specific recognised routes of heroin distribution." (McGuigan et al., 2002). As these deaths were not recorded as heroin-related poisoning deaths, they did not contribute to the increase in the number of deaths in Scotland registered between 2000 and 2001. Indeed, in the short term, the number of heroin-related poisoning deaths may have been lower than otherwise expected as a result of heroin users being advised to avoid injecting heroin and using other routes of administration e.g., 'chasing the dragon' or smoking heroin.

There was such a severe shortage of heroin across the UK and Europe (Hallam, 2011) between September/October 2010 and mid-2011 that it became known the 'heroin drought'. Several theories were advanced to account for this shortage (Simonson and Daly, 2011). The effects of the drought were wide-ranging: street-level purity fell from 32% to 13%; drug users starting using 'black market' diazepam and other 'street tranquillisers'; the number of transactions at

needle and syringe exchanges fell. Transition to polydrug use during the shortage led to higher susceptibility to overdose and additional drug-related vulnerabilities (Harris et al., 2015). The re-appearance of higher purity heroin led to a reported doubling in the number of deaths in some areas (Simonson and Daly, 2011). Indeed, at the UK level the number of 1,207 heroin/morphine deaths registered in 2009 fell to 1,060 in 2010 and dropped further to 817 in 2011 and 821 in 2012. This prolonged fall is also likely due to a continuing heroin shortage, both in the UK and the EU, if street level purity is used as a proxy measure for availability (Wright, 2017).

A much more recent phenomenon that may have not only affected heroin users but also those using opioids and other classes of drugs is the Covid-19 pandemic. Changes were seen not only in the way in which prescribed methadone and buprenorphine were dispensed (Richards-Jones et al., 2023). When measures such as 'lock down', self-isolation, quarantining and restrictions on social mixing were introduced, there were consequent changes in supply chains, prices, and what substances were on offer in terms of physical face to face transactions, with consequent shifts to more online and social media transactions occurring (Arillotta et al., 2021). There were also shifts from illegal drugs to the misuse of prescription and Over the Counter drugs for self-medication (Schifano et al., 2021a). There was an overall fall in the number of hospital stays in Scotland for opioids, cocaine and 'multiple/other' drugs whilst there was an increase for hypnotics/sedatives and cannabis (Public Health Scotland, 2022:23).

Although it is probably too soon to fully assess the impact of the pandemic on drug-related deaths there are some early indications that changes have occurred. For example, a study using NPSAD data for England showed a 64% increase in methadone deaths overall in the first six months of 2020 compared to similar periods in earlier years (Aldabergenov et al., 2022). However, drilling down into this finding, the researchers found there was a noticeable increase in predicted deaths during the first lockdown in England for individuals not prescribed methadone but not for those with a methadone script, which is thought to have functioned as a protective factor. It is likely that the increase in methadone-related deaths in those without a script is due to a greater supply of methadone due to services being advised to move most patients on opioid substitution treatment from daily supervised consumption to take-home doses of methadone or buprenorphine, and to lengthen prescriptions (up to two weeks' supply (Kesten et al., 2021), thereby facilitating greater diversion. To fully understand this difference further studies are required. Another NPSAD study looked at deaths that occurred between January 2018 and December 2021 in England that had been reported by 31 December 2022 (Sekeris et al., 2023). This study confirmed the increase in methadone-related deaths but also found a significant fall in heroin/morphine deaths; there was a rise in the proportion of deaths involving anti-depressants. At the official GMR level, ONS report that the median registration delay for both drug poisoning and drug misuse deaths rose substantially in 2021 compared to 2020 for

both England and Wales “amid disruption caused by the coronavirus (COVID-19) pandemic” (ONS, 2022a:11).

There are a range of factors that can influence the choice of psychoactive substances used by individuals. Changes in availability due to shortages of specific drugs have been outlined in the preceding discussion; tightening up of prescribing; falls in street purity levels; ‘droughts; diseases; contaminated supplies; etc. These have led to changes not only in the type of substances used, i.e., displacement or substitution, but also route of administration, e.g., from injecting heroin to ‘chasing the dragon’.

Other external factors may affect availability or the desirability of psychoactive drugs, including shifts in policy or policy-driven initiatives such as restricting prescriptions and formulations, trading standard initiatives, as well as changes to existing legislation, i.e., the Misuse of Drugs Act 1971 (or its schedules via secondary legislation such as Statutory Instruments and Orders in Council), the introduction of interim measures such as Temporary Class Drug Orders (TCDOs) in November 2011) or even new primary legislation, i.e., the Psychoactive Substances Act (PSA) 2016. There have also been changes in classification under the Misuse of Drugs Act 1971 of some index drugs or groups of substances, e.g., cannabis, some benzodiazepines, ‘Z’ drugs; GHB/GBL, etc.

The effects of TCDOs have not been widely researched. One Scottish study which looked at the introduction in April 2015 of a TCDO to deal with ethylphenidate and related analogues found that it had been effective in reducing infections among people who inject drugs during an infection (Yeung et al., 2017). Another Scottish study looked at the effects of two TCDOs (for methylphenidate and ethylphenidate), trading standards activities and the PSA 2016 on “cohorts of patients with recreational drug toxicity presenting to Edinburgh Royal Infirmary and dying with detectable recreational drugs in Edinburgh” (Pettie et al., 2018). The study found that these initiatives was “associated with effective and sustained prevention”, reduced hospital admissions (and consequent cost saving to the National Health System), together with a reduction in the detection of stimulant NPS in post mortem toxicology.

The effects of the PSA 2016 on several drug indicators have been studied: the availability of specific substances, e.g., the synthetic cannabinoid MDMB-CHMICA (Haden et al., 2017) or classes of drugs, e.g., synthetic cannabinoids, some of which caused unforeseen adverse outcomes (Ralphs et al., 2021); episodes of toxicity related to new psychoactive substances reported to NPIS (e.g., Al-Banaa et al., 2020); hospital presentations following use of synthetic cannabinoids (Craft et al., 2022); and fatalities. Deaths reported to NPSAD following NPS use continued to increase despite the Act’s introduction; however, reductions were seen

in younger individuals and those living in more affluent areas (Deen et al., 2021). A similar conclusion has been drawn by Burgess (2021):

> "In Scotland, deaths in which 'NPS were implicated in or potentially contributed to the death' have soared every year post-PSA, from 74 in 2015; to 286 in 2016; to 337 in 2017; to 575 in 2018. … In England and Wales, NPS-related deaths halved in the year post-PSA, but have since returned to prePSA levels. … While numerous years of data are required to reach firm conclusions, this casts doubt on the preliminary evidence suggesting the PSA might have reduced NPS-related deaths in England and Wales, and the advancement in the [Home Office Report (Home Office, 2018)] that the PSA has reduced overall harms."
> Burgess (2021:26)

Further research could be undertaken to map such changes in legislation against trends in drug-related deaths, using both drug poisoning and drug misuse definitions. This should take the form of 'before and after' studies. As far as the author is aware, there are no studies looking at what effects, if any, changes introduced by bringing substances under control under the provisions of the Misuse of Drugs Act 1971 or changing their classification under it have had on drug-related deaths.

Provision of information on harms caused by drugs, including fatalities, has and continues to feed into such changes in legislation; this aspect is examined further in Chapter 13. However, it is worth recalling here that it is only rarely that the approach used in this chapter, i.e., looking at statistical relationships between drug-related deaths and other drug indicators has been used in the UK context, or even globally. Even the seminal ACMD (2000) report on reducing drug related deaths omitted such an exercise.

Data limitations and strengths

The intention was to have 1990 as the base-year, so as to build on the already published analyses (see Chapter 8); this was achieved to a certain extent.

Limitations

It has not been possible to calculate correlations for all drug classes/index substances because insufficient data items were available at the UK and/or country levels. Although it is possible to calculate correlations across all measures for all geographical levels (i.e., UK and individual countries) combined, the author decided not to present these so as to maintain clarity of presentation of results and their interpretations. However, the author is confident that the exercise described here in this Part demonstrates that it is possible to undertake an epidemiological study using this approach that provides a cohesive view and understanding of the nature, evolution and extent of drug-related deaths in the UK.

If it were possible to align parameters for longer periods and/or across the UK would it lead to stronger associations/correlations, thereby allowing clearer/stronger conclusions to be drawn? That will depend on how case ascertainment, reporting, recording and publication develops in the future. These aspects are discussed in the concluding chapter (Chapter 14).

Many of the limitations described here for the present exercise are, unsurprisingly, the same as those encountered in the previous studies mentioned in the earlier chapters of this Part. For clarity, these limitations are rehearsed here.

Most data sources used to monitor drug indicators such as prevalence of use, law enforcement activities, measuring harms, service provision and treatment, and investigations into toxicology and cause of death have inherent biases derived from the data-generating activities themselves, as well as the nature and purpose of the activities, e.g., epidemiological vs. statistical vs. routine/administrative data. It is important, therefore, to understand and, where possible, take account of any biases or skewness thus generated.

The information collected and published by the UK GMRs has limitations as detailed in Chapters 3 to 5. The number of cases identified here were actually 'mentions' of index drugs/drug classes on death certificates, i.e., no information was available in respect of drugs' dosage, post-mortem reports, toxicology results and setting characteristics. The inclusion of an index drug in information submitted to GMRs does not necessarily mean that this drug directly 'caused' the death, but that it was found at postmortem and/or was identified by toxicological screening. On the other hand, when an index drug is mentioned on its own, one could assume that the substance recorded was somehow more directly implicated in a fatality.

Polysubstance use itself may be a confounding factor. Taking ecstasy as an example, the co-consumption of two stimulants (e.g., amphetamine and/or cocaine with MDMA) might synergically increase both serotonergic and dopaminergic stimulation, thereby increasing the likelihood of the serotonin syndrome (Schifano et al., 2021b). Combined use of hallucinogens (e.g., LSD and/or ketamine) with MDMA may increase the possibility of 'intoxicated behaviours', such as dangerous driving, leading to a greater chance of a deadly outcome. Alternatively, co-use of sedatives with MDMA might lessen an excess of sympathomimetic overactivity (Schifano et al., 2006).

There may also be reporting biases over time. For example, ecstasy and cocaine/crack cocaine may not have been screened for systematically in the first part of the 1990s; consequently, figures for those years may be lower than the actual occurrences.

A major issue from an epidemiological perspective is that the mortality statistics used for the present exercise were deaths registered in a calendar rather than the actual year of death. Although the fact of death of individuals may be registered within a few weeks of death, the actual cause may not be known for some months, even years, and this may not appear in published drug-related death statistics until some considerable time after the death was first registered. Unfortunately, the only consistent published information on DRDs registered across the UK were those on year of registration.

The number of offenders convicted of or cautioned for drug offences and number of seizures may reflect changes in policies, priorities and activities of law enforcement agencies. Historically, the police only submitted those samples to the Forensic Science Service for which they already suspected a drug to be present. This may have had the effect of police data overestimating the purity of street samples. The amounts of drugs seized over time may reflect both variations in intelligence-led activities of law enforcement agencies and fluctuating availability of drugs on the illicit ('black') market.

Although reports on ecstasy prices from the National Crime Intelligence Service were the best available historically from the UK (Corkery, 2002), these data have their own limitations. Even today, such information on average prices is calculated by the National Crime Agency from information submitted by individual officers from different police force areas, and at varying periods, on a non-systematic and non-stratified basis. Most information is probably anecdotal in nature and is not based on routine 'test purchases', although this is sometimes done by some police forces.

Datasets relating to other potential drivers probably have similar issues and limitations. There may be additional confounding variable underlying all the data; the nature of the relationships between the different variables is not straightforward and may change over time. Since the present exercise was an ecological study, it has proved difficult to address the role of confounding variables that may well explain some of the associations noted in this chapter. Therefore, it is important, if not essential, to look for consistency in trends across data sources. Continuity of indicators related to deaths and associated indicators is fundamental to understanding the trends in drug-related deaths.

Strengths

This is the first study of its kind, anywhere in the world, as far as the author is aware, to look at drug-related deaths using such a wide range of both drug indicators and parameters. The

period covered is also probably one of the longest ever undertaken using an ecological approach.

This PhD-related exercise builds on and extends the period covered by earlier studies conducted by the author and colleagues, as well as the range of index drug/drug classes investigated. If the studies were to be repeated in a few years' time, some of the current deficits, in terms of small numbers of data points for some substances, would be remedied and more robust correlations calculated and, thus, more definitive conclusions drawn.

Chapter overview

This Part of the thesis has demonstrated how drug-related death data can be used in conjunction with other drug indicators to provide a more comprehensive and holistic understanding of what higher level or macro factors (including some at the international level) may play a role in causing or contributing to such events, compared to local scenarios as considered in Chapter 7.

Eight sets of drug indicators have been used to try and shed light on their relationships with fatalities across a range of 15 index drugs/drug classes. Some clear narratives have been presented for some of these substances (e.g., heroin/morphine, methadone, diazepam, temazepam, cocaine/crack, amphetamine) whilst others warrant further investigation (e.g., ecstasy, mephedrone, cannabis, ketamine, GHB/GBL, NPS). The limitations of data availability, accuracy, etc. limited what analyses could be conducted. Some of these aspects are revisited in Chapter 14.

The contents of this Part could form the basis for a series of individual papers on the main drug groups covered here, or indeed a monograph, which could help to inform policy development, legislation, professional practice, service and treatment provision, etc. These aspects are discussed in Chapter 13.

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PART 5 – DECISION-MAKING AND THE WAY FORWARD

This final part (Part 5) consists of two chapters which pull together the various themes that have been woven through the fabric of the previous parts and chapters, with the intention that a seamless final product results.

Chapter 13 demonstrates how the empirical data and information on drug-related deaths (DRDs) derived from the processes outlined in Part 2, analysed at both the macro and micro levels in Part 3, and explored in relation to other drug indicators in the United Kingdom (UK) context can be deployed in public health and other scenarios: feeding into policy advice and formulation, informing drug control and regulation, developing education, and providing evidence-based professional guidance and practice. This is evidenced by reference to examples drawn from activities in which the author and colleagues have been engaged during the course of his doctoral research programme.

Chapter 14 provides illustrations of how the themes examined in this thesis coalesce and are complementary. Developments over the past three decades in UK DRDs are reviewed, and the current situation is explored. Changes, continuities, and challenges that may be faced in the future are identified and discussed. Factors that may impact the ways in which future work in this multidisciplinary field will be conducted are outlined.

CHAPTER 13 - DECISION-MAKING USING DATA ON DRUG-RELATED DEATHS

"Careful detailed examination of information on mortality associated with drug use facilitates systematic analyses that can reveal the characteristics of individuals dying as a consequence of drug toxicity. Gaining an understanding of such characteristics, the circumstances and characteristics of the deaths themselves, is fundamental and intrinsic for generating a robust evidence base on harms related to specific drugs, as well as providing clinical and policy intervention opportunities. …

Such scientifically based monitoring data can provide information on the nature and extent of a health risk and possibly its duration, thereby informing public health interventions and service provision, and feeding into policy advice about control and regulation (and whether that would help or hinder). Whether legislation is used or not to restrict the availability and use of particular emerging NPS molecules or groups of molecules, it is important to inform and educate (would-be) users, clinicians and treatment providers in a timely fashion about the adverse consequences that can occur."
Corkery et al (2020)

Previous chapters (Chapters 6 to 12) have looked at the micro- and macro-levels at a range of factors that can impact drug-related deaths and the inter-play between them. These are many and varied, as noted by the ACMD (2016). Earlier in this thesis (Chapters 2 to 5) the processes were detailed whereby such deaths were identified and investigated, and relevant information captured, recorded, analysed and disseminated.

This chapter (Chapter 13) demonstrates how such information from empirical research can be used to feed into policy advice and formulation, drug control and regulation, education, professional guidance and practice. This is done by looking at some examples of the activities in which the author and colleagues have been engaged during the course of this programme of doctoral research, i.e., since August 2018.

Framework for discussion of author's activities

In a sense, this chapter is concerned with the 'impact' of the author's, including the current PhD-related, activities. 'Impact' can be regarded in many ways. For example, for recent Research Excellence Framework (REF) purposes the sub-panels assessed " the 'reach and significance' of impacts on the economy, society, culture, public policy or services, health, the environment or quality of life that were underpinned by excellent research" (REF, 2020:7). This is further elaborated as:

"Definition of impact for the REF

297 .For the purposes of the REF, impact is defined as an effect on, change or benefit to the economy, society, culture, public policy or services, health, the environment or quality of life, beyond academia.

298. Impact includes, but is not limited to, an effect on, change or benefit to:

- the activity, attitude, awareness, behaviour, capacity, opportunity, performance, policy, practice, process or understanding
- of an audience, beneficiary, community, constituency, organisation or individuals
- in any geographic location whether locally, regionally, nationally or internationally.

299. Impact includes the reduction or prevention of harm, risk, cost or other negative effects.

300. For the purposes of the impact element of the REF:

a. Academic impacts on research or the advancement of academic knowledge (whether in the UK or internationally) are excluded. (The submitted unit's contribution to academic research and knowledge is assessed within the 'outputs' and 'environment' elements of REF.)

b. Impacts on students, teaching or other activities both within and/or beyond the submitting HEI are included. The 'Panel criteria' (paragraphs 301 to 302) sets out the panels' expectations for impact in this area.

301. Impacts will be assessed in terms of their 'reach and significance' regardless of the geographic location in which they occurred, whether locally, regionally, nationally or internationally. The UK funding bodies expect that many impacts will contribute to the economy, society and culture within the UK, but equally value the international contribution of UK research."

REF (2020:68)

Whilst this REF definition of impact, including the elements of academic research and environment, provides a useful framework for the present exercise, it is not without its critics; see, for example, Blagden (2019). Another reason for using this framework is that the author was one of the members of UH staff submitted to both REF 2014 and REF 2021 in respect of outputs and was part of the research team covered in some of the submitted relevant impact case-studies for Unit of Assessment 3 (Allied Health Professions, Dentistry, Nursing and Pharmacy). Indeed, he and his Principal Supervisor (FS) played key roles in developing and writing the case-studies. The case-study submitted for REF 2021 "Novel Psychoactive Substances: changing legislation, regulation, clinical practice and drug prevention strategies to protect public health" - which is pertinent in the present context - can be viewed here: https://results2021.ref.ac.uk/impact/fb323a20-6e2a-4a04-8ae2-a6b9d7cd7130?page=1. A copy is also provided as Appendix B. This provides examples of how the author's contributions have fed and continue to feed into the process. The following sections provide details of the impact of the author's PhD-related activities, especially with regard to: policy advice; education; professional guidance and practice.

Policy advice

Over the last three decades, the author, at different times and in different roles, has worked closely, with the Secretariat of the Advisory Council on the Misuse of Drugs and with Council members. These roles included: Home Office official/researcher (1994-2005; contributor to and co-opted member of many Working Groups (1999 to date); and as a co-opted member of two 'Standing Committees', i.e., the Novel Psychoactive Substances Committee since its establishment in 2009, and the Technical Committee since 2016 (see Appendix C for further details).

Appendix G presents an overview of the author's contributions to ACMD Committees and Working Groups and their outputs since mid-2018 when he commenced his PhD programme. An indication is also given of advice provided to the Government, Home Secretary and Ministers, whether information was used or advice was accepted, and any resultant changes in drug control and regulation. Note that some of these activities are still on-going.

Appendix G lists 14 substantive contributions made by the author to ACMD reports since mid-2018; he has made contributions to other advice and recommendations on other topics. One of these reports (on synthetic cathinones) is a 'work in progress' and the outcomes, including recommendations, have yet to be finalised and published.

Control and regulation

Formal responses have been made by the Government to the other nine reports. Advice given in July 2018 led to changes in legislation and commissioning of further advice from the ACMD. Advice and/or recommendations about control/regulation of substances were made in six of other reports.

The April 2020 recommendation that flualprazolam, flunitrazolam and norfludiazepam be controlled as Class C drugs under the Misuse of Drugs act (MDA) 1971 in line with other controlled benzodiazepines, and placed under Schedule 1 of the Misuse of Drugs Regulations (MDR) 2001 was accepted; secondary legislation (statutory instrument) was approved by Parliament and came into effect on 18 August 2021.

The October 2020 recommendations that the current classification of all SCRAs controlled by the MDA, remains appropriate, and should continue to be controlled as Class B, and, therefore, be put in Schedule 1 of the MDR were both accepted; they did not entail any new legislation.

Recommendations made in November 2020 about GHB, GBL and related substances included suggestions that these substances be moved from Class C to Class B and that GBL and 1,4-BD

be placed under Schedule 1 of the MDR. These recommendations were accepted; a statutory instrument brought these changes into effect on 13 April 2022.

July 2022 saw the publication of responses to two separate ministerial commissions on isotonitazene and brorphine, required of the UK Government by obligations under international conventions to control compounds. Detailed recommendations made by the ACMD about specific 'nitazenes' and brorphine being controlled as Class A drugs, and being placed in Schedule 1 of the MDR, and that consultation be had about drawing up generic controls that would capture any possible variants that might emerge. These recommendations were accepted in February 2023, and on 27 November 2023 it was announced that relevant legislation would be brought before Parliament as soon as possible. A statutory instrument brought these changes into effect on 20 March 2024.

The Government's response in March 2023 to the ACMD's conclusion, that the current status of nitrous oxide under the Psychoactive Substances Act 2016 was appropriate, was to note it. However, the Government had previously indicated its position on control, and re-iterated its decision to control this gas as a Class C drug. A statutory instrument was approved by Parliament and came into effect on 8 November 2023.

Cumyl-PeGaClone and other recently encountered SCRAs were the subject of advice published in May 2023. The Government accepted the ACMD's recommendation on 25 July 2023 that this particular SCRA be controlled as a Class B drug and added to Schedule 1 of the MDR. On 27 November 2023 it was announced that relevant legislation would be brought before Parliament as soon as possible. This legislation will enable the UK to comply with its international obligations under the UN conventions. A statutory instrument brought these changes into effect on 20 March 2024.

May 2023 also saw the publication of advice concerning three stimulants with similar effects to ketamine: diphenidine, ephenidine, and methoxyphenidine. The ACMD's recommendation that these be controlled as Class B drugs and be added to Schedule 1 of the MDR was accepted by the Government on 10 August 2023. On 27 November 2023 it was announced that relevant legislation would be brought before Parliament as soon as possible. This legislation will enable the UK to comply with its international obligations under the UN conventions. A statutory instrument brought these changes into effect on 20 March 2024.

A review of the evidence on the use and harms of Xylazine, Medetomidine and Detomidine was published in February 2024 (ACMD, 2024a). The main advice was that xylazine should be added to Class C of the Misuse of Drugs Act 1971. However, as it has legitimate use as a veterinary medicine, it should be placed in Schedule 4 Part 1 of the Misuse of Drugs Regulations 2001 (as amended). The Government' has accepted this recommendation (Home Office, 2024a).

March 2024 saw the release of two ACMD reports. The first report was occasioned by the 66th session of the United Nations Commission on Narcotic Drugs (CND), which added 2-methyl-AP-237 to Schedule 1 of the Single Convention on Narcotic Drugs 1961. The UK was legally obliged to consider how to control this substance, and this was referred to the ACMD for advice. The Council considered its harms and control. They also took the opportunity to look at other acyl piperazine opioids and made recommendations about this group of substances (ACMD, 2024b), which the Government has accepted (Home Office, 2024c).

The second report was initiated internally by the ACMD, as its monitoring group became aware of the detection and non-medical use of a further group of novel benzodiazepines both in the UK and other European countries. The Council, through one of its working groups, considered the evidence of the harms and misuse of recently encountered uncontrolled novel benzodiazepines and related compounds and their prevalence in the UK, including data provided by the author from the EU-MADNESS project. The report makes recommendations on the classification and scheduling of these substances (ACMD, 2024c). These were accepted by the Government (Home Office, 2024b).

May 2024 saw the release of the ACMD's updated harms and advice on control of alkyl nitrites ('poppers') under the Psychoactive Substances Act 2016. This work was undertaken at the behest of the then Home Secretary in August 2020. The key recommendation is that alkyl nitrites should be exempted from the 2016 Act by adding them to Schedule 1 (ACMD, 2024d). It will be interesting to see what the new Government's response will be.

Monitoring, surveillance, drug testing and screening

The author has also contributed to advice and/or recommendations which have also been made regarding the identification and monitoring of new and emerging psychoactive substances. Such recommendations were made in 6 of the reports listed in Appendix G. The aspects covered include:

Systematic screening during toxicological analysis of deaths related to drug poisoning for specific groups of drugs, i.e., fentanyl and fentanyl analogues; 'fourth-generation' SCRAs; GHB, GBL, etc.;

Guidance on a UK-wide minimum standard set of postmortem toxicology tests is developed for apparent drug-related deaths, to include testing for NPS and improve consistency of detection and analyses;

Adequate funding should be made available by government to allow Coroners, Procurators Fiscal and forensic toxicologists to follow the best practice guidelines when developed;

Testing for such substances as GHB and GBL should be routinely undertaken in all cases of unexplained sudden death. Where testing is not possible, then a clear statement should be included in the toxicology report to that effect;

The analysis of seized materials or submitted drug samples thought to contain opioids, as well as the analysis of patient toxicology and postmortem samples should be facilitated by the provision of adequate resources. Information derived from these activities needs to be "collected, collated, and monitored by the relevant public health agencies in the UK and reviewed in a consistent and methodical manner by the UK Government, for example the newly established Synthetic Opioid Taskforce and the Early Warning System" (ACMD, 2024b).

Information about new molecules emerging in the UK should be fed back to Coroners, Procurators Fiscal, and forensic providers, including toxicology laboratories. The latter should be provided with advice and information on analytical techniques, spectra, and access to analytical standards. This approach should encourage data collection.

Enhanced long-term data collection and monitoring, across a range of indicators including deaths, was advocated by the ACMD to enable a better understanding of health and social harms caused by nitrous oxide use.

The provision of information for health professionals (such as TOXBASE) and the general public (such as FRANK) on the health effects of emerging compounds, such as novel psychoactive opioids, should be reviewed and updated. In response to the above recommendation that information on dangers from emerging NPS should be updated, both TOXBASE and FRANK were updated with advice about the health effects of new compounds, including synthetic opioids.

In most instances, the UK Government accepted the recommendations in principle. However, some of these are beyond its remit; for example, on systematic screening for specific compounds. This is because "Coroners are independent judicial office holders who are independent in the discharge of their statutory functions. Coroners are funded by individual local authorities and make decisions in each individual case about the nature of the toxicological examination required. As a result, it is not possible for the Government to require coroners to adopt a particular approach to toxicology" (Home Office, 2020a).

Indeed, with regard to some of these suggestions, Home Office officials have raised them with both the Ministry of Justice and the Office of the Chief Coroner with respect to England and Wales, and relevant stakeholders in Scotland and Northern Ireland, in order that such issues can be

considered as appropriate. The Government stated it would consider matters carefully, along with the devolved administrations, but there would be funding implications in the event of new toxicology guidelines being proposed (ACMD, 2023a).

In many of their responses to these recommendations the Government recognises that these have a broad relevance to postmortem toxicology (Home Office, 2020c).

In respect of long-term monitoring of nitrous oxide, the Government stated that the present arrangements with regard to deaths were adequate (Home Office, 2023d). However, the author would argue that deaths recorded as involving nitrous oxide based on death certificate information alone fails to capture any information on the nature and circumstances leading to death in cases involving poisoning, and will completely miss deaths caused to third parties by drivers etc. under the influence of nitrous oxide. A specialist database, such as NPSAD or the former VSA Mortality Project is needed to capture and fully understand deaths involving substances such as nitrous oxide and alkyl nitrites. This is further underlined in the case of alkyl nitrites ('poppers').

The examples given above demonstrate that the author, with his PhD-related work, has contributed: to informing policy advice, resulting not only in changes to existing legislation but also to the introduction of new laws; making suggestions for improving consistency in the detection, screening and monitoring of newly emerging molecules; improved provision of information to health professionals and the general public.

At a broader policy level, the contribution that the ACMD can make to the national approach to dealing with drug-related challenges facing the UK is acknowledged in the latest Drug Strategy: "We will work with experts, including the Advisory Council for the Misuse of Drugs and experts through experience, to assess emerging threats, review the latest evidence, monitor trends and identify new areas of focus." HM Government (2021:61). Drug-related deaths feature among the Government's aims: "By the end of 2024/25 we expect this whole-of-government mission to have: "… prevented nearly 1,000 deaths, reversing the upward trend in drug deaths for the first time in a decade.." (HM Government, 2021:9). What this actually means is an expectation to reduce drug-misuse deaths in England by 1,000 (HM Government, 2021:33). There is also reference to the challenges that the devolved administrations face in respect of such deaths (HM Government, 2021:30).

Education

‘Education’ is commonly defined in quite narrow terms as a process whereby systematic ‘instruction‘ is provided, typically in the context of school and/or university. However, the author conceives of ‘education’ as also embodying the principle of not only sharing evidence-based information in an as objective way as possible but providing recipients of such information with the tools and skill-sets to understand, interpret and apply it. Dissemination of information can take, and has to take, different forms of communication as different messages (information) has to be conveyed in meaningful ways to different audiences and/or stakeholders.

During the period of the author’s PhD programme, most of the information he has communicated has been aimed at academic and/or scientific audiences, although some presentations have been made to lay people.

The main vehicles for disseminating the results of the author’s research on drug-related deaths have been and are: academic papers (of various types); oral and/or poster presentations at conferences and meetings of professional bodies; drawing on his research when teaching and supervising Masters’ level students undertaking clinical practice or public health research projects; using examples from his research when lecturing on addiction, travel health, and epidemiology; and advising PhD students, both those he co-supervised and others.

Some of the author’s contributions to the academic literature are mentioned in passing in the context of his ACMD-related activities (see above). Appendix D provides details, including abstracts, of the academic papers related to drug-related deaths which the author has led on, together with details of oral and poster presentations and their related abstracts.

Since the start of his PhD-related work in 2018, the author had led on eight academic papers, was sole author on another (which was also published as a book chapter, i.e., Corkery (2018)), and was co-author of one paper (with only one other author, i.e., King and Corkery (2018)). Eight of these were original research (Corkery, 2018; King and Corkery, 2018; Corkery et al., 2018; Corkery et al., 2019b; Corkery et al., 2021; Corkery et al., 2022; Corkery and Schifano, 2022; Corkery et al., 2023), whilst one was more of a conceptual piece (Corkery et al., 2020), and one was a ‘letter to the editor’ (Corkery et al., 2019a). In addition, a further book chapter on synthetic cathinones and related fatalities in the UK was published (Corkery et al., 2018).

The methods used included: ‘state of the art’ reviews; systematic literature reviews’; a case-study and case-series, as well as netnographic approaches. Typically, papers included at least two methods, usually a ‘state of the art’ review/systematic literature review combined with a case series, whilst one paper combined a systematic literature review with a netnographic study and a case-study (Corkery and Schifano, 2022). There was a paper that had a very methodological

focus - development of fatal toxicity indices (King and Corkery, 2018). However, most papers focused either on a range of specific molecules (i.e., 4F-EPH, alprazolam, ibogaine, ketamine, khat, kratom) or groups of related substances (i.e., GHB and related precursors). Specific populations at risk of experiencing a drug-related death were also looked at: those undergoing treatment with ibogaine; drownings; and UK Lesbian, Gay, Bisexual and Transgender communities.

Three oral presentations, two by the author, have been delivered on the following topics: "Synthetic cathinones and related fatalities in the United Kingdom"; " 'Croaking on Kambô': intoxications and fatalities associated with use of secretions from phyllomedusa bicolor (giant leaf frog, giant monkey frog)"; and "Ibogaine/Noribogaine in the treatment of Substance Use Disorders: a systematic review and Meta-analysis of side effects".

Three posters have been presented at conferences. Topics covered were: Alprazolam-related deaths in Scotland; and Investigating relationships between ketamine deaths and other epidemiological indicators. Abstracts of the oral and poster presentations have also been published, together with one on UK kratom deaths.

The oral and poster presentations have been delivered at annual School of Life and Medical Sciences research conferences and International Novel Psychoactive Substances conferences, organised by the University of Hertfordshire (UH) and other international partners.

The author, in his role as Module Lead for several Masters' level research project modules (MSc in Public Health, MSc in Physician Associate Studies, and MSc in Advancing Clinical Pharmacy), uses examples from his own research to illustrate how to conduct literature searches, systematic literature reviews, and netnographic methods. In addition, the author uses his research to illustrate lectures to health professionals following post-graduate programmes of study, including those mentioned in the previous paragraph, on addiction, travel health, and surveillance and monitoring.

This background, as well as previous experience of being Module Lead, teaching and supervising Master of Pharmacy students' research projects on drug-related issues, including deaths (e.g., methadone and kratom), has naturally led to supervision of Public Health and Physician Associate research projects across a range of public health and clinical practice topics - including substance use. This provides many opportunities for sharing both theoretical and practical expertise and experiences from the author's past and current research activities.

Such research insights, as well as subject-knowledge, has enabled the author to contribute constructively to the successful co-supervision (with FS as Principal Supervisor) of three UH PhD students looking at NPS: Dr Barbara Loi, Dr Stefania Chiappini, and Dr Valeria Catalini. In addition, he provided mentoring about conducting suicide research in Coroners' courts to a PhD student in the UH School of Health and Social Work.

Professional guidance and practice

Some of the examples mentioned in the previous section can also be appropriately considered under this heading; for example, lectures and workshops given to Masters' level pharmacy, physician associate, and public health students. He has also sought to introduce these topics into the curricula for such students at UH.

Many of the academic papers are hopefully read by a range of people including: health professionals; forensic scientists, toxicologists, pathologists, coroners and medical examiners; epidemiologists and public health officials; police and other law enforcement agencies; lawyers and other judicial officials; politicians, political advisors, and legislators. Part of the aim of disseminating the author's research findings in this way is to inform discussions on drug-related issues using objective evidence.

The variables or parameters usually covered by these academic papers studies include: age, gender, ethnicity, marital status, living arrangements, employment status, occupation, area deprivation level, substance use history, injecting history, prescription drug history. In respect of certain substances (GHB, GBL, nitrous oxide, alkyl nitrites or 'poppers'), sexual orientation and/or gender identity have been explored/investigated. The key characteristics of the deaths are also usually described, including: *locus* and circumstances of death; pathological findings, underlying health issues, mechanisms and cause(s) of death; substances involved (including combinations thereof) and toxicological results; and intent or mode of death (accidental, intentional, undetermined intent).

In a more formal setting, the author has contributed with his expertise on drug-related deaths and related indicators, within the time-scale of this PhD programme, to the delivery of training "Novel Psychoactive Substances (NPS): new frontiers in addiction?" in July 2021 to health professionals (physicians, nurses, social workers and clinical psychologists) employed by ATS Sardegna (Sardinian Health Protection Agency) in Italy. Further training being provided by a UH-based team led by the author's Principal Supervisor (FS) is planned for late 2024. This will be for addiction health professionals (e.g., recovery workers, social workers, nurses, physicians, and psychologists) working within the Italian NHS service with penal institution inmates.

Continuing the author's current PhD-related activities

Whilst the author continues to contribute to papers related to a range of drug-related issues, in terms of drug-related deaths the papers outlined below are in progress and/or being planned.

Following the current thesis submission, the author is planning to lead on and submit papers on his PhD-related activities to peer-reviewed journals based on data collated and analysed for

several ACMD reports, with the following provisional titles: “Deaths related to use of diphenidine and methoxphenidine”; “Deaths in the UK related to the use of nitrous oxide”; “Deaths in the UK related to use of alkyl nitrites (‘poppers’); and “UK deaths from swallowing ‘poppers’ (case-series)”. These will provide up-to-date information for policy-makers, health professionals and others.

The current PhD-related data on lethality indices will be submitted soon as a systematic review, provisionally entitled “The past, present and future uses of fatal toxicity and lethality indices”. This has its origins in the author’s 2018 paper (King and Corkery, 2018), and is a natural evolution of it. It is hoped it will stimulate further developments in the field.

Taking the author’s oral presentation to the IX International Conference on Novel Psychoactive Substances in October 2022 as the starting point, a paper provisionally entitled “ ‘Croaking on Kambô’: intoxications and fatalities associated with use of secretions from *Phyllomedusa bicolor* (giant leaf frog, giant monkey frog)” will be submitted to an appropriate journal covering natural substances. It will include new cases that have been reported, as well as two deaths in Australia for which the coroner’s verdicts are still awaited (May 2024). A paper will also be prepared, if sufficient cases are identified, on deaths involving bufotenine - a compound found in the secretion of the toads such as *Bufo alvarius* (Sonoran Desert toad) that has hallucinogenic properties. The use of natural products is increasing all the time for a variety of reasons and purposes, but there are risks attached to some of these compounds of which (potential) users and ‘practitioners’ need to be aware.

Through monitoring of scientific and other types of literature databases, the author is aware of further deaths involving substances he has previously written about being reported. He is considering the need for providing updates on substances such as iboga/ibogaine and *Catha edulis* (khat).

Chapter overview

This chapter has outlined and provided details of how the author’s recent research activities have been employed to inform policy advice and formulation, contributed to the development of drug controls and regulations, informed and supported teaching and training of health professionals, and provided guidance and illustrations to Masters’ level and PhD students. Further details are given in Appendices C to F.

The issues to be covered in the proposed activities outlined have a resonance with those discussed in the final chapter (Chapter 14). They will take forward and complete the activities undertaken with the author’s present ACMD activities, inform the knowledge-base for the various stakeholders identified earlier in this chapter, and provide a solid basis for dealing with future compounds,

contexts, changes, and challenges. Chapter 14 pulls together the various themes and issues explored by this thesis, takes stock of the current situation, and takes a look into the future.

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CHAPTER 14 - DRUG-RELATED DEATHS - PAST, PRESENT AND FUTURE?

"We are drowning in information, while starving for wisdom … The world henceforth will be run by synthesizers, people able to put together the right information at the right time, think critically about it, and make important choices wisely".
Wilson (2014:399)

"The measure of greatness in a scientific idea is the extent to which it stimulates thought and opens up new lines of research."
Dirac (1968:17)

"Préparer l'avenir ce n'est que fonder le présent. Il n'est jamais que du présent à mettre en ordre. À quoi bon discuter cet héritage. L'avenir, tu n'as point à le prévoir mais à le permettre." . [Preparing for the future is only establishing the present. It is only ever the present that needs to be put in order. What is the point of discussing this heritage? The future, you do not have to foresee it but enable it.]"
de Saint-Exupéry (1948:167)

Recap

Chapter 1 described the context and scope of this thesis, introduced the over-arching thematic threads that provide coherence to the narrative, stated the rationale, aims and objectives of this programme of research, and, lastly, outlined the structure of the thesis. Chapter 2 explained the key concept underlying this thesis, i.e., the variety of ways in which data on deaths associated with use of drugs have been and are being used. Chapters 3 to 5 provided information on the sources available in the context of the United Kingdom (UK) to provide not only an overview of drug-related deaths (DRDs) but also insights into their nature and extent; this was largely done using narrative analyses (e.g., literature reviews).

Chapter 6 outlined and explored, at a macro level using the published outputs of the General Mortality Registers (GMRs), the changes in UK DRDs over the past three decades from several angles: socio-demographic, spatial, temporal, toxicological (drug involvement), and intention. At the micro level, Chapter 7 outlined how 'at risk' groups and populations can be defined, and approaches that can be employed to identify such groups, using a combination of profiling (a) decedents' socio-demographic characteristics and (b) characteristics of deaths. These are illustrated by way of 15 selected studies, across a range of substances and scenarios, with which the author was directly involved. These primarily used data from a UK Special Mortality Register (SMR) – the National Programme on Substance abuse Deaths (NPSAD). Finally, the purposes of profiling 'at risk' groups are considered.

Chapters 8 to 12 demonstrated how DRD data can be used in conjunction with other drug indicators to provide a more comprehensive and holistic understanding of what higher level or

macro factors (including some at international level) may play a role in causing or contributing to such events. Eight sets of drug indicators were used to shed light on their relationships with fatalities, across a range of 15 index drugs/drug classes. Local scenarios occur against the backdrop of such external factors.

The penultimate chapter (Chapter 13) demonstrated how information from empirical research outlined in Chapters 6 to 12 can be used to feed into policy advice and formulation, drug control and regulation, education, professional guidance and practice. This was achieved by looking at some examples of the activities in which the author and colleagues have been engaged during the course of this programme of doctoral research, i.e., from August 2018 to May 2024.

This closing chapter (Chapter 14) draws together the activities described in the previous ones, illustrating how the themes examined are complementary and coalescent. It takes a look back at what has happened over the last three decades, what the current situation is, and what the future may hold. The latter topic considers a range of factors that may impact the ways in which future work in this now multidisciplinary field will be conducted.

A brief overview of the past three decades

The period since 1993 has seen the development, refinement and implementation of two important definitions of DRDs: drug poisoning deaths - the 'wide' definition used by the Office for National Statistics (ONS), and the Standard definition used by the European Monitoring Centre for Drug and Drug Addiction (EMCDDA). These have been supplemented over the past two decades by the 'drug misuse' definition which is now the key indicator used across the UK. The ONS 'wide' definition allows a more comprehensive comparison of DRDs. The EMCDDA definition has lost its domestic UK relevance because of the UK leaving the European Union, and hence the EMCDDA; however, The National Records of Scotland (NRS) still use it to provide a comparison of Scottish with European data.

Whilst the sources of information on drug-related deaths have remained stable across the last three decades, there have been developments in investigating and reporting DRDs. Whilst guidance has been issued by professional bodies to some groups of emergency responders who may encounter sudden or unexpected deaths, there is still no guidance on how to forensically treat a scene that may relate to a drug-related death. There are on-going concerns about how thorough the police, in particular, are when investigating such sites.

Pressure has been mounting over recent years to improve the quality and consistency of forensic pathology reports; there are still no nationally agreed autopsy protocols, but recent developments are discussed later in this chapter. The emergence of Novel Psychoactive Substances (NPS) has seen stake-holders involved in identifying, investigating, and reporting DRDs pressing for more

standardised approaches to the range of molecules that are screened for and in the reporting of test results. However, one of barriers to this is the funding available to coroners for pathological and toxicological investigations (see Chapters 4 and 13); see later section for current/future developments).

There have been considerable improvements in the ways in which individual suspected and actual drug-related deaths are investigated, documented and assessed. The key starting point is probably the creation, in 1997, of the data collection form used by NPSAD; the author played a key role in its conceptualisation as well as its subsequent refinements and distribution to coroners whilst he was the NPSAD Programme Manager; the form is still in use, increasingly in electronic format (2024). The NPSAD form also served as a template for the development of guidance and documentation used by the Welsh Government and local DRD review teams elsewhere in the UK.

Obviously, the quality of information provided by pathologists and toxicologists influences the details recorded on Medical Certificates of Cause of Death. There is still considerable room for improvement in the instruction of those who complete such forms. In turn, this has the potential for the generation of more accurate and complete mortality statistics, including those related to DRDs. The latter produced by ONS and the Northern Ireland Statistics and Research Agency (NISRA) could also be improved by the provision of toxicological information. Neither ONS nor NISRA receive such information, unlike NRS and NPSAD. The latter also receive some pathological information; this can assist SMRs like NPSAD but also the GMRs (ONS, NRS, and NISRA) to interpret toxicological information.

Correct understanding and interpretation of pathological and toxicological information is vital to the production of meaningful coding of medical cause of death certificates using the International Classification of Diseases (ICD). The introduction of ICD-10 (WHO, 1992) in 1999-2000 saw an improvement in the quality of DRD statistics published in the UK; the possible impact of the UK implementation of ICD-11 in 2025 is examined briefly later in this chapter.

The number and range of agencies collecting, analysing, and publishing data and statistics on DRDs across the UK has grown over the past three decades. Some exercises were ‘one-off’ activities, whereas others have evolved and established themselves as ‘go-to’ places to obtain timely, accurate and detailed information. All three GMRs have become authoritative in their respective fields and continue to improve the accuracy and relevance of their high-level statistics and commentaries. SMRs, especially NPSAD, continue to provide more in-depth analyses and interpretation of information from a range of sources derived from coroners inquests and/or record linkage exercises.

Whilst Chapter 6 details some of the changes that have taken place over time in the types and nature of drugs involved in UK DRDs; the characteristics of both those dying and the deaths themselves are examined in Chapter 7. Taken together, these have provided an understanding and explanation of what has been happening in terms of DRDs in the UK over a considerable period of time.

There have been some continuities over the last three decades. The overall picture is one of increasing numbers of DRDs. However, whilst this is true of the mid- to late- 1990s and from about 2012 to 2021, the intervening period saw some fluctuations. Most deaths are accidental, and thus preventable. Eight of the nine drug classes considered in Chapter 6 showed increased numbers of deaths between 1997 and 2021; only barbiturates showed a fall. Opiates/opioids have always accounted for most DRDs, especially heroin/morphine and methadone; consistently, two-thirds of methadone-related deaths involve individuals who were not prescribed the medication. Whilst benzodiazepines as a class have shown an increasing role in causing and/or contributing to deaths, there was a fall in relation to temazepam but rises for diazepam and 'designer benzos'. The numbers of deaths involving stimulants have all shown significant increases, especially cocaine.

Synthetic cathinones and synthetic cannabinoids were the main NPS classes to emerge in the late 2000s. However, other types of NPS have also emerged in recent years, especially synthetic opioids and 'designer benzos'; these appear to be much more potent than their predecessors and are of increasing concern for health professionals and their clients, as well as course for politicians and law-makers.

Also of concern is the relatively recent identification by a small number of research groups, especially the Psychopharmacology, Drug Misuse and Novel Psychoactive Substances Research Unit at the University of Hertfordshire, using pharmacovigilance and web-crawling approaches of increasing misuse of Prescription Only Medications (POMs) and Over the Counter products (OTCs). Whilst some of these changes may not be unsurprising, e.g., opioids (Chiappini et al., 2022c, Schifano et al., 2019), Selective Serotonin Reuptake Inhibitors (Chiappini et al., 2022b), antihistamines, cough medicines, and decongestants (Schifano et al., 2021), the appearance of such medications as anticholinergics (Chiappini et al., 2022a) and semaglutide (Chiappini et al., 2023) having an abuse potential is somewhat unexpected. The misuse and abuse of such medications is leading to fatalities involving them; in many instances resulting in many deaths being included in the national DRD statistics and reported by the author and co-researchers.

The majority of deaths involve males by a ratio of 2 or 3 to 1 across the UK, reflecting usage patterns. The mean age at death has increased over time for both genders. This may be, in part, due to an ageing cohort of opiate/opioid users.

Underlying all of the aspects outlined above is the continuing trend in polypharmacy that has been noted since the 1970s. It is now rare for a death to be attributable to a single index drug, or indeed a single drug class. This makes it increasingly difficult for pathologists, toxicologists, Coroners and Procurators Fiscal to determine the relative contribution, if any, of post-mortem drugs in an individual case - especially where a NPS is identified.

As Chapter 13 demonstrates, such information and its interpretation feed directly into risk assessments for specific index drugs or drug classes, and consequent policy advice, drug control and regulation. Such Government-led activities have had to react to these changes, try to predict future challenges, and pre-empt them. Often, a range of other drug indicators (see Chapters 8 to 12) are used in conjunction with DRDs to help in these activities. Such macro-level data, as well as more focused micro-level case-studies, case-series, and even case-reports, play a role in providing guidance and education to health professionals and others. The information and data from these sources can inform stake-holders about both current issues and likely future challenges.

The current situation on United Kingdom Drug-Related Deaths

The numbers of both drug poisoning and drug misuse deaths registered in 2022 reached new peaks in England and Wales overall, although there were slight falls in Wales for both types of death (1.24% and 2.37% respectively) compared with 2021 (ONS, 2023a). The rate of increase in England appears to have to slowed for both categories of drug-related deaths; 0.88% for drug poisonings and 2.11% for drug misuse. These differences were largely due to changes in the numbers of accidental deaths, especially heroin/morphine, tramadol and other opiates/opioids (but not methadone), cocaine, and 'Z' drugs. By contrast, there were noticeable falls in deaths where MDMA, NPS, benzodiazepines, antidepressants and antipsychotics were mentioned in the cause of death. The overall number of drug-related death registrations may have been impacted by the effects of the Covid-19 pandemic; ONS (2023b) note that "2022 saw the longest delays since the time series began in 1993."

A more noticeable drop was seen in drug-related deaths registered in Scotland during 2022; 17.38% for drug-poisoning deaths (NRS, 2023b) and 20.98% for drug misuse deaths (NRS, 2023a). These falls are the largest year-on-year decreases seen in the last three decades in Scotland. The major reason for the fall appears to have been a decline in accidental deaths which account for most drug-related deaths. Looking at the mentions of specific types of drugs specified in the cause of death for drug misuse deaths, there were falls for all drug groups, apart from MDMA which remained at a similar level to 2021 registrations. Although NRS do not mention Covid-19 in regard to registrations, it is possible that some DRDs registered may have been caused by issues generated by the pandemic.

There was a significant drop in the number of DRDs registered in Northern Ireland in 2022 compared to the previous year; 27.7% for drug-poisoning deaths and 27.4% for drug misuse cases (NISRA, 2024a). Looking at the mentions of specific types of drugs specified in the cause of death for drug-poisoning deaths, there were falls for all drug groups, apart from antidepressants which remained at the same level as for 2021 registrations (NISRA, 2024b). Cocaine deaths remained stable, but the drug "emerged as the predominant substance mentioned in deaths involving only one drug in 2022, constituting 9.1% of total drug-related deaths and 35.0% of single-drug deaths" (NISRA, 2024a:2). The largest numerical falls were seen for opioids, benzodiazepines, NPS and gabapentinoids. However, NISRA (2024a:5) point out that "registration-based statistics will always be subject to fluctuations in the time which lapses between the date of death and the date the Coroner is able to close the investigation (and thereafter be incorporated in the registration based statistics)."

Whilst the overall number of drug-related deaths registered in 2022 fell in the United Kingdom, it remains to be seen if this was simply a year-on-year 'blip' or the start of a real decline. A more accurate assessment will be possible by looking back at the number of drug-related deaths that have actually occurred in recent calendar years. For this reason, the GMRs tend to employ a technique called 'rolling averages' to look at trends over a number of years, typically three. Nevertheless, any fall in drug-related deaths - which are mostly preventable - is to be welcomed, although numbers remain far too high.

Evolving drug scenarios

A 'spoiler' alert has already been given in this chapter about the emerging issues of novel benzodiazepines and novel synthetic opioids. Although these are the most prominent drug classes dominating discussions amongst relevant stake-holders, there are other drug classes and specific molecules which are also appearing on the horizon, although perhaps below the level for detection by 'early-warning' or 'radar' systems. ('Horizon scanning' is discussed below.)

The top priority for stake-holders in the arena of drug-misuse is currently the rapid emergence in North America over recent years of synthetic opioids, especially fentanyl and related analogues, largely due to possible lax prescribing and monitoring by relevant authorities (e.g., regulators and law enforcement). Some of these analogues are extremely potent, e.g., carfentanil, but do not appear to have had a significant impact in the UK. More recently, however, non-fentanyl novel synthetic opioids have come to the fore, especially the 2-benzylbenzimidazole opioid structural class, more commonly referred to as 'nitazenes'. Not only has the presence of nitazenes made a significant impact in North America in terms of deaths, but this class of drug has also started to make an impact in Europe (Schüller et al., 2023; Giraudon et al., 2024) and elsewhere.

The UK has not been spared this experience, starting in 2019 (ACMD, 2022). Indeed, the scale of the impact appears to have been quite significant, especially in 2023, although no definitive statistics on deaths are available yet. There are reports of nitazenes being found in postmortem toxicology across the UK (ACMD, 2022; PHS, 2023; Homer and Johal, 2023). The author is currently aware (February 2024) of at least 7 (seven) deaths having been registered in Scotland where nitazenes were implicated (personal communication to author from Vital Events Branch, NRS, 9 February 2024). According to reports from the National Crime Agency, nitazenes have been linked to 176 deaths, including 47 in Scotland (Cowan, 2024). A Statutory Instrument related to the control of nitazenes as Class A drugs in the UK recently went through Parliament (see also Chapter 13). It will be interesting to see what happens as a result of this legislation (United Kingdom, 2024).

Typically, the nitazenes are present in heroin, oxycodone and even benzodiazepines (D'Agostino, 2023; ACMD, 2022; Nahar et al., 2023) supplied to end users; the same is also true of xylazine (Booth, 2023; Nahara et al., 2023). Xylazine, an analogue of clonidine, is a potent α_2 adrenergic agonist, is widely used in veterinary medicine to sedate and anaesthetise large animals such as cattle and horses. However, it has been used recreationally as a drug of misuse since the late 1970s, but increasingly so over the last couple of decades in other parts of the world. Mixed with fentanyl, it is known as 'tranq dope' and has been appearing in Europe (EMCDDA, 2023). Concerns about the presence of xylazine in opiates/opioids in the UK led to the setting up of a working group by the Advisory Council on the Misuse of Drugs (ACMD) to investigate the current situation in the UK. The ACMD's report was recently published (ACMD, 2024) with the Government's accepting its recommendations (Home Office, 2024). The first death in the UK involving xylazine occurred in May 2022 was reported by NPSAD (Rock et al., 2023). The author is currently aware (May 2024) of at least 10 deaths in Scotland involving xylazine that occurred throughout 2023 (personal communication to author from Vital Events Branch, NRS, 19 April 2024). Perhaps more worrying is the combined presence of both nitazenes and xylazine, e.g., in a death involving heroin and other drugs in August 2023 (Courts and Tribunals Judiciary, 2024). Furthermore, xylazine has not only been found in heroin supplies but also where the purchasing intent was counterfeit prescription medication tablets and tetrahydrocannabinol (THC) vapes (Copeland et al., 2024).

Ketamine is sometimes used in combination with xylazine in veterinary medicine. However, it is also used recreationally and has caused deaths, as has been seen in earlier chapters. Other dissociative drugs (e.g., diphenidine, ephenidine, and methoxyphenidine) have appeared in recent years. However, as these have become subject to control (see Chapter 13), 'chemists' have sought to develop other ketamine analogues that may have the same properties/effects. An example of such a molecule may be 'CanKet' or 'Canberra ketamine' which was identified first identified in China and then found in Australia in late 2022 (Butler, 2022; Davey, 2022). This is

known in China as 2F-NENDCK or 2-(2-fluorophenyl)-2-(ethylamino) cyclohexan-1-one (Wang et al., 2023; Algar et al., 2024).

The variety of synthetic cannabinoids has evolved considerably since the late 2000s and continues to do so. A new class, i.e., oxizids, was identified in the summer of 2021 in New York. This class is described as having oxindole cores with hydrazide/hydrazone linker moieties (Palamar et al., 2024). This class is also present in Europe (Andrews et al., 2023). A recent paper suggests that oxizids may be cardiotoxic (Hancox et al., 2023). The semi-synthetic cannabinoid hexahydrocannabinol (HHC) has been available on the market for the last three years or so (Graziano et al., 2023). HHC is a hydrogenated tetrahydrocannabinol derivative (Ujváry, 2024). It is present in some e-cigarette liquids (Hachem et al., 2023) and thus has an abuse potential. It is difficult to know what to call such newly emerging molecules (Rossheim et al., 2023). Will HHC turn out to be “Spice 2.0”? (Evans-Brown et al., 2022:10).

The combination of opiates/opioids and benzodiazepines has long been an issue in polypharmacy DRDs. Whilst traditionally this phenomenon concerned prescription drugs, recent developments of fentanyl being combined with not only prescription benzodiazepines but also ‘designer benzos’ have resulted in the term ’benzo-dope’ being added to the vocabulary of treatment agencies, international organisations such as the EMCDDA, and conferences (Krotulski et al., 2022).

The shortage of opium reported recently by the United Nations Office on Drugs and Crime (UNODC) being harvested in Afghanistan may lead to a shortage of heroin in Europe (UNODC, 2023). This could provide organised crime groups from Mexico with an opportunity to broaden their activities to include Europe in terms of both supplying fentanyl and possibly facilitating its production in Europe; fentanyl production facilities have been discovered within the European Union (Carbonaro, 2023). However, such a scenario may not materialise. As the EMCDDA noted in January 2024:

“At present, there are no signs of heroin shortages in Europe. 'Nonetheless, the Taliban’s ban on opium cultivation, if it is sustained, could have a significant impact on heroin availability in Europe in the future', states the report. While it will take time for the developments in Afghanistan to be felt in the EU, a decrease in heroin availability could lead to market gaps being filled by potent synthetic opioids or stimulants (e.g. methamphetamine, cathinones), with significant negative effects on public health and security.”
EMCDDA (2024)

People are increasingly looking to the spiritual realm for insights into/solutions to today’s challenges; this may well involve substances that are natural in origin /derived e.g., plants, fungi, animals. The author has reported on deaths in the UK involving such substances, including: ayahuasca, iboga/ibogaine, khat, kratom, etc. The range of such substances that could be used may well increase as interest in alternative ‘treatments’ derived from (or more likely

misappropriated) from their traditional ‘shamanistic’ origins and repackaged for a ‘Western’ clientele. Hence, deaths involving these molecules should be anticipated.

As has been clearly demonstrated by this thesis, drug scenarios have changed over the decades and continue to evolve in the UK, both at the micro/local and national levels. There is no reason to suppose that this situation will change in the decades to come.

Future information needs

Going forward, it will remain important to obtain as much information as possible on what is currently happening and thereby try to understand the factors at work and the interplay between them, trying to predict what may happen in the future (Corkery et al., 2017), and how such knowledge can inform policy and practice (Corkery et al., 2020). This section takes a brief look at some of the relevant issues.

From April 2024, all deaths In England and Wales became formally subject to either scrutiny by a Medical Examiner or an investigation by a Coroner. The secondary legislation has yet to be approved by Parliament (DHSC, 2023). This should help prevent any substance-related deaths being overlooked.

Comprehensive screening for potentially unknown molecules in post-mortem toxicology can be essential in identifying and thus understanding deaths where common drug screens have failed to find any relevant suspects. It is understood that Coroners justify their decisions not to request testing for additional substances by referring to the fact that they are not allowed to look for things which are considered irrelevant to specific deaths. In the meantime, to identify new molecules Coroners should think of some way of deeming investigations relevant e.g., the possible contribution of xylazine, fentanyls, nitazenes in such cases.

In recent years, on-site drug-screening has taken place at music festivals and similar events in the UK (Barratt and Measham, 2022), and some of the author’s research colleagues have been involved in the first Home Office licensed drug screening/testing in a treatment setting (Guirguis et al., 2020). Self-report data combined with on-site toxicology testing “are important for capturing unintentional or unknown exposure to NPS” (Fitzgerald et al., 2024). A recent commentary by Cooney and Measham (2023), on which the author was an advisor, indicates that drug-checking services at festivals have been demonstrated to “significantly reduce consumption of missold [sic] and adulterated products, to reduce rates of drug use generally and to reduce overdose risks.” Thus, such drug testing has the potential to reduce DRDs at festivals, albeit that such fatalities are rare.

Analysis of waste-water has developed in recent decades to monitor ‘traditional’ drug misuse at a community level (Castiglioni et al., 2014), to identify emerging NPS in specific types of setting, e.g., club-land (Archer et al., 2013) and festivals (Bijlsma et al., 2020), and to monitor NPS diffusion (Castiglioni et al., 2015; Salgueiro-Gonzalez et al., 2024). A more recent development has been to forecast overdoses and deaths associated with opioid use in two US cities (Gushgari et al., 2019), and deaths from the use of amphetamine-type stimulants in Finland (Kriikku et al., 2024).

The implementation of ICD-11 (WHO, 2024) is due to start in the UK in 2025. As noted in Chapter 4, although additional drugs have been specified in this revision, the coding of NPS is going to remain problematic. The coding rules for ICD-10 were revised in a major way three times in the 2002-2010 period leading to issues about which substances to prioritise when applying codes (Denissov et al., 2012). Any changes implemented for ICD-11 must be preceded by appropriate consultations.

Improving the range of information collected and how patterns can be better understood

As the description in Chapter 7 of studies using NPSAD data has demonstrated, the easier identification and better understanding of ‘at risk’ populations can be facilitated through the use of information on a wide range of factors (variables). Data from a number of local sources, including Coroners, Medical Examiners, law enforcement agencies, and forensic toxicology laboratories, can be employed for ‘real-time’ public health surveillance as well as informing prevention and intervention strategies/activities at the local level (Noriega et al., 2023).

To the author's personal knowledge, law enforcement agencies have been applying ‘artificial neural network’ or ‘artificial adaptive systems’ approaches to understanding drug supply networks for at least the last couple of decades. This process has been described in academic papers and books, for example see (Monaghan and Terzi, 2012). This approach is also used to understand criminal organisations, and is being currently used to try and deal with such problems as online sales (Li et al., 2019; Hu et al., 2021). As far as the author can establish through literature searches, these approaches have not been applied to the ‘county lines’ phenomenon in the UK.

If geo-spatial information on the *locus* of death, where events leading to death occurred, or death itself occurs is captured accurately, such information can be used in conjunction with other information to understand more about the dynamics and characteristics of individual events and possible interconnections with other similar events. The level of detail should be at as low a level as possible, e.g., GPS (Global Positioning System) coordinates or address, which can then be used at different geographical levels to match onto geospatial data collected by other stakeholders. The geographical level could be postcode (or lower) which can then be coded to

ward, local authority area, parish council, National Health Trust area, police beat, command or constabulary area, etc. levels.

Where geospatial data are available for other drug indicators and also other possible confounders/ factors such as unemployment rates, deprivation scores, etc. captured by population census and or other official data collection systems, these data items can be linked together for individual events. Relationships between them can then be explored and events could be followed in 'real time', as is done in the USA.

Local information, down to County level, on DRDs can be accessed in the USA by any citizen. One enterprising newspaper, the San Francisco Chronicle, has a developed a 'tracker' that uses information from the public health database CDC WONDER (https://wonder.cdc.gov/). Death certificates from local medical examiners and coroners provide the core information for that database. The tracker was launched on 21 August 2023 to allow individuals to follow the progress of the US 'opioid epidemic' (San Francisco Chronicle, 2023; Lekhtman, 2023). Such a tool would be of immense value to epidemiologists, public health officials, law enforcement agencies, as well as the local citizenry, if one could be developed for the UK and/or its constituent countries. The main hurdle to be overcome in this regard would be the current restrictions placed by statute on the GMRs. However, an SMR – such as NPSAD – may be better placed to investigate such opportunities.

Based on existing systems available in Australia (Coroners Court of Victoria, 2024; Coroners Court of New South Wales, 2023), Canada (Office of the Chief Coroner for Ontario, 2024), and New Zealand (Coronial Services of New Zealand, 2022), Dr Georgia Richards and colleagues (France et al., 2023) have developed a "Preventable Deaths Tracker" (https://preventabledeathstracker.net/) which allows researchers and members of the public to search through the database of Regulation 28 reports on preventable deaths submitted to the Chief Coroner for England and Wales (https://www.judiciary.uk/courts-and-tribunals/coroners-courts/reports-to-prevent-future-deaths/). This limited database has already been used to focus on preventable deaths involving medicines (France et al., 2023) and opioids (Dernie et al., 2023). If this tracker were to be combined with other datasets (e.g., NPSAD) it would be an even more useful resource for researchers, including drug epidemiologists like the present author.

Going forward, more thought could be given to how geo-spatial approaches can be used not only in the investigation and recording of drug-related deaths but also in the way in which such information can be depicted in official published statistics and in research papers/reports. GMRs and SMRs such as NPSAD could investigate ways in which change(s) over time can be displayed electronically through dynamic maps, tables and charts.

If softwares were available (the author is currently unaware of such resources) to map geo-spatial intelligence and temporal data and present them dynamically, 'time-lapse' approaches could be used to present the diffusion of deaths and their links (if any) to illicit drug markets, thereby making such phenomena more readily understood. In turn, this could lead to dynamic 'real time' interventions by law enforcement and public health agencies. Such understanding could also facilitate nuanced public health warnings/messages, targeted drug education, drug treatment provision, distribution of naloxone, etc.

Applying artificial adaptive systems to such geo-spatial information, i.e. 'self-organising maps' (Li and Juhola, 2014) could assist with the identification and prediction of overdoses, deaths, drug-related diseases, drug contaminations, etc. Such approaches are already employed for activities as pharmacophore mapping (Polanski, 2003), drug discovery (Schneider et al., 2009), and comparison of chemical databases (Bernard et al., 1998).

Horizon scanning

Regular and 'real time' scanning of a range of internet (surface web, deep web, and darknet/dark web) and social media sites, and comparing them against each other and with established databases of NPS (e.g. the EMCDDA's European Database on New Drugs (EDND) (https://ednd2.emcdda.europa.eu/) and the UNODC's New Psychoactive Substances Portal (https://www.unodc.org/LSS/Home/NPS) can help inform relevant stake-holders (e.g., law enforcement agencies, health professionals) as to what new molecules may be about to emerge (Corkery, 2017).

The NPS*finder*® (https://npsfinder.com/) web crawler/navigating tool, developed jointly by Damicom, L'Osservatorio sulle Dipendenze, and the UH's Psychopharmacology, Drug Misuse and Novel Psychoactive Substances Research Unit, is a leading example of novel approaches being developed. NPS*finder*®

> "was designed to automatically scan a list of websites for new/novel/emerging NPS and extract a range of information including chemical and street names; chemical formulae; three-dimensional images; and anecdotally reported clinical/psychoactive effects. The scanned websites … [are] representative of online psychonaut websites/fora and other NPS online resources, e.g., vendor websites ..."
> Catalani et al. (2022).

Since November 2017, it has been supporting clinical operators, scientific research and institutional activities, to identify and classify molecules and psychoactive products in 'real time'. Each entry contains information about the substance's chemical family, chemical characteristics, commercial and street names. Furthermore, suggestions regarding the clinical management of intoxication from specific molecules are provided. Information from NPS*finder*® has been provided to bodies such as the ACMD to inform advice to the UK Government when the latter have been

considering changes to drug laws and regulations, included in several peer-reviewed journal articles to alert toxicological and clinical practitioners, as well as to generally indicate to international stake-holders (e.g., EMCDDA and UNODC) that the actual number of molecules is much higher than those listed on these agencies' databases.

A paper by Catalani et al. (2022) highlights the way in which "QSAR and docking studies could be of great advantage in obtaining quick and reliable predictions on biological activity, potency and even provide initial toxicity information. In this way, it will be easier to better understand the possible harms associated with index novel [molecules], and this may constitute a starting point for further investigations (e.g., de novo chemical synthesis; in vitro studies; preclinical studies)." Thus, those who are engaged in investigating overdoses and deaths (toxicologists, pathologists, coroners, etc.) can be alerted to the possibility that an 'unknown' NPS or one that has not been identified in routine drug screening may be worth considering as being potentially present and/or involved.

Employing data from multiple sources, Lim et al. (2022) developed a simulation model to replicate "how risks of opioid misuse initiation and overdose have evolved over time in response to behavioral and other changes and suggests how those risks may evolve in the future, providing a basis for projecting and analyzing potential policy impacts and solutions."

Web-crawling, web-scraping, etc. cannot only be used to identify new molecules being discussed in online fora (Simpson et al., 2018) or advertised online (as per NPS*finder*®), but also to identify possible deaths related to specific index molecules whether new (e.g., 'designer benzos', 'nitazenes') or old (e.g., ayahuasca, kratom, khat).

Other tools, such as Natural Language Processing and Machine Learning can also be used to facilitate and enhance the identification (Wright et al., 2021), classification (Goodman-Meza et al., 2022), surveillance (Ward, 2021), and timeliness in reporting (Ward et al., 2019) of drug-related overdoses and deaths.

The English proverb "Necessity is the mother of invention" is very apt at the present time in the field of DRDs. Slavova et al. (2019) noted that "The opioid overdose crisis [in North America] has brought into focus some of the limitations of US MDI [(medicolegal death investigations)] systems for drug overdose surveillance and has given rise to a sense of urgency regarding the pressing need for improvements in … MDI data for public health action and research." Adapting what these authors wrote: "Epidemiologists [including the author of this thesis] can stimulate positive changes in MDI data quality by demonstrating the critical role of data in guiding public health and safety decisions and addressing the challenges of accurate and timely overdose mortality measures with stakeholders. Education, training, and resources specific to drug overdose surveillance and analysis will be essential as the nation's overdose crisis continues to evolve"

(Slavova et al., 2019), it is hoped that this thesis will, in some ways, contribute to those ends in respect of UK DRDs.

Conclusions

A number of key themes have become evident during the course of conducting research for and writing up this thesis. Going forward, these may present, in the UK context, as outlined in the following paragraphs.

Continuity - deaths will continue to occur. They will need identifying, investigating, and analysing. Statistics will need to be compiled and disseminated. Monitoring and surveillance will need to continue and be evaluated. Clinical and other professional guidance will also need to be issued.

Change - drug scenarios will continue to evolve and change. New molecules will need to be identified and screened for, in turn leading to a need for the timely availability of standard samples against which confiscated drugs can be compared. New modes of delivery (e.g., vaping) are emerging; routes of administration appear to be broadening. The role of Information Technology and other technologies, including Artificial Intelligence and less-invasive post-mortems, is growing. The development of artificial neural networks, web-crawling, etc. has already led to improvements in identifying and monitoring new molecules.

Consistency of approach - is a necessity. This can be a gradual process; for example, the amalgamation of coroners' jurisdictions has been occurring over the past couple of decades. However, regional coroners' groups have been established in recent years, leading to standardisation of approach, training, etc. Standardisation of drug screening protocols, toxicology and pathology reports would also assist in improving the quality and accuracy of data collected and disseminated. The implementation of ICD-11 will help in this respect.

Challenges - these are often outside the control of stake-holders but do impact on their work. A clear example is that of Covid-19, which caused changes in the populations at risk of dying, changes in types of substances being used/misused, changes in routes of administration, and delays in investigating and reporting DRDs. Communication between UK researchers investigating drugs and their effects, including overdose and death, and their European counterparts has been adversely and seriously affected by 'Brexit', i.e., the UK ceasing to be a member of the European Union. This has meant that the UK is no longer part of the EMCDDA (European Union Drugs Agency from 2 July 2024), with a consequent loss of access to the EDND, discontinuity in terms of published statistics, etc. The author advocates that the UK Government seeks to become an associate member of the European Union Drugs Agency, which begins operation on 2 July 2024, in the same way as Norway and Turkey have been members of the EMCDDA. Brexit also led to the UK ceasing to be part of Europol (European Union Agency for

Law Enforcement Cooperation), thereby losing access to key intelligence. Fortunately, the UK remains a member of the International Criminal Police Organization (INTERPOL) and the World Customs Organization.

At the heart of these issues are GMR statistics and SMR investigations and research. Their roles are, in turn, dependent on: case identification and investigation; data collection, collation, curation and analysis. The data have to be disseminated using suitable vehicles and language, so that stake-holders can use them in interpretation, advice, application and implementation in policy formulation and practice.

Chapter overview

This concluding chapter has briefly summarised the findings of the previous ones. An overview has been provided of patterns of drug-related deaths in and across the UK over the past three decades. An update on the position regarding DRDs registered in 2022 (the latest year for which data are available) has been presented. An attempt has been made (without the use of a 'crystal ball') to look at: evolving drug scenarios, future information needs; improving the range of information collected and how DRD patterns can be better understood; and 'horizon scanning'. The conclusions revisit the themes that run through this work: continuity, change, consistency, and challenge.

To paraphrase F. Scott Fitzgerald (1920):
To write this thesis it took two years; to conceive it two hours; to collect the data in it all my research life (three decades).

FINIS

The end? No! The story of drug-related deaths in the United Kingdom continues: fatalities continue; 'new' and 'traditional' substances play their parts; the roles of the 'usual suspects' ('chemists', drug traffickers and retailers, police and other law enforcement agencies, coroners, toxicologists, pathologists, public health officials, etc.) are executed; the 'script-writers' such as journalists and researchers guide our focus and provide critiques; politicians and law-makers provide oversight and the narrative. However, there are other 'actors' waiting in the wings to prompt or distract the key players. The pivotal roles are lived out on this stage by the individuals consuming and administering these substances; it is their reaction to these varying stimuli that determines how things play out.

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APPENDICES

This section of the thesis contains the following listed appendices.

Appendix A - Information on National Programme on Substance Abuse Deaths (see Chapter 3)

Appendix B - REF 2021 impact case-study

Appendix C - Author's activities with the Advisory Council on the Misuse of Drugs (ACMD), July 2018 to date

Appendix D - Author's academic outputs on drug-related deaths, July 2018 to date

Appendix E - Author's additional achievements and esteem factors

Appendix F - Correlation matrices for Chapters 9 to 11 – available as separate Word document containing Excel workbooks

Appendix G - Author's contribution to ACMD activities and resultant outcomes, 2018 - 2024

APPENDIX A - INFORMATION ON THE NATIONAL PROGRAMME ON SUBSTANCE ABUSE DEATHS

NATIONAL PROGRAMME ON SUBSTANCE ABUSE DEATHS (np-SAD)

INTERNATIONAL CENTRE FOR DRUG POLICY

ST GEORGE'S, UNIVERSITY OF LONDON

Introduction

This paper first outlines the benefits to be derived from using a Special Register - that maintained by the National Programme on Substance Abuse Deaths (np-SAD) - to conduct surveillance and research on and analysis of drug-related mortality in the UK. Second, a comparison is made between the Office for National Statistics (ONS) and np-SAD databases. Finally, the 'added value' of the np-SAD is summarised.

Enhanced monitoring of drug-related mortality by using np-SAD

The principal advantages of using the np-SAD are as follows:

- **Rapid and early provision of statistics** and analysis on surveillance; identifying new and emerging trends.
- **Monitoring patterns of death amongst specific populations of drug users** and provision of information to inform intervention (Oyefeso *et al*, 1999b; 2000). Other risk factors amongst drug users have been identified, e.g. suicide – a Department of Health target (Oyefeso *et al*, 19999a). These have implications for clinical practice and prescribing.
- **Part of an early warning system** in respect of misuse of new substances, or new consumption patterns, e.g. GHB/GBL, ketamine, oxycodone, PMA, methylamphetamine, piperazines
- **Issuing alerts about potential new risk factors/substances**
- **Wide range of data items collected** by np-SAD means that analyses undertaken can inform prevention and intervention strategies at local, regional, and national levels.
- **Multidisciplinary team** with expertise in the field of substance use, prescribing and clinical practice, statistical analysis, and epidemiology, provides informed commentary on the interpretation and implication of findings. This is fed back to health professionals, policy-makers and service providers. For example, the significant proportion of cases where illicit supplies of methadone were implicated in death has relevance for prescribing and supervised consumption.
- **Ongoing close collaboration with data suppliers** (coroners and their staff) regarding gaps in information, clarification of facts, and quality assurance.

These benefits are derived through employing the information collected, analysed, interpreted and disseminated by the np-SAD:

- **Active participation in the formulation of guidance on drug issues.** For example, input is provided to the Drug-Related Deaths Steering Group of the National Treatment Agency. The ICDP is also a registered stakeholder with the NICE, and NPSA.
- **Informing issues in the area of prescribing**, for example, the use of anti-depressants (Oyefeso *et al*, 2000; Cheeta *et al*, 2004), and the relationship between prescribing benzodiazepines and their role in drug-related deaths (recent request from the Department of Health). The paper by Cheeta *et al* (2004) informed the NICE guidelines on anti-depressant prescribing.
- **Dissemination of information** on the effects and role of specific substances in causing death, e.g. methadone (Valmana *et al*, 2000; Corkery *et al*, 2004), ecstasy (Schifano, 2004;

Schifano *et al*, 2003a, 2003b), ketamine (Schifano et al, 2008).

- **Relating drug-related mortality to other key indicators**, for example buprenorphine (Schifano *et al*, 2005a), ecstasy (Schifano et al, 2006), cocaine (Schifano and Corkery, 2006), methylamphetamine (Schifano et al, 2007), or in new ways of obtaining drugs i.e. 2C-T-7 (Schifano *et a*l, 2005b).
- **Identification of the roles of polypharmacy** (prescribing of multiple substances) and polysubstance abuse in deaths in regular np-SAD reports and academic papers.
- Information on the cause of death is published by np-SAD.

Comparison between ONS and np-SAD information on drug-related deaths

This section of the paper outlines the commonalities and differences between the information and services provided by the drug poisoning deaths database of the Office for National Statistics (ONS) and the National Programme on Substance Abuse Deaths (np-SAD).

Aspect	ONS	np-SAD
Status	Government department	Independent International Centre within the University of London
Function	The Office for National Statistics (ONS) is the government department that provides UK statistical and registration services. The Office also incorporates the General Register Office for England and Wales (GRO). The GRO is responsible for ensuring the registration of all births, marriages and deaths in England and Wales, and for maintaining a central archive dating back to 1837.	The Programme's principal function is one of surveillance[1] so as to reduce and prevent drug-related deaths in the UK due to the misuse of drugs, both licit and illicit, by collecting, analysing and disseminating information on the extent and nature of death. The Programme offers a comprehensive prevention package to Drug (and Alcohol) Action Teams (D(A)ATs), Primary Care Trusts (PCTs) and Strategic Health Authorities (SHAs) with a mission to tackle the problem of drug-related deaths.
Accountability	From 1 April 2008, ONS has been under the governance of the UK Statistics Authority, which itself is directly accountable to Parliament. . The operational management of ONS is delegated to the Director of ONS.	Managed within the overall structure of the International Centre for Drug Policy St. George's, University of London. Accountable to the Medical School Council. Has a national (UK-wide) Steering Group composed of policy-makers, experts, and user groups to advise on the surveillance aspects of the Programme's activities.
Funding	From central Treasury funds.	Surveillance activities are funded for 2 years by grant from Department of Health.
Legal restrictions	Functions are governed by statute and cannot be changed easily or quickly. Has to comply with Data Protection Act.	No legal constraints and able to adapt to changes circumstances and needs quickly. Follows good academic practice guidelines and reports to the National Steering Group, on which there are representatives of the Department

[1] One of the aims of np-SAD is to provide national drug-related death surveillance through the Special Register, and routinely inform clinicians and policy makers on risks associated with premature death due to substance misuse. Health-related surveillance has been described as the 'ongoing systematic collection, analysis, and interpretation of outcome-specific health data, closely integrated with the timely dissemination of these data to those responsible for preventing and controlling disease or injury' (Thacker and Stroup 1998:106).

		of Health, Home Office, Department for Constitutional Affairs, the Devolved Administrations and other Government Departments. Has to comply with Data Protection Act.
Staffing	Statisticians within Mortality section of Vital Statistics in central London, plus general coding staff located in Hampshire.	Two full-time paid staff (Programme Manager and Demographer), part-time database & administrative officer, and 4 other team members. Broad range of expertise is brought to bear from different professional backgrounds – psychiatry, psychology, social science, pharmacology, epidemiology, addictive behavioural science, database, project management, etc. Heritage of 40 years of experience in collecting and analysing data on UK-wide drug-related mortality data. In addition to the Director of the ICDP, two current team members have been associated with the Programme for more than a decade. This gives continuity of approach. Located in an academic centre with input from relevant disciplines National and international experience, collaboration and networking.
Mortality database(s)	Historic archive of general deaths in England and Wales from 1837. Drug poisoning deaths from 1993 onwards (Christophersen *et al*, 1998; ONS, 2006).	Dead Addicts Database covered deaths of addicts notified to the Home Office (1967-1994). Home Office Addicts Index deaths (1982-1997). Coroners Database from 1997 (Ghodse *et al*, 2005: 13-15). Official custodians of the Home Office Addicts Index Access database and paper files covering the period 1968-1997.
Current data sources	Death certificates and Part V of Coroner's Inquisition form.	Special data collection form, plus post-mortem and toxicology reports.
Method of collection	Submission of death certificates and Part V forms to central database by local Registrars of Births, Deaths and Marriages.	Coroners or their staff, plus personal visits by np-SAD staff to some coroner's offices, filling in data collection form, extracting information from all documents available to the coroner at the time of inquest. These include: post-mortem and toxicology reports; witness statements; reports by emergency services and hospital staff; medical reports (including psychiatric history, prescribing history, and contact with services).
Data collection unit	Individual deaths	Inquests completed on the deaths of individuals

Reporting periods	Deaths registered in a particular calendar year (from 1993)	Inquests completed in particular 6-month (surveillance) periods, deaths occurring in a particular calendar year when an inquest has been completed.
ICD coding	ICD-9 1993-2000; ICD-10 from 2001	ICD-10 from outset (1997)
Definitions	Captures a wide range of 'acute' or 'direct' drug-related deaths, but focuses on poisoning-related ones. An ONS case is usually expressed in terms of the following ICD-10 codes for underlying cause of death: F11–F16, F18–F19 Mental and behavioural disorders due to drug use (excluding alcohol and tobacco); X40–X44 Accidental poisoning by drugs, medicaments and biological substances; X60–X64 Intentional self-poisoning by drugs, medicaments and biological substances; Y10–Y14 Poisoning by drugs, medicaments and biological substances, undetermined intent; X85 Assault by drugs, medicaments and biological substances. Cases can be extracted using narrower definitions, e.g. to monitor the UK Drug Strategy targets for DRDs or to provide information for the EMCDDA.	Captures a wide range of 'acute' or 'direct' drug-related deaths, but focuses on psychoactive substances. An np-SAD case is defined as a death where any of the following criteria are met at an inquest or similar investigation: one or more psychoactive[2] substances directly implicated in death; or history of dependence or abuse[3] of psychoactive drugs; or presence of Controlled Drugs[4] at post mortem. Cases can be extracted using narrower definitions, e.g. to monitor the UK Drug Strategy targets for DRDs or to provide information for the EMCDDA. The same definitions are used for the 'Drug Strategy' cases, but there are different definitions and selection criteria applied as between General Mortality Registers and Special Registers for the EMCDDA.
Geographical coverage	England and Wales	UK and Islands (England, Wales, Scotland, Northern Ireland, Isle of Man, Guernsey, Jersey)
Compliance	Compulsory. Since 1982, 100% compliance by registrars.	Voluntary system. England & Wales – 95% of all areas have reported at some stage to the Programme. Annual report includes complete information on cases notified to Scottish police forces, via MoU with Scottish Crime & Drug Enforcement Agency
Coverage of drug-related deaths	Assumed to cover all 'acute' or 'direct' drug-related deaths such as	Assumed to cover all 'acute' or 'direct' drug-related deaths such as

[2] 'Psychoactive' substances are those having a direct effect on perception, mood, cognition, behaviour or motor function. Typically these include opiates and opioid analgesics, hypnotics, sedatives, antidepressants, anti-epileptics, anti-psychotics, hallucinogens and stimulants such as amphetamines and cocaine.

[3] A drug abuser/dependent case is defined as one with a history of substance abuse where one or more of the following criteria are met:

- reported as a known illicit drug user by the coroner, based on evidence obtained at inquest;
- prescribed substitute medication for drug dependence;
- presence of an illicit drug at post mortem, where not prescribed, or
- presence of any additional information on the coroner's report suggestive of a history of drug abuse, and where such a history fulfils ICD-10 criteria.

[4] 'Controlled Drugs' are those drugs specifically mentioned in the Misuse of Drugs Act (1971) – these include opiates, cocaine, amphetamines, cannabis, GHB, ketamine, hallucinogens and most benzodiazepines.

	poisonings, overdoses, etc. but experience of identifying GHB and ketamine cases on both databases suggests otherwise, i.e. additional cases found on both databases that were not identified on the other database. Indirect deaths involving diseases such as HIV/AIDS and hepatitis, and conditions like cirrhosis are difficult to identify without special registers and databases (e.g. as with HIV/AIDS).	poisonings, overdoses, etc. but experience of identifying GHB and ketamine cases on both databases suggests otherwise, i.e. additional cases found on both databases that were not identified on the other database. Information on indirect deaths involving diseases such as HIV/AIDS and hepatitis, and conditions like cirrhosis are not currently collected unless they have gone to inquest and are identified as drug-related deaths.
Data fields	Demographic: personal details, age, gender, place of birth, Usual address Occupation Marital status Circumstances of death: place, date, Substances mentioned on death certificate or by coroner, Medical causes of death Coroner's verdict Other relevant information Whether post mortem was held Circumstances if an "accident"	Demographic: personal details, age, gender, place of birth, ethnicity, Usual address Occupation Living arrangements Circumstances of death: place, date Prescribed medication, substances found at post mortem, including levels, Substances implicated in death, including psychoactive ones Drug/substance abuse status Medical and psychiatric history, injection behaviour, recently released from prison, etc. Medical causes of death Coroner's verdict or determination Other relevant information Inquest: coroner, area, date of inquest, whether post mortem was held
Statistics generated	Frequencies, percentages, trend analysis, age-standardised rates. Breakdown by regions and at lower levels published occasionally	Frequencies, percentages, rates per 100,000 population, proportion ratios, trend analysis, etc. Regular publications include breakdowns by coroners', DAAT, PCT, SHA areas of rates of DRDs per 100,000 adult population, and more detailed breakdowns by DAAT area.
Publications	Main output are yearly figures on drug poisoning deaths and deaths due to drug misuse (i.e. Drug Strategy cases) released in February each year in Spring issue of *Health Statistics Quarterly*. These figures are published 14 months after the end of the year being reported on. This delay in information provision limited the usefulness of such data for surveillance and, therefore, for informing prevention and treatment policies and practices.	Two annual publications: short briefing update for coroners, etc early in year (replacing the former 6-monthly surveillance reports); Annual Report looking at deaths occurring in calendar year preceding year of publication. The reports include information cases profiles; *associated risks* (sex and accidental/intentional death; age and accidental/intentional death; prescribed psychoactive drugs; methadone; antidepressants; other opioid analgesics and hypnotics/sedatives); *drug abuse*

	Commentary gives information on trends over time for a limited range of variables. Ad hoc papers in *Health Statistics Quarterly* and *Population Trends*.	(cases with a history of illicit drug use are compared to those without) and a *commentary.* The latter highlights the main findings and discusses implications for clinical practice and policy development at the local, regional and national levels. Interpreting the findings and translating them into terms that can be understood by both policy makers and clinicians in the field, is a very good example of the 'added value' of a Special Register. Academic input to the evidence base: peer-reviewed academic papers, conference presentations, books, monographs, etc.
Dissemination	Printed copies and downloadable PDF files of Health Statistics Quarterly appear on ONS website on day of publication. Also Excel tables can be downloaded for data back to 1993.	Downloadable pdf from ICDP web-page on day of release. Printed copies are sent free to all coroners, professional bodies, Ministers, central government and devolved administrations, international bodies (WHO, UN, etc). Printed copies also available for sale to academics, libraries, DATs, etc. Executive Summaries put on np-SAD website on day of release.
Common problems	Description of 10% of drug-related deaths in England and Wales as 'drugs overdose' or 'multiple drugs overdose'. (The proportion in Northern Ireland may be higher. This is only relevant for np-SAD.) Identification of indirect 'drug-related' deaths (see above) and other deaths such as accidents, fatalities arising from disputes over drugs, etc Not all relevant cases necessarily identified.	
Benefits of two data collection systems	Since both databases collect information on a broad range of drug-related deaths, they can each be used to cross-check or validate the findings of the other (i.e. triangulation). They are not alternatives since they have different functions, but they do complement each other both in terms of the information they publish and in the services they provide.	
Collaboration	It would be beneficial to both organisations to be able to exchange information on named individuals on a regular and routine basis so that all relevant cases are identified, and thus both databases made more complete and accurate. However, legislation restricts the way in which the ONS can share information with non-Governmental bodies; this limits the extent to which information can be exchanged between the two bodies. For ad hoc studies, e.g. to examine the number of GHB-related deaths, it is necessary for the np-SAD to register that specific project as a medical study (as in the case of the Addict Index study). Consideration could be given to see if such an arrangement could be extended to the surveillance work as a whole, or to an alternative mode of working.	

Additional 'added value' of Special Register

The benefits already demonstrated by the np-SAD can be summarised as follows:

- The principal benefits are those of a voluntary data collection scheme and an independent academic body.

- Provision of DRD data that are specific to local drug policies and practices
- Utilisation of data collection procedures that allow for additional information to be collected, that cannot be provided on death certificates
- Availability of staff with expertise in the field of drug addiction, thus providing more informed commentary on the interpretation and implication of findings for clinical practice
- Immediate access to new information that can feed quickly into prevention initiatives. Acting as part of an early-warning system.
- The publication of six-monthly surveillance reports that provide indication of the extent of drug-related deaths, thus assisting policy makers to modify priorities and redirect intervention initiatives that are sensitive to current patterns
- Ability to identify cases of drug-related deaths with a history of drug abuse/dependence enables the development of evidence-based prevention programmes for this vulnerable group
- Retention of data in a readily accessible electronic format to facilitate understanding further studies of predictors, trends and patterns of drug-related deaths
- Ability to undertake special local surveillance reports and psychological autopsies
- Participation in local, national, and international conferences, work groups, etc. e.g. ACMD and Technical Working Group, NTA Steering Group on drug-related death
- Facilitation of training in drug-related mortality – training, e.g. REITOX Academy in Lisbon April 2004, lectures to health professionals on diploma and degree courses

A specialist register is a major element in a response framework in the reduction of drug-related deaths. Special registers, such as DAWN in the USA and other surveillance systems in Germany, Sweden and other major European countries, are essential supplements to GMRs. The key elements of specialist registers that make them useful surveillance tools are the speed of data being made available, and their accessibility to relevant policy makers and clinicians.

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National Programme on Substance Abuse Deaths (np-SAD)

September 2009

APPENDIX B - REF 2021 IMPACT CASE-STUDY

Novel Psychoactive Substances: changing legislation, regulation, clinical practice and drug prevention strategies to protect public health

Download case study PDF

Submitting institution

University of Hertfordshire

Unit of assessment

3 - Allied Health Professions, Dentistry, Nursing and Pharmacy

Summary impact type

Political

Request cross-referral to

-

Is this case study continued from a case study submitted in 2014?

No

Underpinning research subjects

- Clinical Sciences
- Pharmacology And Pharmaceutical Sciences
- Psychology

1. Summary of the impact

Research at the University of Hertfordshire (UH) into rising misuse and severe ill-health effects of Novel Psychoactive Substances (NPS) has led to more effective legislation and regulation, and new measures to protect public health. The research contributed to UK law changes that reclassified two psychostimulants (4F-EPH and ethylphenidate) as Class B substances and two anticonvulsants (pregabalin and gabapentin) as Class C. It was key to recommendations by the UK Advisory Council on the Misuse of Drugs (ACMD) on misuse of Fentanyl and Gamma Hydroxybutyrate (GHB). UH studies informed reviews by the Home Office, Public Health England, NHS England and the United Nations Office on Drugs and Crime, and changed clinical and prescribing guidelines in the UK and Italy. The research led to the first Home Office license for a drug checking service, which informed a select committee inquiry into UK drugs policy and underpinned recommendations arising from an inquest into drug-related deaths at music festivals in Australia.

2. Underpinning research

The last decade has seen the rapid emergence of an increasingly diverse group of recreational psychotropic drugs marketed colloquially as ‘legal highs’, ‘bath salts’ or ‘research chemicals’. These Novel Psychoactive Substances (NPS) pose a significant risk to public health; understanding of their chemical composition and toxicity is limited and the nature and severity of

their adverse health effects are unpredictable and often unknown. The use of NPS can lead to acute anxiety, psychosis and addiction, and has been repeatedly linked to emergency hospitalisations and deaths.

Multidisciplinary research by UH's Psychopharmacology, Drug Misuse and NPS Unit (led by Schifano) has investigated several issues associated with NPS: negative health consequences arising from their use; the epidemiology of NPS use and related mortality and 'near misses'; the abuse potential of prescription and over-the-counter NPS; identification and classification of illicit psychoactive substances. This body of work has made a leading contribution to the global knowledge base for this fast-evolving phenomenon, through over 200 peer-reviewed articles by members of the UH Unit since 2010. Studies under three EU programmes sought to provide health and law enforcement communities with evidence of the pharmacological properties and effects of NPS, how they are obtained and how to identify them. The UH-led, multi-centre Recreational Drugs European Network (ReDNeT) [**G1**] profiled emerging NPS and consumption patterns. The project led to a database of 650 NPS combinations, expanded upon the role of web-monitoring tools in mapping NPS diffusion and disseminated advice to EU health professionals, policymakers and crime agencies [**3.1**].

The UH-led EU-MADNESS research programme [**G2**] identified the NPS that were causing the most harm. The data was used to develop educational resources for health professionals and policymakers, with Corkery leading the analysis of anonymised data on drug-related deaths for correlations with misuse of NPS. The Unit were Co-Is on the 'Enhancing Police Skills concerning NPS' programme [**G3**], providing expertise in substance epidemiology and monitoring, chemical and mathematical modelling, and knowledge of the dark web to facilitate early recognition of NPS. Both programmes fed into the design of the Unit's novel web crawler software NPS.Finder®, which searches online discussion forums frequented by NPS users to identify the emergence of NPS and profile them. It has identified around 4,300 unique NPS, a figure four times higher than that reported by EU and UN agencies [**3.2**]. Under **G3**, the Unit developed a novel approach for the in-field identification and classification of NPS using Raman spectroscopy coupled with Principal Components Analysis (PCA). For the first time key structural features of potential 'unknown' NPS could be identified [**3.3**].

The Unit has investigated the misuse of prescription medications as recreational NPS. Studies highlighted concerns around the misuse of gabapentinoids (notably gabapentin and pregabalin), which are prescribed to treat epilepsy, neuropathic pain and anxiety [**3.4**, **3.5**]. Researchers found that many gabapentinoid experimenters had a history of recreational polydrug misuse, who self-administer with very high dosages [**3.4**]. They found 6.6% and 4.8% of adverse drug reactions were associated with pregabalin and gabapentin respectively, with 27 and 86 fatalities [**3.5**]. A study with Sapienza University of Rome flagged the intravenous and potentially fatal misuse of tropicamide eye drops, which can lead to hyperthermia, convulsions and coma [**3.6**].

Fentanyl is a powerful opioid similar to morphine but 50-100 times more potent. A UH study [**3.7**], involving the analysis of fentanyl-related misuse over ten years, revealed a spike in adverse drug reactions between 2016 and 2018, especially when fentanyl was mixed with heroin. Large numbers of cases required prolonged hospitalisation or resulted in death, leading the team to conclude that fentanyl abuse should be considered a public health issue with significant implications for clinical practice. A separate study [**3.8**] of the misuse of GHB and gamma-butyrolactone (GBL), which had increased greatly since the 1990s, particularly among LGBT individuals in recreational settings (e.g., 'chemsex'), concluded that significant caution is needed when ingesting GHB/GHL, especially alongside alcohol, stimulants, benzodiazepines and ketamine. It found that risk of death is increased due to their CNS-depressant properties.

3. References to the research

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3.8 Corkery JM, Loi B, Claridge H, Goodair C, Schifano F. Deaths in the Lesbian, Gay, Bisexual and Transgender United Kingdom communities associated with GHB and precursors. Current Drug Metabolism, 2018. **http://doi.org/10.2174/1389200218666171108163817**.

Key underpinning grants

G1 European Commission, 2010-12. 'Recreational Drugs' European Network (ReDNet): An ICT prevention service addressing the use of novel compounds in vulnerable individuals. Total award: €833,333; amount to UH (coordinator): £195,258. **Winner of 2013 European Health Award.**
G2 European Commission, 2014-16. EU-MADNESS (EUropean-wide, Monitoring, Analysis and knowledge Dissemination on Novel/Emerging pSychoactiveS): integrated EU NPS monitoring & profiling to prevent health harms and update professionals. Total award: €635,215; amount to UH (coordinator): £226,378.
G3 European Commission, 2014-16; Project EPS/NPS – Enhancing Police Skills concerning NPS. Total award: €692,850; amount to UH: £193,105.

4. Details of the impact

UH research on NPS has: directly influenced action by the UK Government and public bodies to introduce new legislation, regulation and guidance to protect public health; changed NPS clinical and prescribing guidelines for health professionals; secured the first Home Office license for a drug checking service; and informed drug prevention strategies in the UK and overseas.

Impact on UK drug legislation, regulation and policymaking

UH research into NPS has been used by UK policymakers to identify the scale and nature of NPS use and its associated risks. Several papers published by the UH Unit were cited in the Home Office's *New Psychoactive Substances in England: A review of the evidence* (2014) [**5.1**]. The research has fed directly into the deliberations and recommendations of the ACMD on some of the most potentially harmful NPS on the market. Schifano was a full ACMD member until reaching his term limit in 2019; Corkery was a member of the ACMD's NPS Committee [**5.2**].

In 2015 the ACMD reviewed the harms associated with the misuse of pregabalin and gabapentin. ONS data had shown a sharp rise in deaths related to pregabalin (four in 2012 to 38 in 2014) and gabapentin (nine in 2013 to 26 in 2014). Studies led by Schifano had been raising safety concerns over the drugs; as an ACMD member, Schifano contributed his research insights, specifically **3.4** and **3.5**, to the Review. The ACMD chair wrote to the Home Office Minister in January 2016, recommending the control of pregabalin and gabapentin as Class C substances. Paper **3.4** was cited in the recommendation [**5.3**]. This also referenced a review published by PHE and NHSE (2014) which in turn cited research by Schifano and Corazza as part of its evidence base [**5.4**]. Responding to the ACMD, the Government announced, in 2018, the reclassification of pregabalin and gabapentin as Class C controlled substances. Stronger controls were put in place to minimise the risk of stockpiling by patients.

Under [**G2**], in 2016 Corkery identified the first known death from ' *complications of 4F-EPH*' (4-Fluoroethylphenidate). This molecule is an analogue of the medication Ritalin (methylphenidate). He also identified five deaths where ethylphenidate, an amphetamine-like psychostimulant, was implicated in the cause of death. As an ACMD NPS Committee member, Corkery published this

data in the ACMD's report sent to the Home Office minister in March 2017 [**5.5**]. It recommended the control of 12 methylphenidate-related NPS, including 4F-EPH and ethylphenidate, as Class B substances. Only two months later, the molecules became Class B drugs following the passing of secondary legislation under the Misuse of Drugs Act 1971 and a Home Office circular was immediately sent to police forces and criminal justice bodies drawing their attention to the law change [**5.5**].

Fentanyl is a licensed medicine for anaesthesia and pain management; it is also classified as an illegal Class A substance in the UK. In 2017, the Home Secretary, responding to increasing fentanyl-related deaths, commissioned the ACMD to review the number of known fentanyl analogues – and their known and likely risk factors. The ACMD's NPS Committee analysed the misuse potential of fentanyl compounds and associated harms. Key evidence was UH's 10-year assessment of fentanyl misuse in the UK, EU and US [**3.7**], which Corkery, as a committee member, fed directly into the review process [**5.6**]. The conclusions in the ACMD report, published in January 2020 and covered widely in the media, mirrored those in **3.7**: ' *fentanyl and fentanyl analogues present a significant risk to UK public health*' and ' *current monitoring and surveillance systems should be adapted to help identify the true scale of this threat*'. It warned, as noted in **3.7**, that a rise in the number of deaths in the UK was being driven by fentanyl being added to heroin. The Home Office said it would ' *carefully consider*' the recommendations in its policy response.

In January 2020 the Home Secretary asked the ACMD to urgently review GHB, GBL and closely related compounds, responding to the use of GHB by the serial killer Stephen Port and suspected use of GHB by serial rapist Reynhard Sinaga. The ACMD published its report, widely covered in the media, in November 2020, recommending that GHB should become a Class B drug. Corkery's studies at UH, including **3.8**, were cited 25 times as key evidence for the conclusions [**5.7**].

Impact on clinical and prescribing guidelines and practice

In July 2017 the Department of Health published *Drug misuse and dependence: UK guidelines for clinical management* for healthcare professionals. The chapter *Misuse of or dependence on gabapentinoids* used **3.4** as key evidence, warning that ' *prescribers need to be aware of the risk that some patients may wish to accumulate supplies with a view to taking excessive doses for a psychoactive effect*'. It noted ' *accumulating*' evidence of gabapentinoid misuse, particularly in those who misuse other drugs [**5.8**]. In 2018 the Royal College of Psychiatrists published *Our Invisible Addicts*, a report setting out the extent of substance-related health problems amongst older people. Citing **3.5**, it highlighted the increase in adverse drug reactions associated with pregabalin and advised that ' *vigilance is needed when co-prescribing pregabalin with opioid drugs*' [**5.9**]. Through a collaboration with the Royal Pharmaceutical Society (RPS), research under **G2** and **G3** formed the basis of a new section in the Society's 2018 edition of its *Medicines, Ethics and Practice* textbook, informing pharmacists about how NPS are controlled and

associated harms. The textbook is accessed by all pharmacies in the UK and is part of both undergraduate pharmacy studies and pharmacy pre-registration national assessment. To accompany this, Guirguis co-authored an online NPS 'quick reference guide' that was made available in April 2018 to 27,000 RPS members, along with a factsheet for pharmacists available to both members and non-members [**5.10**].

Research into misuse of tropicamide [**3.6**] was carried out in response to an ' *alarming*' rise in the non-prescription sale of tropicamide in pharmacies in Trentino, Italy [**5.11**]. The peer-reviewed paper and UH's follow-up review in *Human Psychopharmacology* in 2015 led to the Provincial Health Services Agency issuing an advisory notice to all physicians and pharmacists in Italy that tropicamide should not be sold without prescription. Product sales dropped as a result [**5.11**].

Impact on authorities' drug prevention strategies and the legal profession

Novel UH research into identifying emerging NPS via handheld spectroscopy [**3.3**, **G3**], in order to support police and staff in prisons and substance misuse units, resulted in the first drug checking service to be licensed by the UK Home Office. The drop-in service, a partnership between UH (PI: Guirguis) and charity Addaction, was run for the first time in Somerset in 2019; it allows people to have a sample of their drugs tested (using handheld spectroscopy) anonymously and to receive specialist advice. Covered widely in the media, an article in the *Guardian* [**5.12**] said the service ' *marks a milestone for the harm reduction movement as well as a significant shift in government support for the approach*'. It quoted the drugs strategy lead at Avon and Somerset police as saying: ' *We are confident that this approach will help those who are determined to take drugs keep safe from harm, inform them of the health dangers and remind them of the criminal consequences they could face'* [**5.12**]. In June 2019 the service was cited by a witness giving oral evidence on the benefits of drug testing to the Health and Social Care Select Committee inquiry into UK drugs policy. The Committee's report, published in October 2019, highlighted such testing as ' *an effective early warning system … about particular batches of drugs and the dangers they might pose, enabling public health messages to be put out to reduce wider harm*' [**5.13**].

The spectroscopy studies have helped coroners assess NPS-related fatalities. Guirgius acted as an Expert Witness for an inquest held in July 2019 in New South Wales, Australia into the deaths of six young people at music festivals. The coroners' report cited **3.3**, discussed the Home Office-licensed checking service at length and referred to Guirguis's evidence 46 times [**5.14**]. The state premier and police had previously made their opposition to drug checking clear but the report made this key recommendation: ' *That the Department of Premier and Cabinet permits and facilitates Pill Testing Australia, The Loop Australia, or another similarly qualified organisation to run front of house medically supervised pill testing/drug checking at music festivals in NSW'* [**5.14**].

Based on the Unit's combined research and collaboration with UN agencies under **G2** and **G3**, the UN Office on Drugs and Crime (UNODC) asked Corazza to carry out the evidence analysis and prepare the first draft of Volume 21 of its Global Synthetics Monitoring: Analyses, Reporting and Trends (SMART) Update: *Understanding the global opioid crisis*. Published in English, Russian and Spanish, the UNODC emphasised its importance ' *in enhancing international understanding of the threats posed by the non-medical use of opioids and identifying options for response'* [**5.15**].

5. Sources to corroborate the impact

5.1 Home Office: New Psychoactive Substances in England: A review of the evidence, 2014. **www.tinyurl.com/akrgpam8** (pp. 42, 43, 49, 50)

5.2 Letter from the Home Secretary confirming Schifano's position as a full ACMD member.

5.3 ACMD advice to the Home Office re the misuse of pregabalin and gabapentin, 2016. **www.tinyurl.com/48pvmdyb** (p. 2)

5.4 PHE/NHS: Advice for prescribers on the risk of the misuse of pregabalin and gabapentin, 2014. **www.tinyurl.com/378zdlhp** (p. 6)

5.5 ACMD report to the Home Office: Further advice on methylphenidate-related NPS. **www.tinyurl.com/1m371sy2** (para 31); Home Office Circular 008/2017 on the control of 12 methylphenidate-related NPS: **www.tinyurl.com/1rd306ht**

5.6 ACMD report to the Home Secretary: Misuse of Fentanyl and Fentanyl Analogues, 2020. **www.tinyurl.com/1t37rl0b** (p. 58)

5.7 ACMD report to the Home Secretary: An assessment of the harms of GHB, GBL, and closely related compounds: **www.tinyurl.com/3cryvo43** (Corkery's studies cited 25 times throughout).

5.8 Dept of Health: Drug misuse and dependence: UK guidelines on clinical management, 2017. **www.tinyurl.com/49urgqhp** (pp. 208, 254)

5.9 Royal College of Psychiatrists: Our Invisible Addicts, 2018. **https://bit.ly/3qNrYPX** (p. 159)

5.10 Royal Pharmaceutical Society: NPS reference guide and factsheet for pharmacists, 2018. **www.tinyurl.com/bc9gfycs**; **www.tinyurl.com/4i53cq1z**

5.11 Corroborating statement from Addiction Service, Provincial Health Services Agency, Italy.

5.12 'It's about saving lives': inside the UK's first licensed drug testing service, The Guardian 2019. **www.tinyurl.com/3kxvz22c**

5.13 Health and Social Care Committee inquiry into Drugs Policy (oral evidence and report), 2019. **www.tinyurl.com/n3kpurnn** (p. 14 and Q143)

5.14 State Coroners' Court of New South Wales inquest report, 2019. **https://coroners.nsw.gov.au/coroners-court/download.html/documents/findings/2019/Music_Festival_Redacted_findings_in_the_joint_inquest_into_deaths_arising_at_music_festivals_.pdf** (46 citations throughout the report)

5.15 Corroborating statement from the Chief of the Laboratory and Scientific Section, UNODC.

Additional contextual information

Grant funding

Grant number	Value of grant
1	£719,418
2	£548,102
3	£598,035

Countries

- European Union
- United Kingdom
- Italy
- Australia

Formal partners

- St George’s University of London
- Universita di Cagliari
- University of Budapest
- European Institute for Health Promotion
- Universita Politecnica dele Marcha
- Universitat Duisburg Essen
- The University of Edinburgh
- Universita degli Studi G d'Annunzio
- Eötvös Loránd University
- "University of Szczecin "

Funding programmes

- Health Programme 2008-2013
- "Drug Prevention and Information Programme"

Global research identifiers

- grid.270680.b

Name of funders

- European Commission

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APPENDIX C - AUTHOR'S ACTIVITIES WITH THE ADVISORY COUNCIL ON THE MISUSE OF DRUGS (ACMD), JULY 2018 TO DATE

- Co-opted member of ACMD's Working Group on New Psychoactive Substances (2009 >)
- Co-opted member of ACMD's Technical Committee (February 2016 >)
- As member of ACMD's NPS Committee, submitted EU-MADNESS analysis of NRS data to "Advisory Council on the Misuse of Drugs - Methylphenidate-related Novel Psychoactive Substances: A review of the evidence of use and harms" (2017). Paper subsequently published in December 2022
  https://doi.org/10.1177/19253621221142480
- Member of NPS Committee that produced ACMD's Report "Misuse of Fentanyl and Fentanyl Analogues" (2020)
- Member of NPS Committee that produced ACMD's Report "Benzodiazepines - A review of the evidence of use and harms of Novel Benzodiazepines" (2020)
- Member of NPS Committee that produced ACMD's Report "Synthetic cannabinoid receptor agonists (SCRA) - An updated harms assessment and a review of classification and scheduling under the Misuse of Drugs Act 1971 and its Regulations. (2020)
- Two papers cited by ACMD's Report "An assessment of the harms of gamma-hydroxybutyric acid (GHB), gamma-butyrolactone (GBL), and closely related compounds" (2020):
  https://doi.org/10.1016/j.neubiorev.2015.03.012
  https://doi.org/10.2174/1389200218666171108163817
- As member of ACMD's "Nitazene" Working Group (28 January 2022? - 6 October 2023), contributed EU-MADNESS data on NRS information for "ACMD advice on 2-benzyl benzimidazole and piperidine benzimidazolone opioids" published on 18 July 2022.
- Member of ACMD's Nitrous Oxide Working Group (9 September 2022 to 6 September 2023) ACMD's Report "Nitrous Oxide– Updated Harms Assessment" was published 6 March 2023; Led on the section about mortality, including a "bespoke analysis" which will be written up for publication.
- Member of ACMD's 4th generation SCRA (including cumyl-PeGaClone) Working Group 14 April 2022 to 22 October 2022. ACMD's Report "Cumyl-PeGaClone and other recently encountered synthetic cannabinoid receptor agonists - A review of the evidence on their use and harms" was published 22 October 2022 and updated 25 May 2023. Contributed on deaths.
- Member of ACMD's Diphenidine Working Group 14 April 2022 to 25 May 2023. ACMD's Report "A review of the evidence on the use and harms of Diphenidine and other related substances" was published 25 May 2023; addendum published 6 October 2023. Provided EU-

MADNESS data and led on deaths research and writing of sections, which will be written up for publication.

- Member of ACMD's Alkyl Nitrites Working Group 3 May 2023 > to date - Contributing on deaths, including EU-MADNESS data from NRS
- Member of ACMD's Synthetic Cathinones Working Group - 3 May 2023 to date - Contributing on deaths, including EU-MADNESS data from NRS
- Member of ACMD's Desalkyl gidazepam (bromonordiazepam) Working Group3 May 2023 > May 2024 - Contributing on deaths, including EU-MADNESS data from NRS
- Member of ACMD's Xylazine Working Group – 3 May 2023 > February 2024 - Contributing on deaths, including EU-MADNESS data from NRS, etc. to draft report

APPENDIX D - AUTHOR'S ACADEMIC OUTPUTS ON DRUG-RELATED DEATHS, JULY 2018 TO DATE

Academic papers, with abstracts

Corkery, J.M. (2018). Ibogaine as a treatment for substance misuse: Potential benefits and practical dangers. Prog Brain Res. 242:217-257.
https://doi.org/10.1016/bs.pbr.2018.08.005
ABSTRACT:
Ibogaine is an indole alkaloid found in the root bark of the Iboga shrub native to west Africa possessing hallucinogenic properties. For centuries it has been used in religious ceremonies and to gain spiritual enlightenment. However, since the early 1960s, its apparent ability to reduce craving for psychoactive substances including alcohol, cocaine, methamphetamine, opiates, and nicotine has led to its use in detoxification treatments. In many instances, clients receive treatment in non-medical settings, with little by way of robust scientific clinical trials. This chapter provides an overview of the potential benefits that could arise from such research. This is balanced against the serious adverse effects that can occur due to undiagnosed health conditions and/or concomitant use of other drugs. A detailed update is provided of the 33 deaths known to have occurred, including 5 in the UK. Looking forward, there is a need to develop better opiate detoxification treatment against a background of increasing opioid-related fatalities. A congener of ibogaine, 18-MC, appears to be safer and is to undergo clinical trials. In the meantime, would-be consumers and treatment providers must make more careful, detailed risk-assessments before using ibogaine. Treatment outcomes, including deaths, need to be accurately recorded and published.

Corkery, J.M., Loi, B., Claridge, H., Goodair, C., Schifano, F. (2018). Deaths in the Lesbian, Gay, Bisexual and Transgender United Kingdom Communities Associated with GHB and Precursors. Curr Drug Metab. 19(13):1086-1099.
https://doi.org/10.2174/1389200218666171108163817
ABSTRACT:
Background: Misuse of gammahydroxybutyrate (GHB) and its prodrugs gammabutyrolactone (GBL) and 1,4 butanediol (1,4-BD) has increased greatly since the early 1990s, particularly amongst lesbian, gay, bisexual and transgender (LGBT) individuals in recreational and sexual settings, e.g. 'chemsex'. Objective and Method: This paper presents an overview of GHB pharmacotoxicology and provides analyses of cases in the LGBT population associated with the use of these substances extracted from the UK's National Programme on Substance Abuse Deaths database, to which notification is voluntary. Results: From 1995 to September 2013, 21

GHB/GBL-associated fatalities were reported. None involved 1,4-BD. Typical victims were: Male (100%); White (67%), young (mean age 34 years); employed (90%); with a drug misuse history (81%). Most deaths were accidental (67%) or related to recreational drug use (19%), the remaining (potential) suicides. The majority of fatalities (83%) occurred in private residences, typically following recreational use; others occurred in specific 'gay'-oriented locales including clubs and saunas. Three London boroughs accounted for 62% of all notified deaths, reflecting the concentration of both resident and visiting 'gay' individuals. However, this may be an artefact of the voluntary nature of the data submission procedure in particular areas. GHB/GBL alone was implicated in 10% of fatalities. The following substances were implicated either alone or in combination in the remaining cases (percentages may add to more than 100%): cocaine (38%); alcohol (33%); amphetamines (29%); ecstasy (29%); diazepam (24%); ketamine (24%); mephedrone (24%). Post-mortem blood levels: mean 660 (range 22-2335; S.D. 726) mg/L. Conclusion: Significant caution is needed when ingesting GHB/GBL, particularly with alcohol, benzodiazepines, stimulants, and ketamine. Risk of death is increased due to their CNS-depressant properties. Of these, 'chemsex' drugs such as cocaine, mephedrone and ketamine are of note. More awareness is needed in the 'gay' community about risks associated with the consumption of such substances.

King, L.A., Corkery, J.M. (2018). An index of fatal toxicity for new psychoactive substances. J Psychopharmacol. 32(7):793-801.
https://doi.org/10.1177/0269881118754709

ABSTRACT:
An index of fatal toxicity for new psychoactive substances has been developed based solely on information provided on death certificates. An updated index of fatal toxicity (Tf), as first described in 2010, was calculated based on the ratio of deaths to prevalence and seizures for the original five substances (amphetamine, cannabis, cocaine/crack, heroin and 3,4-methylenedioxymethylamphetamine)*. These correlated well with the 2010 index. Deaths were then examined for cases both where the substance was and was not found in association with other substances. This ratio (sole to all mentions; S/A) was then calculated for deaths in the period 1993 to 2016. This new measure of fatal toxicity, expressed by S/A, was well-correlated with the index Ln (Tf) of the original reference compounds. The calculation of S/A was then extended to a group of new psychoactive substances where insufficient prevalence or seizure data were available to directly determine a value of Tf by interpolation of a graph of Tf versus S/A. Benzodiazepine analogues had particularly low values of S/A and hence Tf. By contrast, γ-hydroxybutyrate/γ-butyrolactone, α-methyltryptamine, synthetic cannabinoid receptor agonists and benzofurans had a higher fatal toxicity.

Corkery, J.M., Schifano, F., Guirguis, A. (2019). Commentary on: Attafi IM, Albeishy MY, Oraiby ME, Khardali IA, Shaikhain GA, Fageeh MM. Postmortem Distribution of Cathinone and Cathine in Human Biological Specimens in a Case of Death Associated with Khat Chewing. Arab J Forensic Sci Forensic Med. 2018 Jun 7;1(7). Arab Journal of Forensic Sciences and Forensic Medicine, 1(10): 1473-1475.

https://doi.org/10.26735/16586794.2019.039

ABSTRACT:

The interpretation of post-mortem human tissue toxicology levels may be affected by the sampling site chosen. It is important to bear this in mind when looking at the psychoactive constituents of khat (Catha edulis Forsk) that have been consumed and have con-tributed to or caused death. The post-mortem levels of cathine, cathinone and norephedrine/ norpseudoephedrine are very rarely reported, thereby making it impossible for toxicologists, pathologists and others investigating khat-related fatalities to decide if a level is toxic or fatal. This paper presents all the published data that exists to help start documenting this neglected area. Such information should be collected and reported on a systematic basis to facilitate correct interpretations in the future.

Corkery, J.M., Streete, P., Claridge, H., Goodair, C., Papanti, D., Orsolini, L., Schifano, F., Sikka, K., Körber, S., Hendricks, A. (2019). Characteristics of deaths associated with kratom use. J Psychopharmacol. 33(9):1102-1123.

https://doi.org/10.1177/0269881119862530

ABSTRACT:

BACKGROUND: Kratom (Mitragyna speciosa Korth) use has increased in Western countries, with a rising number of associated deaths. There is growing debate about the involvement of kratom in these events. AIMS: This study details the characteristics of such fatalities and provides a 'state-of-the-art' review. METHODS: UK cases were identified from mortality registers by searching with the terms 'kratom', 'mitragynine', etc. Databases and online media were searched using these terms and 'death', 'fatal*', 'overdose', 'poisoning', etc. to identify additional cases; details were obtained from relevant officials. Case characteristics were extracted into an Excel spreadsheet, and analysed employing descriptive statistics and thematic analysis. RESULTS: Typical case characteristics (n = 156): male (80%), mean age 32.3 years, White (100%), drug abuse history (95%); reasons for use included self-medication, recreation, relaxation, bodybuilding, and avoiding positive drug tests. Mitragynine alone was identified/implicated in 23% of cases. Poly substance use was common (87%), typically controlled/recreational drugs, therapeutic drugs, and alcohol. Death cause(s) included toxic effects of kratom ± other substances; underlying health issues. CONCLUSIONS: These findings add substantially to the knowledge base on kratom-associated deaths; these need systematic, accurate recording. Kratom's safety profile remains only partially understood; toxic and fatal levels require quantification.

Corkery, J.M., Schifano, F., Martinotti, G. (2020). How deaths can help clinicians and policy-makers understand the risks of novel psychoactive substances. Br J Clin Pharmacol. 86(3):482-498.
https://doi.org/10.1111/bcp.14183
ABSTRACT:
Novel psychoactive substances (NPS), especially those newly created, are largely an unknown quantity, particularly in terms of their potential serious adverse effects. This means that policy-makers and clinicians are under-informed about appropriate responses. Collation of detailed information on deaths related to NPS use can help in providing knowledge and understanding these aspects of the NPS phenomenon. The purpose of this review is to outline the role(s) which such evidence-based data can play in this respect. UK NPS-related cases demonstrate differences in definitions used by the General Mortality Registers, and differences between countries, not only in terms of the type of NPS implicated in deaths, but the number and extent of such deaths over time. NPS deaths are continuing to increase numerically and as a proportion of all drug-poisoning deaths. In order to better understand how specific molecules contribute to and/or cause death, detailed information collected by Special Mortality Registers can provide examples of substances' modes of action, adverse effects, symptomatology, treatment interventions, mechanisms of death, etc. This information can provide clinicians and policy-makers with objective information on the serious harms from such emerging molecules. Such evidence-based advice informs public health interventions, service provision and policy decisions on regulation and control of NPS. However, without reliable, accurate and complete information that is correctly collated, scientifically analysed and disseminated in a timely manner, an understanding of the phenomenon of what deaths can be ascribed to NPS, their characteristics and nature will remain unachieved, and thus limit what can be done to reduce them.

Corkery, J.M., Hung, W.C., Claridge, H., Goodair, C., Copeland, C.S., Schifano, F. (2021). Recreational ketamine-related deaths notified to the National Programme on Substance Abuse Deaths, England, 1997-2019. J Psychopharmacol. 35(11):1324-1348.
https://doi.org/10.1177/02698811211021588
ABSTRACT:
BACKGROUND: Ketamine is a phencyclidine derivative with dissociative anaesthetic properties. Increasing numbers of individuals in England take ketamine recreationally. Information on deaths arising from such use in England is presented. METHODS: Cases were extracted on 31 January 2020 from the National Programme on Substance Abuse Deaths database, based on text searches of the cause of death, coroner's verdict and positive toxicology results for the terms 'ketamine' or 'norketamine'. FINDINGS: During 1997-2005, there were <5 deaths p.a. in which ketamine was implicated. Numbers increased until 2009 (21), plateauing until 2016; thereafter, deaths have risen to about 30 p.a. Decedents' characteristics (N = 283): male 84.1%, mean age

31.2 (SD 10.0) years, employed 56.5%, drug use history 79.6% and living with others 60.3%. Ketamine was detected with other substances in most cases. Main (74.6%) underlying cause of death was accidental poisoning. Ketamine may have impaired judgement in other cases. CONCLUSIONS: Although controlled, recreational ketamine use and related fatalities continue to increase. Consumers need to be more aware of the potentially fatal risks they face.

Corkery, J.M., Guirguis, A., Chiappini, S., Martinotti, G., Schifano, F. (2022). Alprazolam-related deaths in Scotland, 2004-2020. J Psychopharmacol. 36(9):1020-1035.
https://doi.org/10.1177/02698811221104065
ABSTRACT:
BACKGROUND: The benzodiazepine drug alprazolam, a fast-acting tranquiliser, cannot be prescribed on the National Health Service in the United Kingdom. Illicit alprazolam supply and consumption have increased. Concern about increasing numbers of alprazolam-related fatalities started circulating in 2018. However, statistics on this issue are very limited. This study examined patterns in such mortality in Scotland. METHODS: Statistics on deaths where alprazolam was mentioned in the 'cause of death' were obtained from official mortality registers. Anonymised Scottish case-level data were obtained. Data were examined in respect of the characteristics of decedents and deaths using descriptive statistics. RESULTS: Scotland registered 370 deaths in 2004-2020; 366 of these occurred in 2015-2020: most involved males (77.1%); mean age 39.0 (SD 12.6) years. The principal underlying cause of death was accidental poisoning: opiates/opioids (77.9%); sedatives/hypnotics (15.0%). Two deaths involved alprazolam alone. Main drug groups implicated: opiates/opioids (94.8%), 'other benzodiazepines' (67.2%), gabapentinoids (42.9%), stimulants (30.1%), antidepressants (15.0%). Two-thirds (64.2%) involved combinations of central nervous system (CNS) depressants. DISCUSSION: Alprazolam-related deaths are likely due to an increasing illicit supply. The fall in deaths in 2019-2020 is partially due to increased use of designer benzodiazepines. Treatment for alprazolam dependence is growing. Clinicians need to be aware of continuing recreational alprazolam use. When such consumption occurs with CNS depressants, overdose and death risks increase. CONCLUSIONS: More awareness of alprazolam contributing to deaths, especially in conjunction with other CNS depressants, is needed by consumers and clinicians. Improved monitoring of illicit supplies could identify emerging issues of medicines' abuse.

Corkery, J.M., Schifano, F. (2022). First Death Involving 4-Fluoroethylphenidate (4F-EPH): Case Report, User Experiences, and Review of the Related Literature. Acad Forensic Pathol. 12(4):149-166.
https://doi.org/10.1177/19253621221142480
ABSTRACT:
BACKGROUND: 4-Fluoroethylphenidate (4F-EPH) is a psychoactive substance, sold primarily

over the Internet as a `research chemical'. Recreational and `functional' use of this drug has been reported by online user fora. Scientifically-based data on the pharmacological, physiological, psychopharmacological, toxicological, and epidemiological characteristics of this molecule is non-existent. The aim of this paper is to remedy this situation. METHODS: Recent literature (including 'grey') was searched to update what is known about 4F-EPH, especially its toxicity. This was supplemented by netnographic examinations of internet sites. RESULTS: The resultant information is presented, including details of the first reported death involving 4F-EPH use in 2016. There are no international controls imposed on 4F-EPH. However, it has been made a controlled drug in several European countries, including the United Kingdom since 31 May 2017, as well as Canada. CONCLUSIONS: It is vital that any other cases, including non-fatal overdoses, are documented so that a firmer scientific evidence-base can be established for this molecule. This will then help inform clinical practice

Corkery, J.M., Martinotti, G., Schifano, F. (2023). Contribution of Drugs to Drowning in Scotland from 1996 to 2020. Curr Neuropharmacol. 21(11):2217-2226.
https://doi.org/10.2174/1570159x20666220830110758

ABSTRACT:

OBJECTIVE: Psychoactive substance use (including alcohol) can affect risk perception, leading to accidents and deaths. There is little detailed or up-to-date information on the role of drugs in drownings in the United Kingdom (UK). This Scottish case-study aimed to fill this knowledge gap. METHODS: Anonymised data for individual drug-poisoning-related drowning registered from 1996 to 2020 were provided by the National Records of Scotland. Statistical analyses were performed for socio-demographics, ICD coding, cause of death, and substances implicated. RESULTS: It has been reported that death registrations increased from 7 in 2017 to over 20 during 2019-20. These deaths (n=160) accounted for <1% of all drug-related poisoning deaths; this proportion rose to record levels (c.1.5%) during 2019-20. Most deaths (69%) involved males. The mean age was 39.8 (range 16-81, SD 15.0) years. The main drug classes implicated were: opiates/opioids (41%), benzodiazepines (31%), stimulants (19%), and antidepressants (14%). Moreover, 57% of benzodiazepines were 'designer' drugs. CONCLUSION: Scottish drownings associated with drug consumption are increasing rapidly. It has been observed that central nervous system depressant drugs (e.g., opioids, benzodiazepines, alcohol) are often involved in drowning. 'Designer' benzodiazepines are a principal factor in increasing Scottish drug-related poisoning deaths; they may be partially responsible for increasing numbers of related drownings. Evidence-based strategies to further reduce the number of preventable drownings should include reference to the dangers of drugs.

Poster Presentations

Corkery, J.M., Claridge, H., Goodair, C., Schifano, F., Martinotti, G. UK Kratom-related deaths. Poster presentation. School of Life & Medical Sciences Research Conference, University of Hertfordshire, 16 April 2019.

Poster abstract and poster given

Corkery, J.M. (2021). Poster "Alprazolam-related deaths in Scotland" for VIII International Conference on Novel Psychoactive Substances, online 17-19 November 2021. Poster submitted 1 November 2021.

Corkery JM, Schifano F, Martinotti G. (2021). Investigating relationships between ketamine deaths and other epidemiological indicators. Poster presentation. School of Life & Medical Sciences Research Conference, University of Hertfordshire, Hatfield, 22 June 2021.

Corkery, J.M.*, Guirguis, A., Chiappini, S., Martinotti, G., Schifano, F. (2022). Alprazolam-related deaths in Scotland, 2014-2020. Poster presentation. School of Life & Medical Sciences Research Conference, University of Hertfordshire, Hatfield, 21 June 2022.

Abstract and oral presentations given

Corkery, J.M., Claridge, H., Goodair, C. (2019). Synthetic cathinones and related fatalities in the United Kingdom. Oral presentation. Sixth International Conference on Novel Psychoactive Substances (NPS). University of Maastricht, The Netherlands, 8-9 April 2019. Abstract in Research and Advances in Psychiatry, 6(1): 16-17.
https://www.rapjournal.eu/common/php/portiere.php?ID=4bb326a39863532a7084a49d0c68ae98

Corkery J.M.* (2022). 'Croaking on Kambô': intoxications and fatalities associated with use of secretions from phyllomedusa bicolor (giant leaf frog, giant monkey frog). IX International Conference on Novel Psychoactive Substances Panama City (hybrid event), 24-26 October 2022. Delivered on 25 October.

Mosca A.*, Chiappini S., Miuli A., Mancusi G., Santovito M.C., Di Carlo F., Pettorruso M., Corkery J.M., Canessa C., Martinotti G., Di Giannantonio M. (2022). Ibogaine/Noribogaine in the treatment of Substance Use Dis-orders: a systematic review and Meta-analysis of side effects. IX International Conference on Novel Psychoactive Substances, Panama City (hybrid event), 24-26 October 2022. Delivered 24 October.

Book chapters published

Corkery, J.M. (2018). Ibogaine as a treatment for substance misuse: potential benefits and practical dangers. Pp. 217-247, in
Tanya Calvey (ed.) Progress in Brain Research: Psychedelic Neuroscienc2 (Volume 242). Academic Press. eBook ISBN: 9780128142561; Hardcover ISBN: 9780128142554
https://doi.org/10.1016/bs.pbr.2018.08.005
https://www.sciencedirect.com/science/article/pii/S0079612318300979?dgcid=raven_sd_aip_email

Corkery, J.M., Goodair, C., Claridge, H. Synthetic cathinones and related fatalities in the United Kingdom. Chapter 11 (pp. 185-210) in Ornella Corazza, Andres Roman-Urrestarazu (eds.) *Handbook of Novel Psychoactive Substances - What Clinicians Should Know about NPS.* Submitted 26 April 2018. Published 17 October 2018. London: Routledge.
ISBNs: Paperback: 9781138068308; Hardback: 9781138068292
https://www.routledge.com/Handbook-of-Novel-Psychoactive-Substances-What-Clinicians-Should-Know/Corazza-Roman-Urrestarazu/p/book/9781138068308

APPENDIX E - AUTHOR'S ADDITIONAL ACHIEVEMENTS AND ESTEEM FACTORS

Information on the inclusion of the author's publications in REF2021 is given in Appendix C. The author's ACMD activities during the period of his doctoral programme are listed in Appendix D. Academic outputs on drug-related deaths produced by the author since July 2018 are listed in Appendix E. This appendix provides details of the additional achievements made by the author during the period of his doctoral programme of research and previously in connection with his research and related activities, and associated esteem factors.

Publications during PhD programme

Since 1 July 2018, at least 10 papers dealing directly with drug deaths have been published with JC as lead author (see Appendix E) and two as co-author. In addition, the author (JC) has also contributed to 22 papers that include reference to drug-related deaths/mortality. Reference is also made in the thesis to many other relevant papers/reports with JC as lead author or as a co-author that were published between January 1994 and 30 June 2018. There are also numerous other outputs such as presentations, conducted both before and during the timeframe of the PhD programme, which are relevant to the thesis and are drawn on in the writing.

Key research database profiles

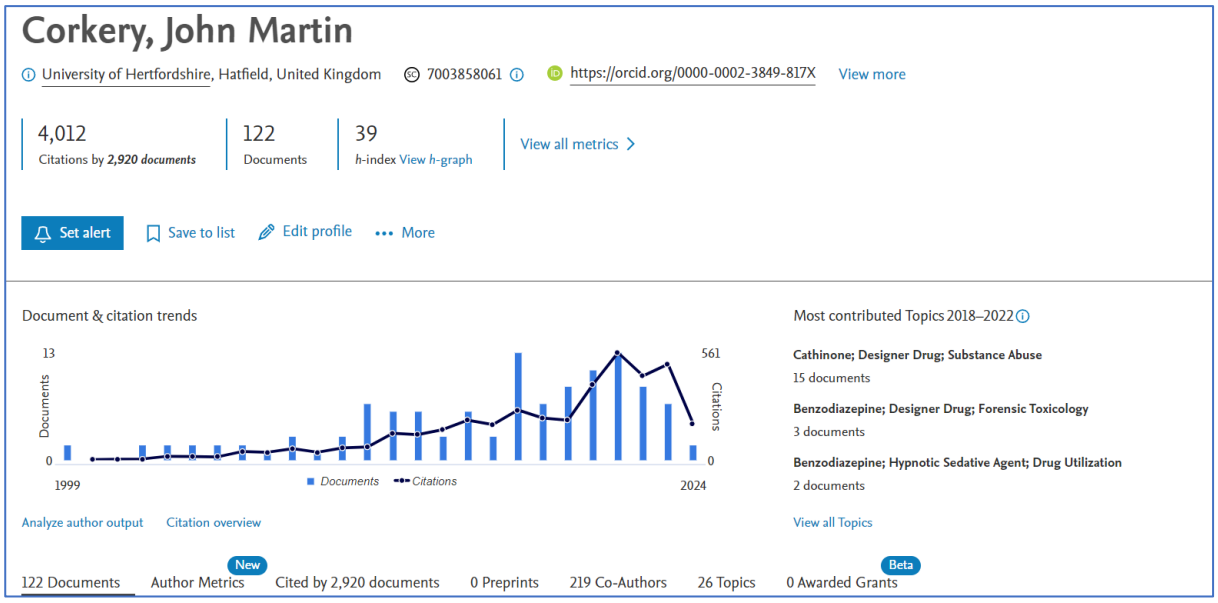
Below are the key metrics for the author provided by the major academic literature databases.

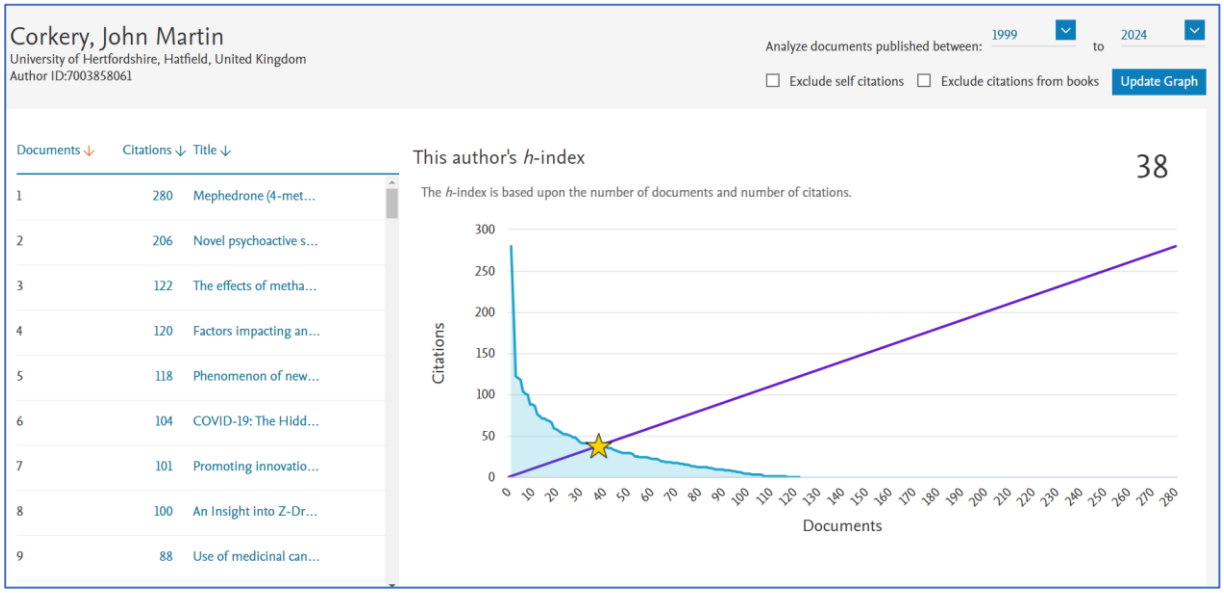
University of Hertfordshire

The author's UH research profile can be found here:
https://researchprofiles.herts.ac.uk/en/persons/john-corkery
There are 186 research outputs listed @ 29 May 2024, and 9 projects.
University of Hertfordshire Research Archive (UHRA) - https://uhra.herts.ac.uk/ 271 items listed @ 29 May 2024.

Scopus @ 29 May 2024

https://www.scopus.com/authid/detail.uri?authorId=7003858061





ResearchGate @ 29 May 2024

https://www.researchgate.net/profile/John-Corkery-2

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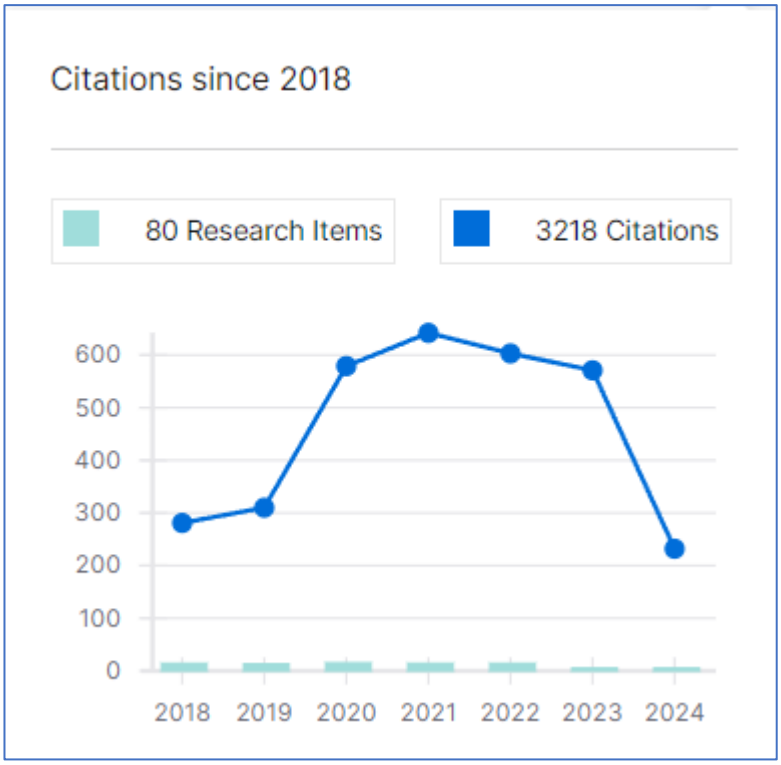
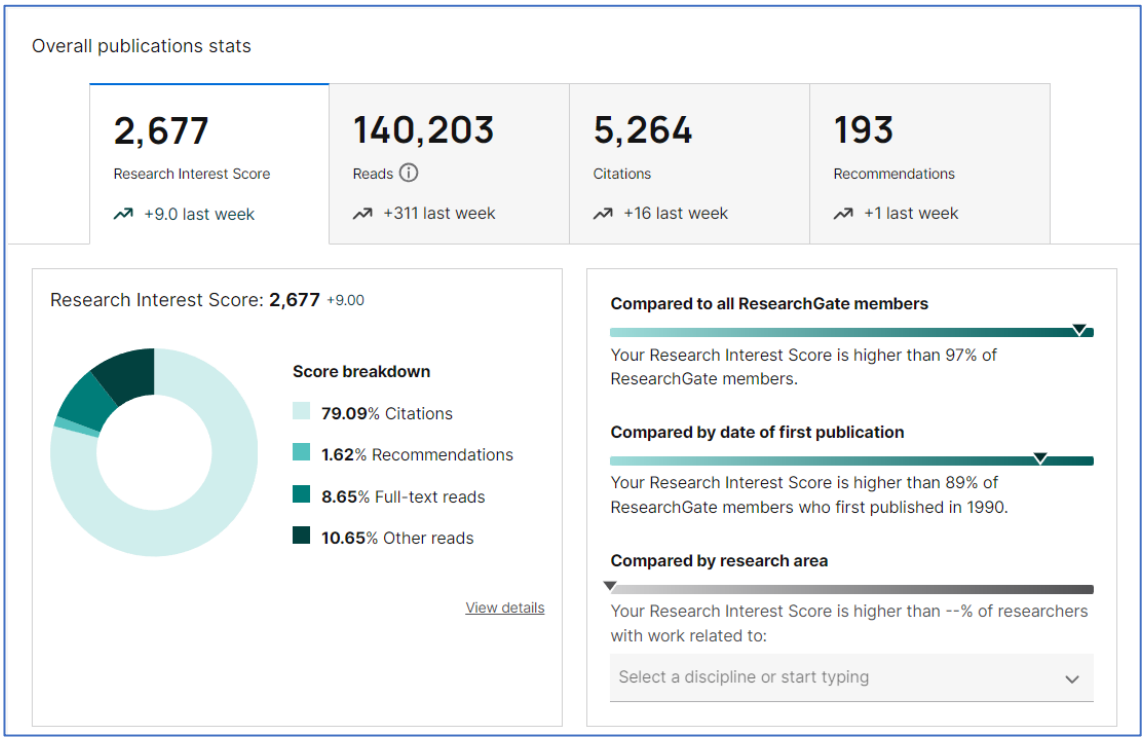
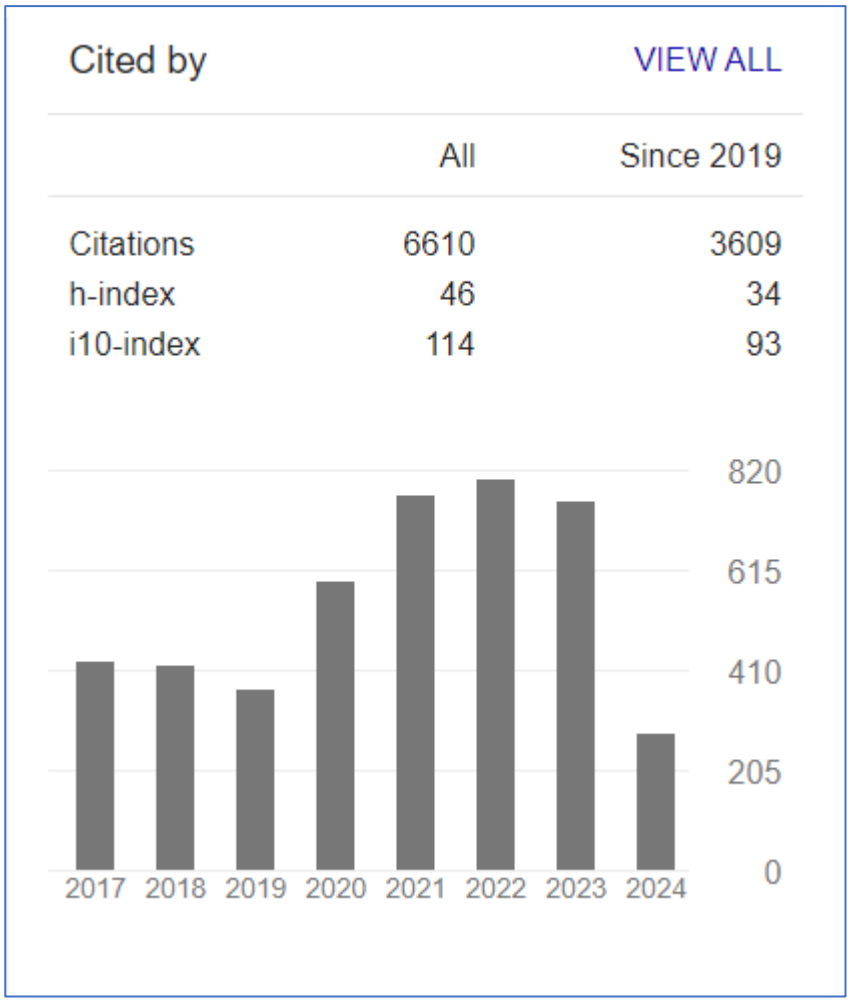




Google Scholar @ 29 May 2024

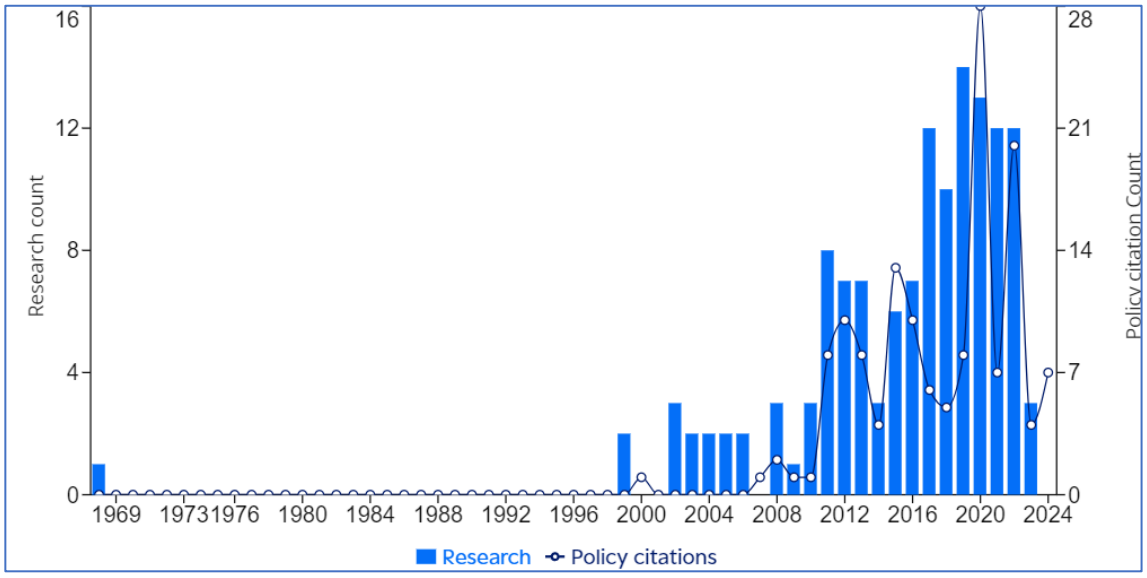
https://scholar.google.com/citations?user=iDkVEywAAAAJ&hl=en



Sage Policy Profile (https://policyprofiles.sagepub.com/dashboard) @ 29 May 2024
https://policyprofiles.sagepub.com/profile/8390/john-corkery

- 144 citations across 108 policy documents
- 59 policy documents which cite my work have been cited a further 1,181 times in 500 other policy documents
- 3 name mentions in 3 policy documents

https://policyprofiles.sagepub.com/dashboard



Editorial panel memberships

- Editorial Committee of European Collaborating Centres on Addiction Studies (ECCAS) from 2001.
- Case Reports in Toxicology
- Review Editor in Addictive Disorders, part of the journal(s) Frontiers in Psychiatry. July 2017.
- Frontiers Editorial Board.
- Appointed Associate Editor for Frontiers in Psychiatry, section Addictive Disorders18 April 2022.

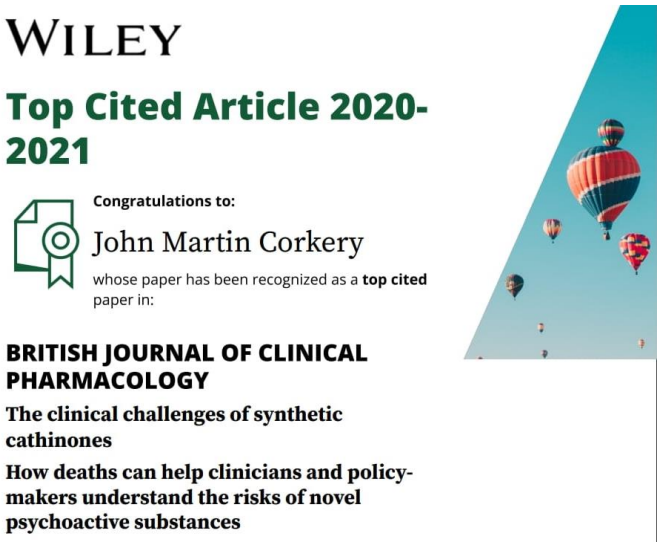
Reviewer/referee for journals

- International Journal of Drug Policy
- Arab Journal of Forensic Sciences & Forensic Medicine
- Case Reports in Toxicology
- Toxics
- Signa Vitae
- Lancet
- British Medical Journal
- BMJ Case Reports
- BMJ Open
- Addiction
- Current Pharmaceutical design
- Drug and Alcohol Dependence
- Drugs & Alcohol Today
- Drug & Alcohol Review
- BMC Psychiatry
- BMC Public Health
- PloS ONE
- Nicotine & Tobacco Research
- Toxicology Letters
- Human Psychopharmacology: Clinical & Experimental
- Addictive Disorders, part of the journal(s) Frontiers in Psychiatry
- Forensic Science International
- Journal of Public Health
- Open Journal of Pain Medicine
- Frontiers in Pharmacology
- Frontiers in Psychiatry
- British Journal of Clinical Pharmacology

- Expert Review of Clinical Pharmacology
- Journal of Psychopharmacology
- Journal of Medical Internet Research
- The American Journal of Drug and Alcohol Abuse
- Emerging Trends in Drugs, Addictions, and Health
- Psychoactives
- Drug Science, Policy and Law
- Psychiatry Research Case Reports
- Journal of Dual Diagnosis
- Regulatory Toxicology and Pharmacology
- Science Progress
- Online Journal of Public Health Infomatics

Testimonials from publishers/journals

Top-cited articles during 2020-21 in British Journal of Clinical Pharmacology:
The clinical challenges of synthetic cathinones (Schifano et al. https://doi.org/10.1111/bcp.14132)
How deaths can help clinicians and policy-makers understand the risks of novel psychoactive substances (Corkery et al. https://doi.org/10.1111/bcp.14183)



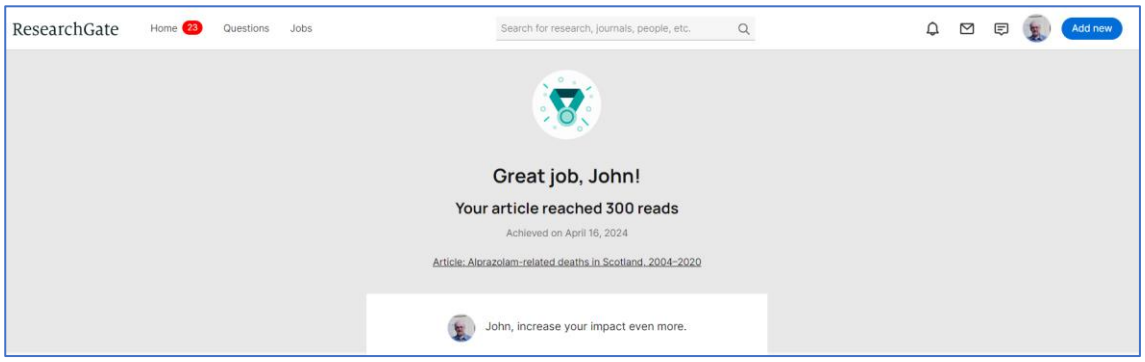
The paper "A Focus on Abuse/Misuse and Withdrawal Issues with Selective Serotonin Reuptake Inhibitors (SSRIs): Analysis of Both the European EMA and the US FAERS Pharmacovigilance Databases" led by PhD student, Dr Stefania Chiappini, with author and Principal Supervisor (FS) listed as co-authors, was short-listed for the "Pharmaceuticals 2022 Best Paper Award".

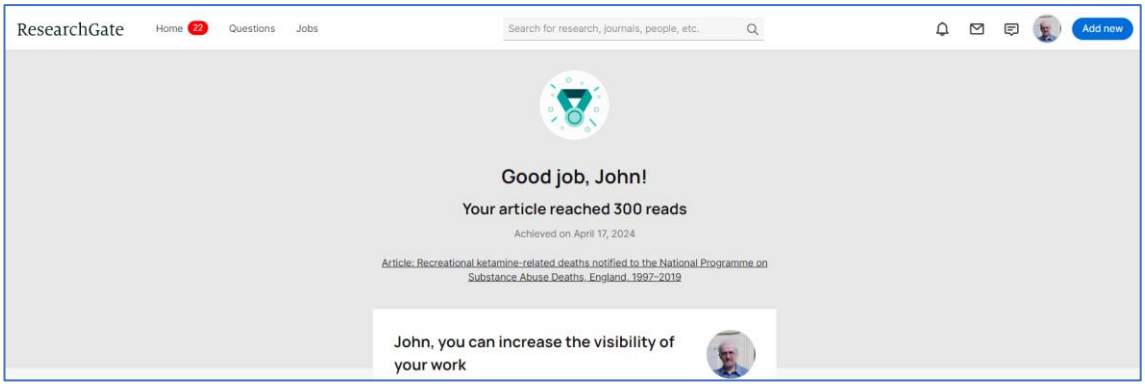
‘Mentions in dispatches’

The author is mentioned by name in an article on ketamine by Dominic Kennedy in “The Times” on 16 May 2023: ‘Freshers deluged with dealers’ offers before their first lectures’, pp. 9-10. https://www.thetimes.co.uk/article/students-targeted-by-drug-dealers-touting-potentially-deadly-drugs-5qhvdr5sg#:~:text=%E2%80%9CIn%20freshers'%20week%20you%20are,young%2C%20they%20are%20pretty%20lax. https://www.thetimes.co.uk/article/how-ketamine-became-the-uks-hidden-campus-killer-9mp3pm6ht

The author’s paper on alprazolam deaths (https://doi.org/10.1177/02698811221104065) was included in January 2023 in a paper by Dr Amira Guirguis giving advice to the Sentencing Council for England and Wales concerning a large seizure of alprazolam.

The author’s achievements in terms of his publications, citations, reads and downloads are often mentioned in internal UH newsletters. Some examples are given below, some relate to the author’s publications being the highest read by UH researchers:

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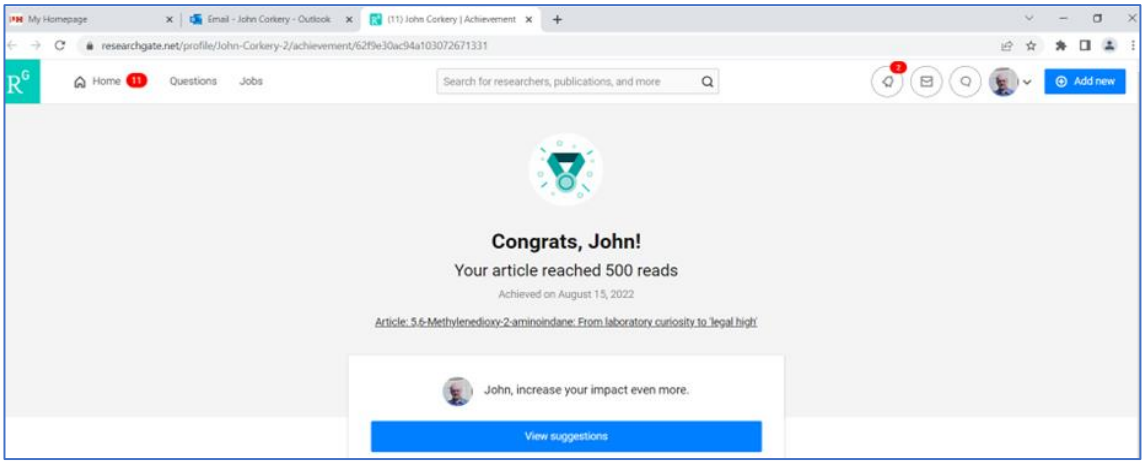
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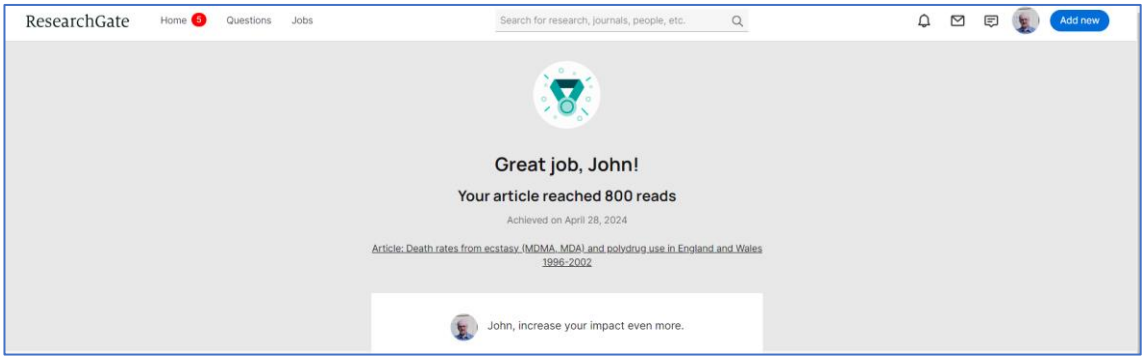
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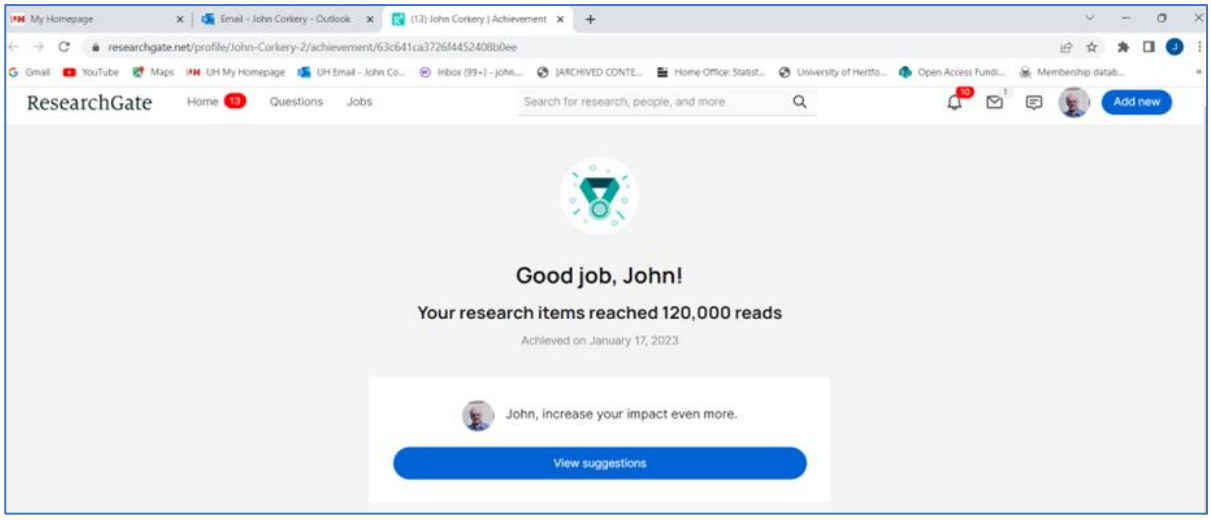
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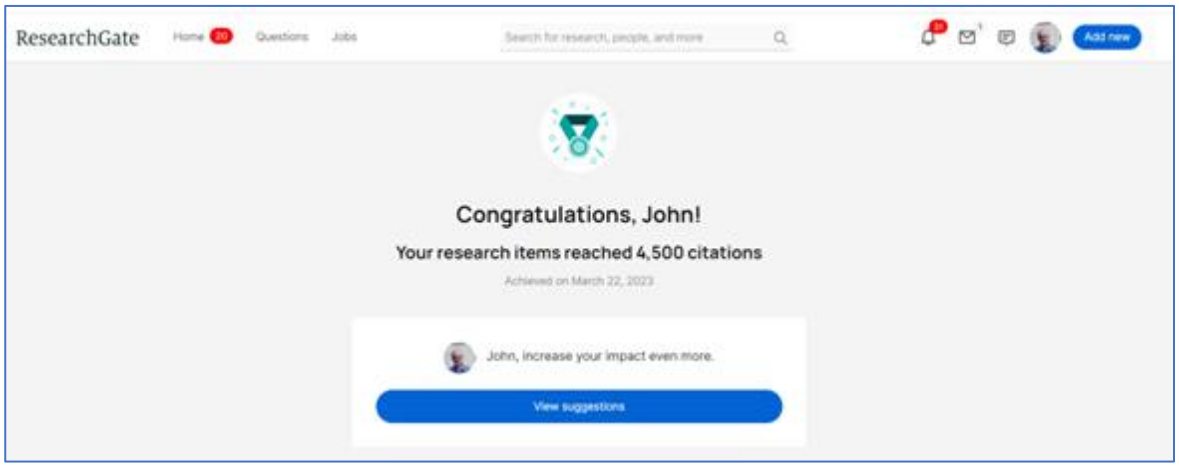
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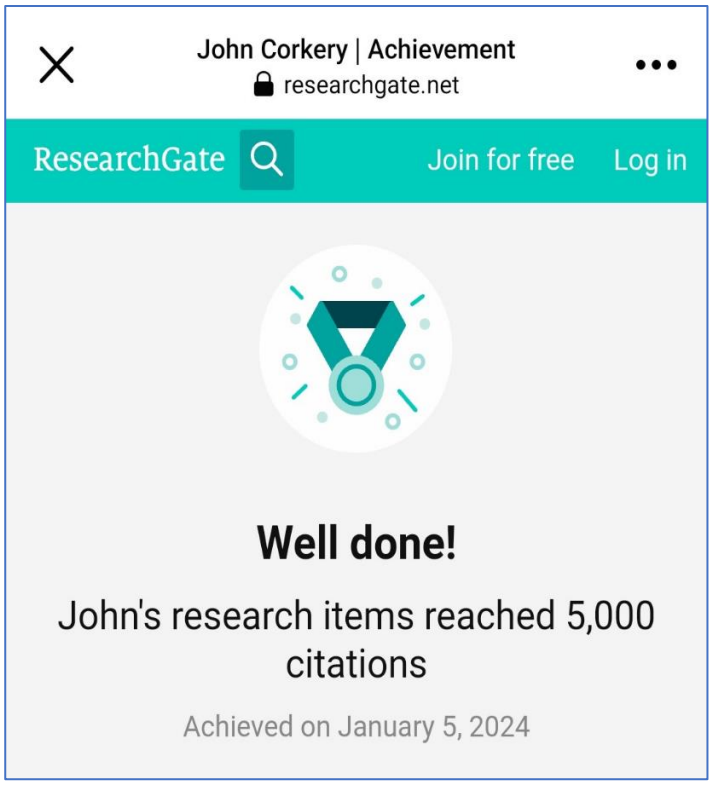
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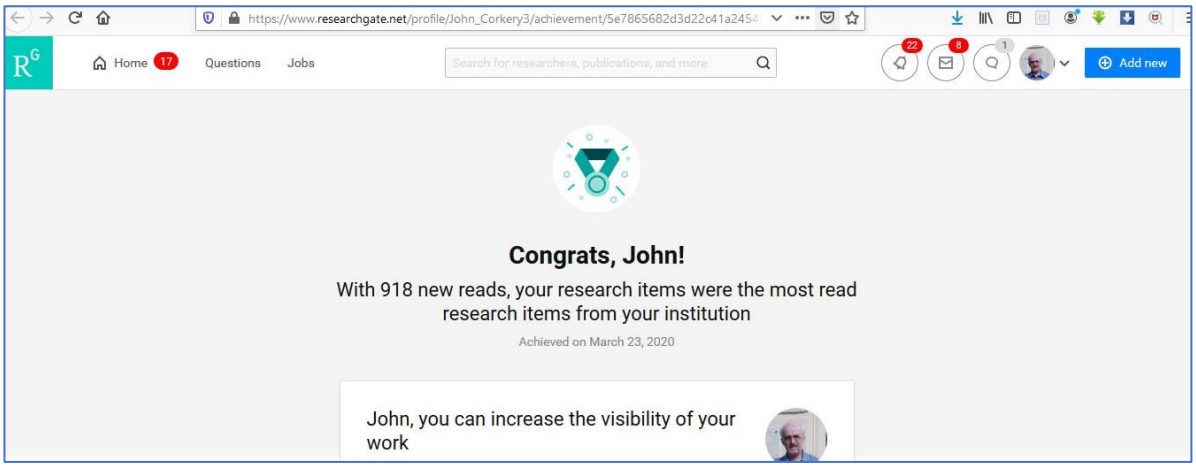
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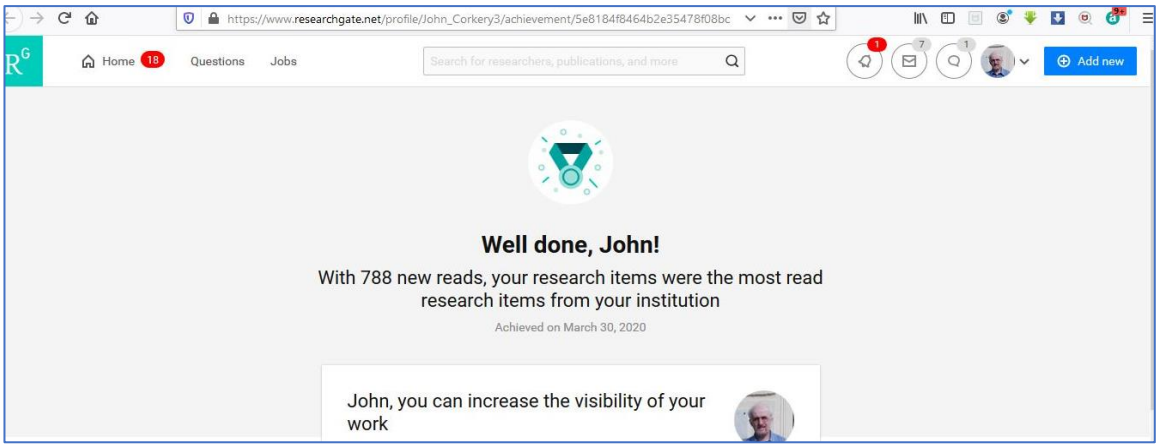
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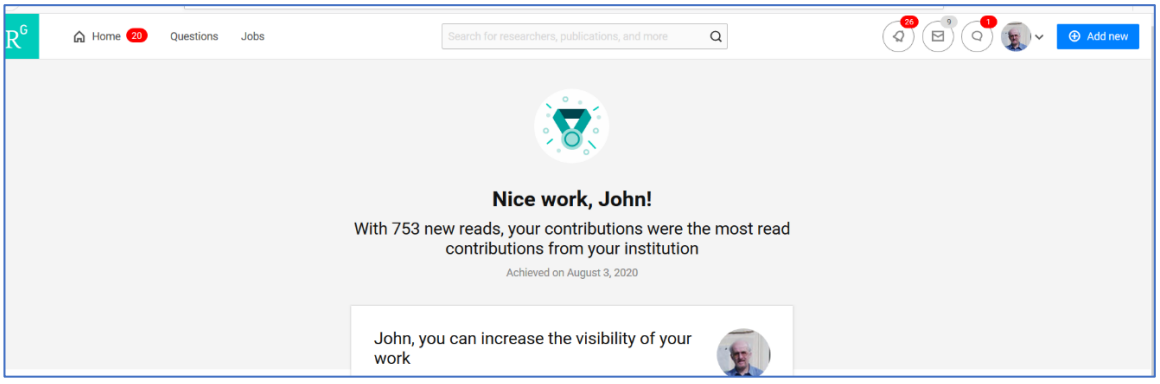
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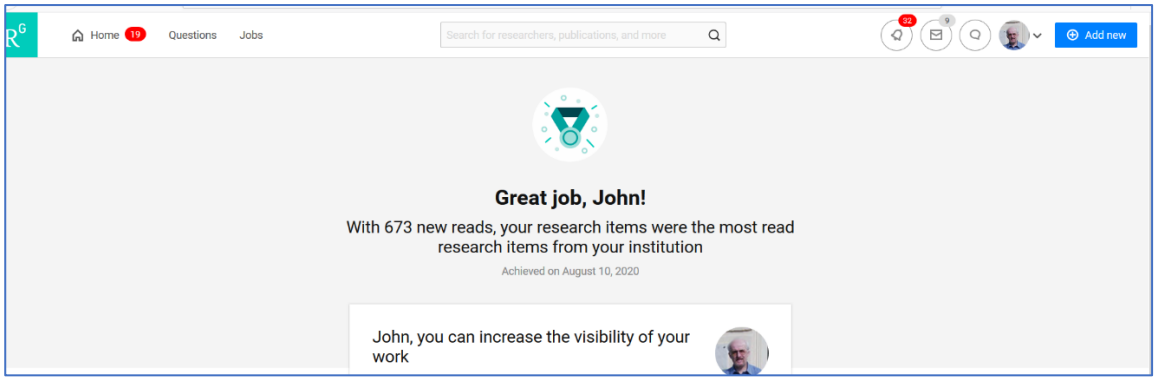

Quotes in newspaper and magazine articles

Some recent examples:

24 April 2024 – The Face
https://theface.com/society/kratom-drug-british-travellers-thailand-tom-birchy-potions-tiktok

21 May 2023 - The Times
https://www.thetimes.co.uk/article/how-ketamine-became-the-uks-hidden-campus-killer-9mp3pm6ht

UH Ethics Committee

Reviewer of ethics applications to the University of Hertfordshire Health, Science Engineering and Technology Ethics Committee with Devolved Authority from December 2018 to date

Additional Advisory Council on the Misuse of Drugs (ACMD) matters

Mentions in many ACMD reports as a contributor, member of the Technical and/or Novel Psychoactive Substances standing committees, Working Group member. This has also resulted in the author being invited to become a member of many ACMD Working Groups - see also Appendix D.

PhD student co-supervisions

Barbara Loi: “Neurochemical and Neuropharmacological Studies on a Range of Novel Psychoactive Substances”, submitted November 2017. Passed viva, with minor amendments, on 2 March 2018. http://hdl.handle.net/2299/21073

Stefania Chiappini: “Assessing the extent and characteristics of non-medical use of a range of prescribed drugs: epidemiological and pharmacovigilance approaches”, submitted March 2022. Passed viva, with minor amendments, on 15 June 2022.
http://hdl.handle.net/2299/25706

Valeria Catalani: “Assessing the pharmacological properties of Novel Psychoactive Substances (NPS) identified online: *in silico* studies on designer benzodiazepines and novel synthetic opioids”, submitted October 2022. Passed viva, no amendments, 6 December 2022.
http://hdl.handle.net/2299/27734

Additional training obtained during the PhD programme

The author successfully completed the following three online modules offered by the CFSRE (The Center for Forensic Science Research & Education) - https://www.cfsre.org/

- Introduction to Drug Caused and Related Death Investigation – 23 and 24 September 2021
- The Evaluation and Certification of Drug Caused and Related Deaths for Forensic Pathologists, Toxicologists and Death Investigators – 27 to 29 October 2021
- Specialized Forensic Toxicology, Pathology and Certification of Drug Related Death for Forensic Pathologists – 1 and 2 December 2021

APPENDIX G – AUTHOR's CONTRIBUTION TO ACMD ACTIVITIES AND RESULTANT OUTCOMES, 2018 - 2024

See Chapter 13 for full details of References.

Month and year	Type of activity	Contribution (s)	ACMD output(s)	Policy outcome(s)	Changes in control/regulation
July 2018	Technical Committee	General contributions	Advice on Scheduling of Cannabis-derived medicinal products [CBPM] (ACMD, 2018a)	On 1 November 2018, following further short-term ACMD advice on the refinement of the proposed CBPM definition and additional recommendations intended to strengthen the proposed legislative change for CBPMs (ACMD, 2018b) – CBPMs were added to Schedule 2 of the Misuse of Drugs Regulations 2001. An Order was laid before Parliament on 11 October 2018 and came into effect on 1 November 2018 (Great Britain, 2018)	Following this legislative change, in February 2019 the ACMD was formally commissioned to conduct a longer-term review of CBPMs (Home Office, 2019).
January 2020	NPS Committee	General contributions	Report on Misuse of Fentanyl and Fentanyl Analogues (ACMD, 2020a)	Recommendation: "4 A) Toxicology analysis of samples of all deaths related to drug poisoning should include analysis for fentanyl and fentanyl analogues as nonsystematic screening hinders our capacity to understand trends in drug death. B) Toxicology reports from all deaths related to drug poisoning should include a clear statement as to whether fentanyl and/or its analogues were included in the testing. Importantly, it should be made explicit if fentanyl and/or its analogues have not been tested for. This would enable meaningful monitoring of trends in fentanyl-associated deaths."	"The UK Government agreed to this recommendation in principle in the reply of October 2020. Ultimately, the recommendation is beyond the remit of Government as Coroners are independent judicial office holders who are independent in the discharge of their statutory functions. Coroners are funded by individual local authorities and make decisions in each individual case about the nature of the toxicological examination required. As a result, it is not possible for the Government to require coroners to adopt a particular approach to toxicology. However, the Government recognises that the ACMD's recent report A review of the evidence on the use and harms of 2- benzyl benzimidazole ('nitazene') and piperidine benzimidazolone ('brorphine-like') opioids contains recommendations that have a broad relevance to post-mortem toxicology." (Home Office, 2020a)
April 2020	NPS Committee	General contributions	Benzodiazepines A review of the evidence of use and harms of Novel Benzodiazepines (ACMD, 2020b)	Recommendation that flualprazolam, flunitrazolam & norfludiazepam be controlled as Class C drugs in line with other controlled benzodiazepines, and placed under Schedule 1 of the Misuse of Drugs Regulations 2001 because they have no medicinal use.	Recommendation was accepted on 8 September 2020 (Home Office, 2020b). Orders were laid before Parliament on 18 August 2021 and came into effect on 18 August 2021 (Great Britain, 2021; United Kingdom, 2021).

October 2020	NPS Committee	General contributions	Synthetic cannabinoid receptor agonists (SCRA): An updated harms assessment and a review of classification and scheduling under the Misuse of Drugs Act 1971 and its Regulations (ACMD, 2020c)	Recommendations included (1) that the current classification of all SCRA controlled by the MDA, remains appropriate, and (2) should continue to be controlled as Class B & be put in Schedule 1 of MDR as they have no recognised medicinal use. (4) Guidance on a UK-wide minimum standard set of post-mortem toxicology tests is developed for apparent drug-related deaths, to include testing for NPS. (5) Toxicology analysis of samples from deaths thought to be drug-related, where there is no obvious toxicological cause, should include prevalent SCRA, including 'fourth-generation' SCRA reported in global drug markets.	6 December 2022 - Recommendations 1 and 2 were accepted. Recommendations 4 and 5 were "beyond the remit of Government as it falls to Coroners, who as independent judicial office holders are independent in the discharge of their statutory functions. Coroners are funded by individual local authorities and make decisions in each individual case about the nature of the toxicological examination required. … However, the Government recognises that the ACMD's recent report A review of the evidence on the use and harms of 2- benzyl benzimidazole ('nitazene') and piperidine benzimidazolone ('brorphine-like') opioids contains recommendations that have a broad relevance to post-mortem toxicology." (Home Office, 2020c)
November 2020	NPS Committee	General contributions; one of author's papers was used extensively, i.e., Corkery et al. (2015). A second paper was also referenced, i.e., Corkery et al. (2018).	An assessment of the harms of gamma-hydroxybutyric acid (GHB), gamma-butyrolactone (GBL), and closely related compounds (ACMD, 2020d)	Recommendations included that these substances be moved from Class C to Class B and that GBL and 1,4-BD are placed under Schedule 1 of the Misuse of Drugs Regulations 2001. Testing for such substances should be routinely undertaken in all cases of unexplained sudden death. Where testing is not possible … then a clear statement should be included in the toxicology report stating this. Where a blood sample is positive for these substances, if possible, this should be confirmed in another sample type, e.g., urine.	Recommendations regarding legislative changes were accepted on 30 March 2021 (Home Office, 2021). An Order was laid before Parliament on 16 March 2022 and came into effect on 13 April 2022 (United Kingdom, 2022). Recommendations regarding testing for these substances were deemed to be "beyond the remit of Government as it is ultimately the responsibility of Coroners, who, as judicial office holders, are independent in the discharge of their statutory functions. Coroners are funded by individual local authorities and make decisions in each individual case about the nature of the toxicological examination required. Nevertheless, Home Office officials have raised this matter with both the Ministry of Justice and the Office of the Chief Coroner in order that it can be considered as appropriate." "The Coroners Service for Northern Ireland are content with this recommendation but would defer to the Forensic Service for Northern Ireland." Scottish Government: "The testing of GHB is relatively simple and a test which is carried out fairly frequently…. If required to test all casework for GHB, this would require a significant increase in resource is not necessarily required. With regards to stating on the report that they have not been tested for GHBRS the tox lead does not think this would be sensible or necessary." (Home Office, 2022)

July 2022	NPS committee	General contributions; contributed EU-MADNESS data on NRS information	Advice on 2-benzyl benzimidazole and piperidine benzimidazolone opioids (ACMD, 2022)	"Two separate ministerial commissions on Isotonitazene and Brorphine requested ACMD to provide advice on the appropriate classification and scheduling of these compounds under the Misuse of Drugs Act 1971 and associated Regulations. This was required to be in line with international controls of those compounds, as they were recently added to the relevant schedules of the Single Convention on Narcotic Drugs of 1961 as amended by the 1972 Protocol and the Convention on Psychotropic Substances of 1971." "Recommendation 1 The following compounds [9 'nitazenes' and brorphine] should be added to Class A of the Misuse of Drugs Act 1971, consistent with the classification of other potent opioids. As these materials have no medical use it is recommended that they should be placed in schedule 1 of the Misuse of Drugs Regulations 2001 (as amended)." "Recommendation 2 The following compounds should be deleted from Schedule 2 and added to Schedule 1 of the Misuse of Drugs Regulations 2001 (as amended): Etonitazene Clonitazene." "Recommendation 3 The ACMD recommends that a consultation should be undertaken with stakeholders, including academia and the chemical and pharmaceutical industries on the introduction of a generic control on 2-benzyl benzimidazole variants, as new examples may be encountered and could present a serious risk of harm. Following this consultation, materials covered by the generic should be added to Class A of the Misuse of Drugs Act 1971, consistent with the classification of other potent opioids. As these materials have no medical use it is recommended that they should be placed in Schedule 1 of the Misuse of Drugs Regulations 2001 (as amended). …" "Recommendation 4 In light of the continuing emergence of NPS and particularly synthetic opioid NPS, a working group should be established to consider and provide recommendations on a UK-wide minimum standard set of post-mortem toxicology tests for apparent drug-related deaths, to include testing for relevant novel psychoactive	The Government responded in February 2023 (ACMD, 2023a) Recommendation 1, with the addition of N-Desethylisotonitazene, included in the ACMD's addendum advice to the report was accepted and will be implemented when Parliamentary time allows. Recommendation 2 was similarly accepted and will be implemented when Parliamentary time allows. The Government agreed with Recommendation 3 and will seek to consult relevant interested parties, including academia and the chemical and pharmaceutical industries. The Home Office will update the ACMD on the results of this. The Government agreed with the principle of Recommendation 4. "However, given that coroners are independent judicial office holders and independent in the discharge of their statutory functions, it would not be appropriate for the government to seek to establish minimum standards for post-mortem toxicology tests. However, we would encourage coroners to consider this recommendation carefully and we will continue to raise this with relevant officials, including those in devolved governments." Recommendation 5: "The government will carefully consider funding implications in the event of new guidelines being proposed as the result of the process recommended in this report." The Government agreed with Recommendation 6; both TOXBASE and FRANK were updated with advice about the health effects of new synthetic opioids, including benzimidazole opioids. On 27 November 2023 a press release was issued that stated: "Following advice from the Advisory Council on the Misuse of Drugs (ACMD), 15 new dangerous synthetic opioids will become Class A drugs under the Misuse of Drugs Act 1971. Possession of a Class A drug carries a sentence of up to seven years imprisonment, an unlimited fine or both. If caught supplying, an offender can face

				substances to improve consistency of analysis and detection. The best practice recommendations agreed would include standards for reporting … “ “Recommendation 5 Adequate funding should be made available by government to allow coroners, procurators fiscal and forensic toxicologists to follow the best practice guidelines developed via recommendation 4.” “Recommendation 6 Information for health professionals (such as TOXBASE) and the general public (such as Frank) on the health effects of NSO should be reviewed and updated, ensuring that information is available in an appropriate format on NSO compounds including benzimidazole and piperidinyl benzimidazolone opioids and the risks that result from the inclusion of compounds of varying and sometimes very high potency in heroin preparations and counterfeit medicines.”	up to life imprisonment, an unlimited fine or both. Many of these substances are incredibly dangerous and have similar effects to heroin and fentanyl, posing a higher risk of accidental overdose. This has been a widespread problem in other countries. Although there is no current evidence to show these substances are prevalent in the UK, there have been some deaths linked to the drugs which is why the government is taking decisive action to safeguard communities. … The fifteen new synthetic opioids … [will] be added to Class A of the Misuse of Drugs Act 1971, subject to parliamentary approval …” (Home Office and ACMD, 2023) An Order was laid before Parliament on 21 February 2024 and came into effect on 20 March 2024 making them Class A drugs (United Kingdom, 2024).
March 2023	Nitrous Oxide Working Group	General contributions. Led on the section about mortality, including a detailed ”bespoke analysis” drawing on data from the VSA Mortality Project6, NPSAD and Re-Solv resources. This will be written up for publication.	Nitrous Oxide– Updated Harms Assessme nt (ACMD, 2023c)	Recommendation 5 The ACMD recommends there should be enhanced long term data collection to better understand the health and social harms of nitrous oxide. This includes additional UK monitoring of: a. Type, prevalence and severity of neurological, neuropsychiatric, and psychological harms attributable to nitrous oxide. b. Number and type of anti-social behaviour incidents associated with nitrous oxide. c. Number of road traffic accidents associated with nitrous oxide use. d. Number of deaths in the UK associated with nitrous oxide use e. Mechanism to monitor the environmental impact of littering associated with nitrous oxide use.”	The Government’s response in March 2023 was: “The ACMD came to the conclusion that nitrous oxide’s current status under the Psychoactive Substances Act 2016 was appropriate. We note this recommendation has been made on the best available scientific evidence and are grateful for the diligence in this work, despite the challenges with evidence gaps. However, given the reported recent rise in health and social harms, and the widespread use and availability of the drug particularly amongst children and young people, the Government has decided to bring forward legislation to control nitrous oxide under the Misuse of Drugs Act 1971 as a Class C drug.” (Home Office, 2023a) The Government responded on 15 June 2023 in respect of Recommendation 5 indicating they accepted it in part: “5 a. OHID monitors trends in hospital admissions for drug poisonings including those relating to solvents and inhaled anaesthetics and in those seeking help for issues with nitrous oxide from substance misuse services via the National Drug Treatment Monitoring system (NDTMS). OHID will continue to monitor trends on nitrous oxide, following its control under the 1971 Act, through the data available and, in collaboration with NHS

					England, will keep under consideration if further data collection is required in future based on future change in trends. b. The decision to control nitrous oxide under Class C of the 1971 Act means that offences involving nitrous oxide would be recorded under statistics related to prosecutions and action taken against Class C drugs. The Drug Misuse Module of the Crime Survey for England and Wales, which is annual, and the Smoking, Drinking and Drug Use among young people in England survey will provide us with specific data on nitrous oxide use. c. DfT will work with the Home Office, Police, and other agencies to consider an analytical product on the prevalence of nitrous oxide use. d. Deaths in England and Wales associated with nitrous oxide are reported in statistics published by the Office for National Statistics which is sufficient to enable monitoring of these deaths. e. Defra's latest litter composition survey data (from 2019) shows that nitrous oxide canisters are not a commonly littered item at the national level. Defra has no plans to conduct another litter survey at this time. However, Defra will consider including a category for nitrous oxide canisters in any future litter survey that may be commissioned in future. Defra will continue to monitor the available data from external sources such as environmental charities Keep Britain Tidy and the Marine Conservation Society and will share this with the Home Office for the purposes of monitoring, where appropriate." (Home Office, 2023c) An Order was laid before Parliament on 11 October 2023 and came into effect on 8 November 2023 making it a Class C drug (United Kingdom, 2023).
May 2023	4th generation SCRA (including cumyl-PeGaClone) Working Group	General contributions, especially on deaths.	Cumyl-PeGaClone and other recently encountered synthetic cannabinoid receptor agonists - A review of the evidence on their use and harms	"In light of the continuing emergence of New Psychoactive Substances (NPS) including SCRA, there is a need to improve surveillance of compounds involved in episodes of severe toxicity or deaths. The ACMD has previously recommended that a working group should be established to consider and provide recommendations on a UK-wide minimum standard set of postmortem toxicology tests for apparent drug-related deaths, to	The Government responded on 25 July 2023: "The government accepts this recommendation and will conduct a consultation with relevant stakeholders on modifications to the current generic control for SCRA as soon as possible. However, in order to meet our international obligations more quickly, and to ensure that Cumyl-PeGaClone is controlled in the interim, the government intends to bring forward legislation to control

			(ACMD, 2023c)	include testing for relevant NPS to improve consistency of analysis and detection." Options for control were outlined. "Recommendation: A consultation should be undertaken with stakeholders, including academia and the chemical and pharmaceutical industries on modifications to the current generic control for SCRA. This modification would capture currently uncontrolled SCRA that have been detected in the UK and internationally, as listed in Annex A. The proposed wording for the generic definition for addition to the MDA is provided in Annex C. This would include Cumyl-PeGaClone, which has been added to Schedule II of the Convention on Psychotropic Substances 1971. Compounds covered by the revised generic would, therefore, be classified as Class B compounds under the MDA 1971. As yet, no medical use of any of these compounds has been established, so those covered by the revised generic definition should appear in Schedule 1 of the MDR 2001 (as amended) and added to schedule 1 of the Misuse of Drugs (Designation) (England, Wales and Scotland) Order 2015, to which section 7(4) of the Misuse of Drugs Act 1971 applies." (ACMD, 2023c)	Cumyl-PeGaClone as a Class B drug under the Misuse of Drugs Act 1971 and place Cumyl-PeGaClone in Schedule 1 of the Misuse of Drugs Regulations 2001 and the Misuse of Drugs (Designation) (England, Wales and Scotland) Order 2015, subject to Parliamentary approval." (Home Office, 2023d) On 27 November 2023 a press release was issued that stated: "Five other drugs will also be controlled as part of the recent ban, including cumyl-PeGaClone, a synthetic cannabinoid receptor agonist (SCRA) which can cause complications such as seizures and liver failure." (Home Office and ACMD, 2023) An Order was laid before Parliament on 21 February 2024 and came into effect on 20 March 2024 making it a Class B drug (United Kingdom, 2024).
May 2023	Diphenidine Working Group	General contributions; Provided EU-MADNESS data and led on deaths research and writing of sections. These will be written up for publication.	A review of the evidence on the use and harms of Diphenidine and other related substances (ACMD, 2023e)	Recommendation 1: The ACMD recommend the compounds diphenidine, ephenidine and methoxyphenidine (also known as methoxphenidine) should be added to Class B of the Misuse of Drugs Act 1971, consistent with the classification of ketamine and other controlled dissociatives such as methoxetamine and PCP related materials." "Recommendation 2: As these materials have no medical use it is recommended that they should be placed in Schedule 1 of the Misuse of Drugs Regulations 2001 (as amended) and added to Schedule 1 of the Misuse of Drugs (Designation) (England, Wales and Scotland) Order 2015, to which section 7 (4) of the Misuse of Drugs Act 1971 applies. • Diphenidine • Ephenidine • Methoxyphenidine (also known as methoxphenidine)." (ACMD, 2023d)	On 10 August 2023 the Government accepted both recommendations and indicated that it intended to bring forward legislation to implement them, subject to Parliamentary approval. (Home Office, 2023e) On 27 November 2023 a press release was issued that stated: "Three stimulants which create similar effects to ketamine - diphenidine, ephenidine and methoxyphenidine - will also be controlled as Class B drugs." (Home Office and ACMD, 2023) An Order was laid before Parliament on 21 February 2024 and came into effect on 20 March 2024 making them Class B drugs (United Kingdom, 2024).
May 2023 –	Akyl Nitrites	General contributions; Led on deaths,	Alkyl nitrites ("poppers")	Recommendation 1: Remove the risk of prosecution under the PSA of those importing, selling	Government response awaited

May 2024	Working Group	including data from VSA Mortality Project, and EU-MADNESS data from NRS. Papers to be written up from analyses undertaken	– updated harms assessment and consideration of exemption from the Psychoactive Substances Act (2016). (ACMD, 2024d)	or supplying alkyl nitrites to those who wish to use them as an aid to atraumatic sexual intercourse. The ACMD recommends that alkyl nitrites should be exempted from the PSA 2016 by addition to Schedule 1 of the Act. The ACMD does not recommend that the exemption should be limited to specific alkyl nitrites as there is currently inadequate information about the efficacy and safety of individual products and such a limitation could also cause supply issues in the short to medium term. The ACMD acknowledges that the exemption would also remove the risk of prosecution under the PSA for those importing, selling or supplying alkyl nitrites for their psychoactive effects. This recommendation should not be seen as an endorsement of the use of alkyl nitrites for their psychoactive effects, or of their efficacy and safety when used to aid intercourse. Further recommendations are therefore also made with respect to other salient legislation, monitoring of unintended consequences (including health and social harms) and research. Recommendation 2: Ensuring appropriate regulation, safeguards and guidance. If Government is minded to exempt alkyl nitrites from the Psychoactive Substances Act 2016, as with all existing exemptions under the Act, Government should ensure that: a) appropriate safeguards are in place for use of alkyl nitrites, b) appropriate regulation is in place to govern the quality of alkyl nitrites products sold (purity, dose, use of childproof containers etc), c) appropriate regulation is in place to govern the import and sale of alkyl nitrites, including the amounts that can be sold. In particular, sales of alkyl nitrites to children and young people should not be permitted, focussing on those under the legal age of consent for sexual activity (16 years). The opinion of the ACMD 24 is that alkyl nitrites would be unsafe in the hands of children and young people under this age. Government should consider what alternative legislation to the PSA or MDA should be used to prevent widespread sales of alkyl nitrites to those over 16 years of age for their psychoactive effects. d) appropriate guidance is in place for safe use by consumers (e.g. provision of appropriate	

				information on methods and routes of use, interactions with medicines, potential adverse effects, risks of fire etc. Recommendation 3: Monitoring and evaluation The impact of legislative changes in the UK should be monitored to ensure that these do not result in unexpected increases in use for psychoactive effects or in other unintended adverse consequences, including health or social harms. Effects on use of other substances should also be monitored. Use of alkyl nitrites should be included in the Crime Survey for England and Wales (CSEW). Health harms can be monitored by quantifying and publishing annual episodes of severe toxicity recorded by the National Poisons Information Service (NPIS) and registered deaths before and after legislative changes involving alkyl nitrites recorded by the Office for National Statistics (ONS), National Records of Scotland (NRS) and the Northern Ireland Statistics and Research Agency (NISRA). The Royal College of Ophthalmologists (RCO) should also be consulted on the feasibility of tracking episodes of poppers-related maculopathy. Recommendation 4: Further research In the event of an exemption being enacted, research should be commissioned to better establish the safety of short and long-term exposure to specific individual alkyl nitrites, including carcinogenicity and effects on vision. This should include systematic reviews of currently available evidence, with further primary research commissioned to address those evidence gaps identified. Although unlikely to be identified as a research priority by funding bodies, it would be irresponsible for government not to ensure that the NIHR or other funding bodies commission appropriate research to ensure that legislative changes do not result in health harms that are currently unrecognised. Recommendation 4: The impact of legislative changes on health harms in the UK should be monitored to ensure that these do not result in unexpected increases in adverse health effects. This can be done by quantifying and publishing annual episodes of severe toxicity recorded by the National Poisons Information Service and	

				registered deaths before and after legislative changes involving alkyl nitrites recorded by ONS, NRS and NISRA …	
May 2023 - to date	Synthetic Cathinones Working Group	General contributions; Contributing on deaths, including EU-MADNESS data from NRS	Working title - "Synthetic cathinones – an updated harms assessment"	Home Office commission to "consider the evidence available on the harms of 3',4'-Methylenedioxy-α-pyrrolidinohexiophenone (MDPHP) and other synthetic cathinones". Home Office (2023b) [Work started March 2024]	
May 2023 - May 2024	Desalkylgidazepam (bromonordiazepam) Working Group	General contributions; Contributing on deaths, including EU-MADNESS data from NRS	Recently encountered uncontrolled novel benzodiazepines and related compounds (2024 update) (ACMD, 2024c)	Recommendation 1: The ACMD recommends that the following 15 substances are classified under Class C of the Misuse of Drugs Act 1971, consistent other classified benzodiazepines. • Gidazepam • Desalkylgidazepam • Methylclonazepam • Cloniprazepam • Difludiazepam • Thionordazepam • Clobromazolam • 4'-Chloro-deschloroalprazolam • Fluclotizolam • Deschloroclotizolam • Flubrotizolam • Fluetizolam • Bentazepam • Bretazenil, • Rilmazafone Recommendation 2: The ACMD recommends that the following should be added to Schedule 1 of the Misuse of Drugs Regulations 2001 (as amended) because they have no medicinal use in the UK. They should also be designated as controlled drugs to which section 7(4) of the 1971 Act applies. • Gidazepam • Desalkylgidazepam • Methylclonazepam • Cloniprazepam • Difludiazepam • Thionordazepam • Clobromazolam • 4'-Chloro-deschloroalprazolam • Fluclotizolam • Deschloroclotizolam • Flubrotizolam • Fluetizolam • Bentazepam • Bretazenil, • Rilmazafone	On 14 May 2024 the Government accepted both recommendations and stated that it intends to introduce legislation to implement them, subject to Parliamentary approval. (Home Office, 2024b)
May 2023 - February 2024	Xylazine Working Group	General contributions; Contributing on deaths, including EU-MADNESS data from NRS	ACMD Report – A review of the evidence on the use and harms of Xylazine, Medetomidine and Detomidine (ACMD, 2024a)	Recommendation 1: Although there is no evidence of intended use of xylazine at this time in the UK, given the acute toxicity of xylazine and the similarity to the enhanced toxicity seen when benzodiazepines are co-used with opioids, xylazine should be added to Class C of the Misuse of Drugs Act 1971. As xylazine has legitimate use as a veterinary medicine, it should be placed in Schedule 4	On 21 March 2024 the Government accepted all three recommendations and indicated that it intended to bring forward legislation to implement Recommendation 1, subject to Parliamentary approval. (Home Office, 2024a)

				Part 1 of the Misuse of Drugs Regulations 2001 (as amended). Recommendation 3: Responsible agencies need to be vigilant and monitor for substances, such as xylazine and related compounds such as detomidine and medetomidine that might be used to augment the opioid market in the UK. This can be done by analysis of seized or submitted drug samples (especially seized heroin and other opioid samples) and analysis of patient toxicology and post mortem samples. These data can then be collected, collated and monitored by the relevant public health agencies in the UK and reviewed by the newly established Synthetic Opioid Taskforce.	
June 2023-March 2024	NPS Committee	General contributions; Contributing on deaths, including EU-MADNESS data from NRS	Acyl Piperazine Opioids, Including 2-Methyl-AP-237 (ACMD, 2024b)	Recommendation 1 The following named compounds which have appeared on the international illicit drug scene, should be added to Class A of the Misuse of Drugs Act 1971, consistent with the classification of other potent opioids. As these materials have no medicinal use in the UK, it is recommended that they should be placed in Schedule 1 of the Misuse of Drugs Regulations 2001 (as amended) and Schedule 1 of the Misuse of Drugs (Designation) (England, Wales, and Scotland) Order 2015, to which Section 7(4) of the Misuse of Drugs Act 1971 applies. The control of the compounds should extend to include any stereoisomeric forms, any salts of such compounds and any preparation or product containing such compounds. (i) 2-Methyl-AP-237 (1-[2-methyl-4-[2E]-3-phenyl-2-propen-1-yl]-1-piperazinyl-1-butanone) (ii) AP-237 (1-[4-([2E]-3-phenyl-2-propen-1-yl)-1-piperazinyl]-1-butanone) (bucinnazine) (iii) para-methyl-AP-237 (1-[4-[2E]-3-(4-methylphenyl)-2-propen-1-yl]-1-piperazinyl-1-butanone) (iv) AP-238 (1-[2,6-dimethyl-4-[2E]-3-phenyl-2-propen-1-yl]-1-piperazinyl-1-propanone). Recommendation 2 Consistent with the classification of other potent opioids, the following compounds should be added to Class A of the Misuse of Drugs Act 1971 as a short-term approach, due to their potencies as μ agonists, relative	On 14 May 2024 the Government announced that it accepted Recommendations 1 and 2. They also accepted Recommendation 3 and stated they “will consult relevant stakeholders, including academia and the chemical and pharmaceutical industries on the introduction of a generic definition for acyl piperazine opioids.” Recommendations 4 and 5 were also accepted; the Government said it would consult with the Devolved Administrations in respect of the latter’s implementation of these recommendations. (Home Office4, 2024c)

				ease of synthesis and potential to become drugs of misuse. As these materials have no medicinal use in the UK, it is recommended that they should be placed in Schedule 1 of the Misuse of Drugs Regulations 2001 (as amended) and Schedule 1 of the Misuse of Drugs (Designation) (England, Wales, and Scotland) Order 2015, to which Section 7(4) of the Misuse of Drugs Act 1971 applies. (i) Azaprocin (1-[3-[(E)-3-phenyl-2-propen-1-yl]-3,8-diazabicyclo[3.2.1]octan-8-yl]propan-1-one) (ii) para-nitroazaprocin (1-[3-[(E)-3-(4-nitrophenyl)-2-propen-1-yl]-3,8-diazobicyclo[3.2.1]octan-8-yl)propan-1-one). **Recommendation 3** The ACMD recommends that a consultation should be undertaken with stakeholders, including academia and the chemical and pharmaceutical industries on the introduction of a generic control to cover 2-methyl-AP-237-related variants, as new examples may be encountered and could present a serious risk of harm. Following this consultation, materials covered by the generic should be added to Class A of the Misuse of Drugs Act 1971, consistent with the classification of other potent opioids. As these materials have no medicinal use in the UK, it is recommended that they should be placed in Schedule 1 of the Misuse of Drugs Regulations 2001 (as amended) and the Misuse of Drugs (Designation) (England, Wales, and Scotland) Order 2015, Northern Ireland 2001, to which 7(4) of the Misuse of Drugs Act 1971 applies. … Recommendation 4 Information should be provided in an appropriate format to the general public, including people vulnerable to drug related harms (such as through Frank) and to harm reduction services on the potential harms that acyl piperazines, such as 2-methy-AP-237, might cause if they become available on the illicit drug markets in the UK. This should include information on the potential health effects. Recommendation 5 In the view of the highly dynamic synthetic opioids landscape in the UK and the associated risks	

				they present, responsible agencies in the devolved administrations should monitor for the appearance of acyl piperazines and other emerging new synthetic opioids in the opioid market across the UK. Adequate resources should be provided to facilitate the analysis of seized materials or submitted drug samples thought to contain opioids, as well as the analysis of patient toxicology and postmortem samples. These data should be collected, collated, and monitored by the relevant public health agencies in the UK and reviewed in a consistent and methodical manner by the UK Government, for example the newly established Synthetic Opioid Taskforce and the Early Warning System. To encourage ongoing collection of data, information about compounds appearing in the UK should be fed back to coroners / procurators fiscal and toxicology laboratories with, where necessary, information about analytical methods and access to appropriate analytical standards.	