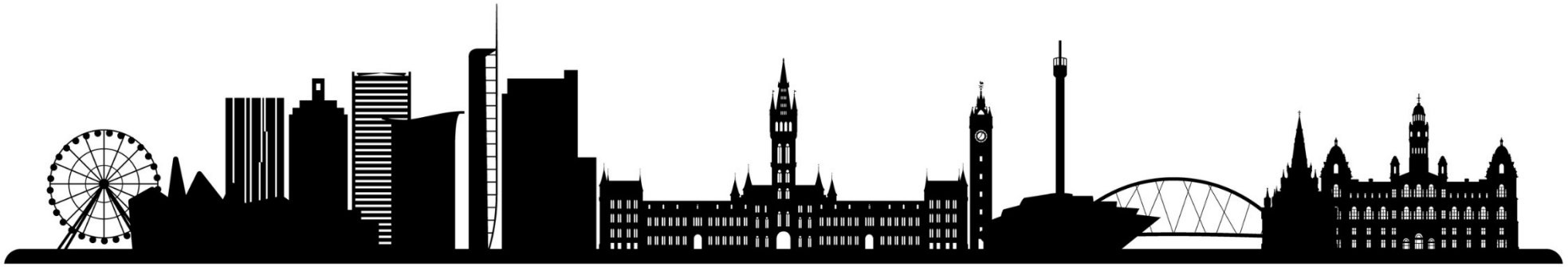
Glasgow City HSCP
Health and Social Care Partnership

Trends in Treatment – Providing MAT for people with Benzodiazepine Dependency

Trina Ritchie, Lead Clinician
NHS GGC Alcohol and Drug Recovery Services

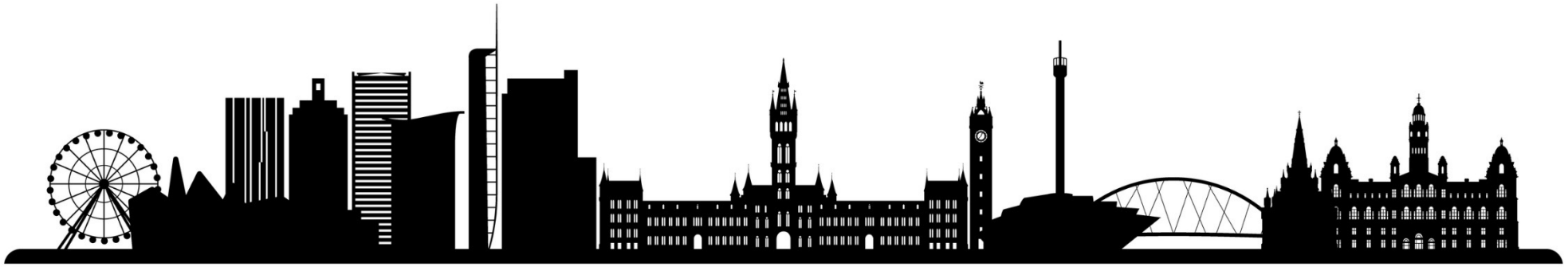


NHS Greater Glasgow and Clyde

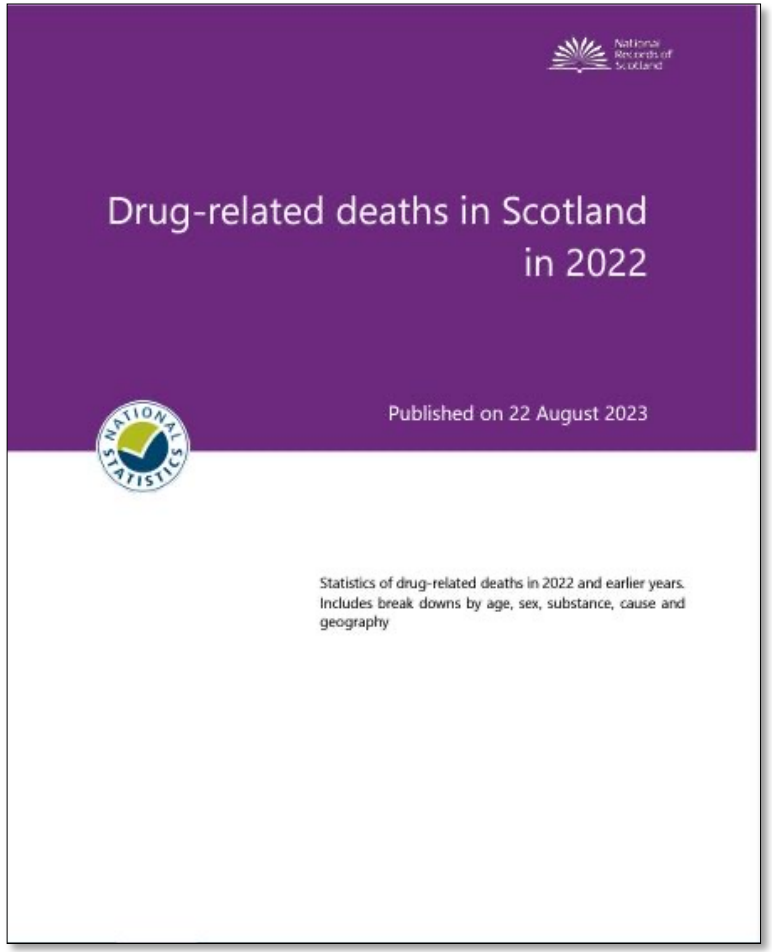
Glasgow City Council

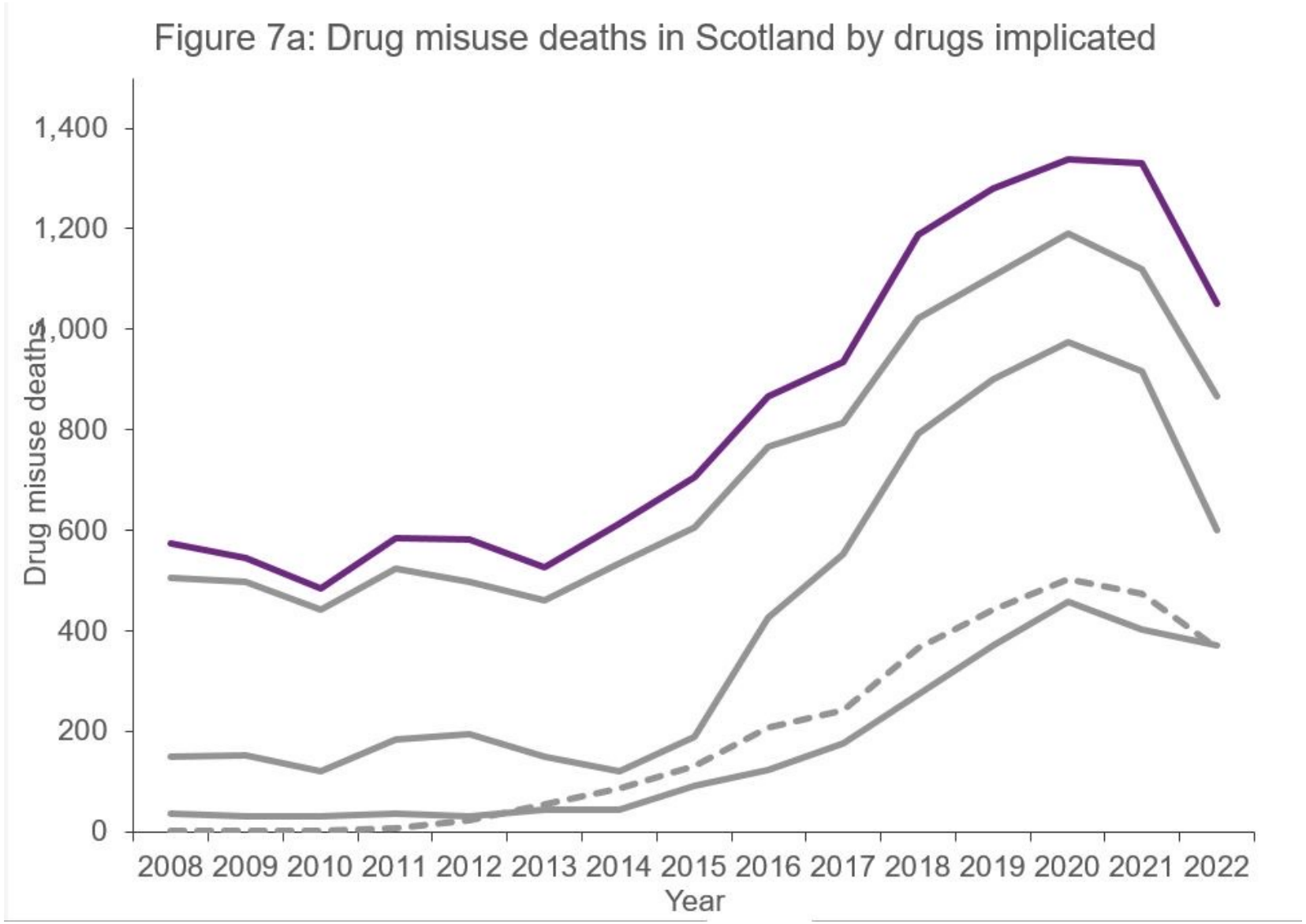
Disclosures

- Consultancy work for Camurus



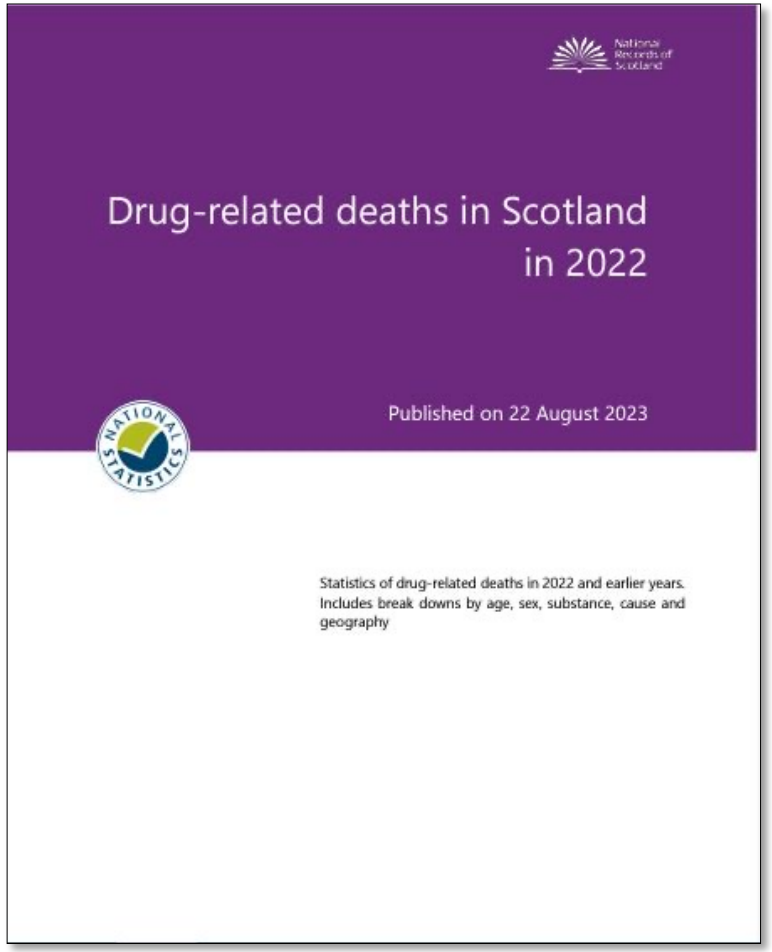
NRS Drug-related deaths in Scotland 2022

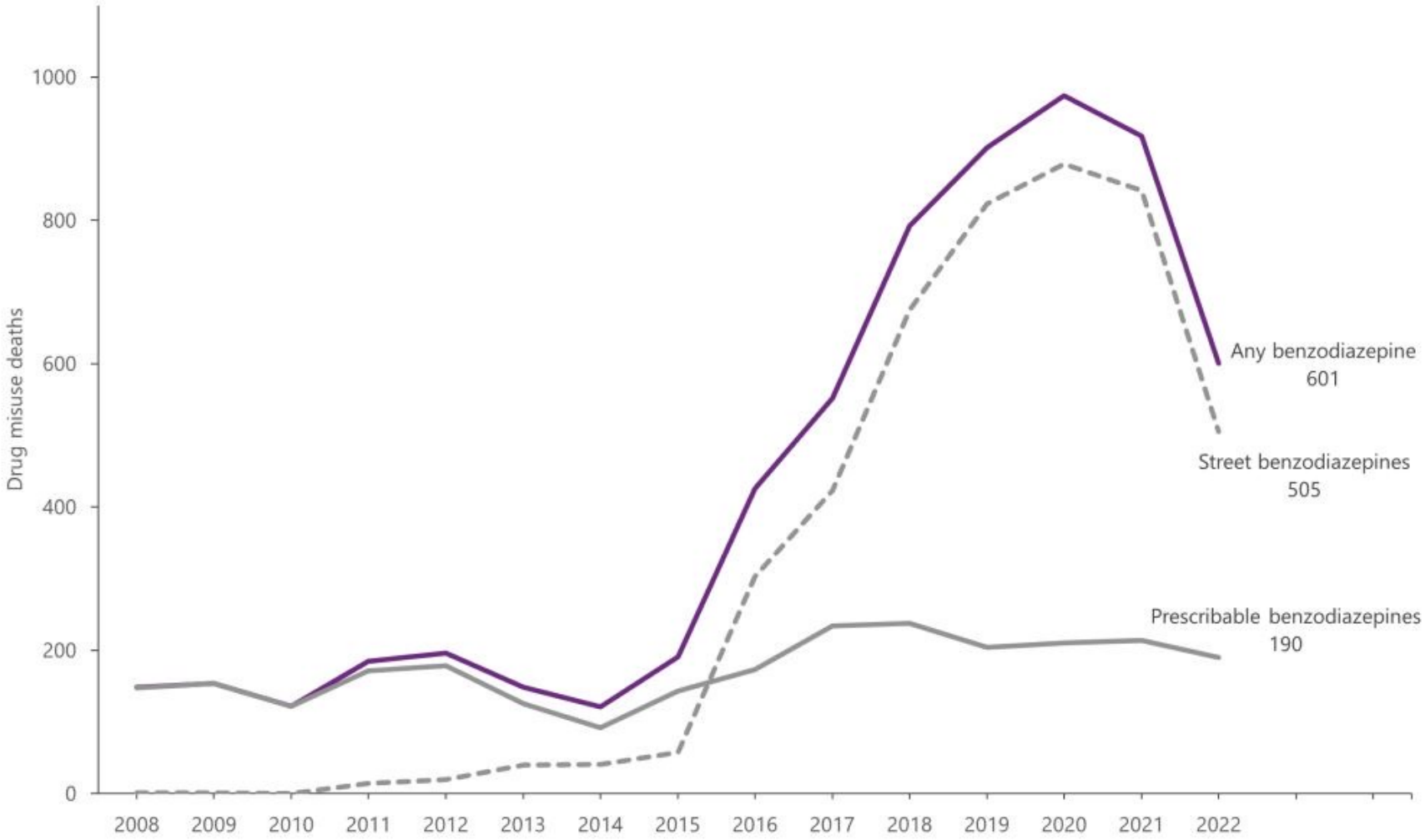




Glasgow City HSCP
Health and Social Care Partnership

NRS Drug-related deaths in Scotland 2022





2002 The Ashton Manual “benzo.org.uk”

Newcastle University

The Institute of Neuroscience

Professor Heather Ashton

CONTENTS PAGE

BENZODIAZEPINES: HOW THEY WORK AND HOW TO WITHDRAW

(aka The Ashton Manual)

- PROTOCOL FOR THE TREATMENT OF BENZODIAZEPINE WITHDRAWAL
- Medical research information from a benzodiazepine withdrawal clinic

Professor C Heather Ashton DM, FRCP
Revised August 2002

Glasgow City HSCP
Health and Social Care Partnership

2012 British Association Psychopharmacology

BAP Guidelines

Psychopharm

BAP updated guidelines: evidence-based guidelines for the pharmacological management of substance abuse, harmful use, addiction and comorbidity: recommendations from BAP

Journal of Psychopharmacology
0(0) 1–56
© The Author(s) 2012
Reprints and permissions:
sagepub.co.uk/journalsPermissions.nav
DOI: 10.1177/0269881112444321
jop.sagepub.com
SAGE

AR Lingford-Hughes[1], S Welch[2], L Peters[3] and DJ Nutt[1]
With expert reviewers (in alphabetical order): Ball D, Buntwal N, Chick J, Crome I, Daly C, Dar K, Day E, Duka T, Finch E, Law F, Marshall EJ, Munafo M, Myles J, Porter S, Raistrick D, Reed LJ, Reid A, Sell L, Sinclair J, Tyrer P, West R, Williams T, Winstock A

Abstract

The British Association for Psychopharmacology guidelines for the treatment of substance abuse, harmful use, addiction and comorbidity with psychiatric disorders primarily focus on their pharmacological management. They are based explicitly on the available evidence and presented as recommendations to aid clinical decision making for practitioners alongside a detailed review of the evidence. A consensus meeting, involving experts in the treatment of these disorders, reviewed key areas and considered the strength of the evidence and clinical implications. The guidelines were drawn up after feedback from participants. The guidelines primarily cover the pharmacological management of withdrawal, short- and long-term substitution, maintenance of abstinence and prevention of complications, where appropriate, for substance abuse or harmful use or addiction as well management in pregnancy, comorbidity with psychiatric disorders and in younger and older people.

Keywords
Substance misuse, addiction, guidelines, pharmacotherapy, comorbidity

Introduction

The first *British Association for Psychopharmacology* evidence-based guidelines for 'the pharmacological management of substance misuse, addiction and comorbidity' were published in 2004 (Lingford-Hughes et al., 2004). This is a substantial revision of that original document but using the same criteria (Table 1) and taking into account a number of recent documents from the National Institute for Health and Clinical Excellence (NICE) and other organisations which significantly enhanced the knowledge base. As before, the guidelines are not intended to provide an equivalent comprehensive review of psychosocial interventions since this is a major topic in its own right. In addition, the word 'patient' is used throughout the document for consistency, although it is acknowledged that in many treatment centres, 'client' or 'user' is the preferred term.

Scope of these guidelines

Our aim is to provide helpful and pragmatic guidelines for clinicians such as psychiatrists and GPs involved in prescribing to people with substance abuse or harmful use or addiction alone and with psychiatric comorbidity. However, the update should also be of interest to other practitioners in the substance misuse field, non-specialists, patients and their families. This revision was undertaken to update the guidelines in the light of new evidence focussing on areas not covered by guidelines published since the original BAP guidelines (e.g. from NICE). We have searched for new evidence concerning pharmacological management of alcohol, nicotine, opioids, benzodiazepines, stimulants and associated comorbidity with mental health problems and substance use or abuse in pregnancy. In addition we have covered pharmacotherapy for younger and older people, for those with personality disorder, as well as for 'club drugs' and cannabis and polydrug users. We review pharmacotherapies in common clinical use as well as those with limited but promising evidence and highlight important areas of 'key uncertainty'. We have reviewed the evidence in as brief a format as possible and refer readers to the other guidelines such as NICE, where more detail is provided. Whilst some avenues have developed, it is notable that many key uncertainties remained unchanged since 2004.

[1]Imperial College London, CNWL NHS Foundation Trust, London, UK
[2]Gaskell NHS Foundation Trust, Gloucester, UK
[3]Pennine Care NHS Foundation Trust, Ashton-under-Lyne, UK

Other invited participants at the consensus meeting who contributed to the discussion and commented on the guidelines were Drummond C, Farrell M, Gilvarry E, Strang J. John, a user representative, read and commented on the written guidelines. Prof W van den Brink reviewed the written guidelines.

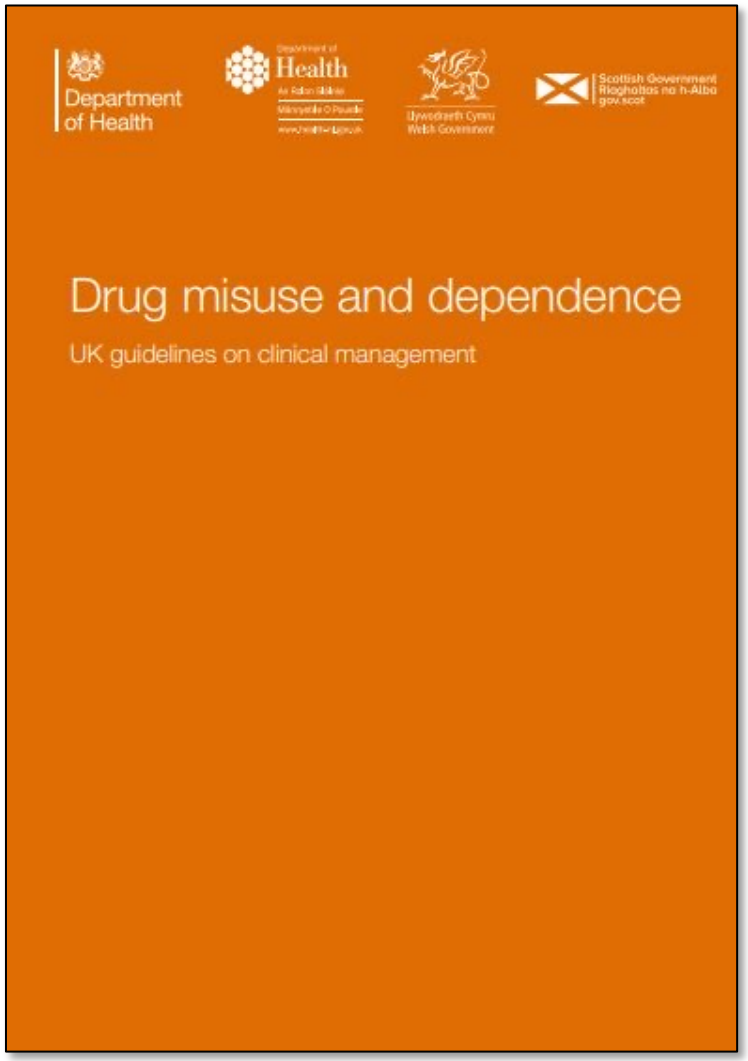
Corresponding author:
AR Lingford-Hughes, Imperial College London, Burlington Danes Building, Hammersmith Hospital site, Du Cane Rd, London W12 0NN UK
Email: anne.lingford-hughes@imperial.ac.uk

- Separates “therapeutic dose” and “high dose/street use”
- Increased mortality OST plus benzos
- Extended assessment of benzo use
- Optimise OST
- Single, long acting benzodiazepine
- Diazepam 30mg daily maximum dose
- Clear treatment plan, goals and time frame
- Agree dose reductions and timescales
- If maintenance ensure regular review
- Suggests research questions

NHS Greater Glasgow and Clyde

Glasgow CITY COUNCIL

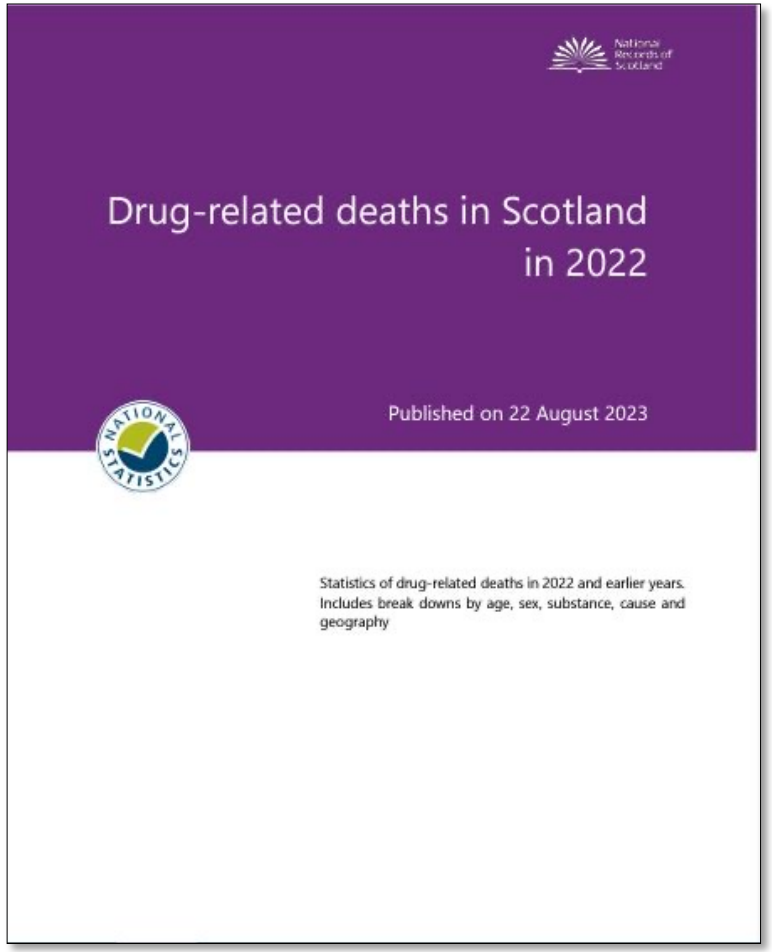
2017 UK Drug Misuse Guidelines

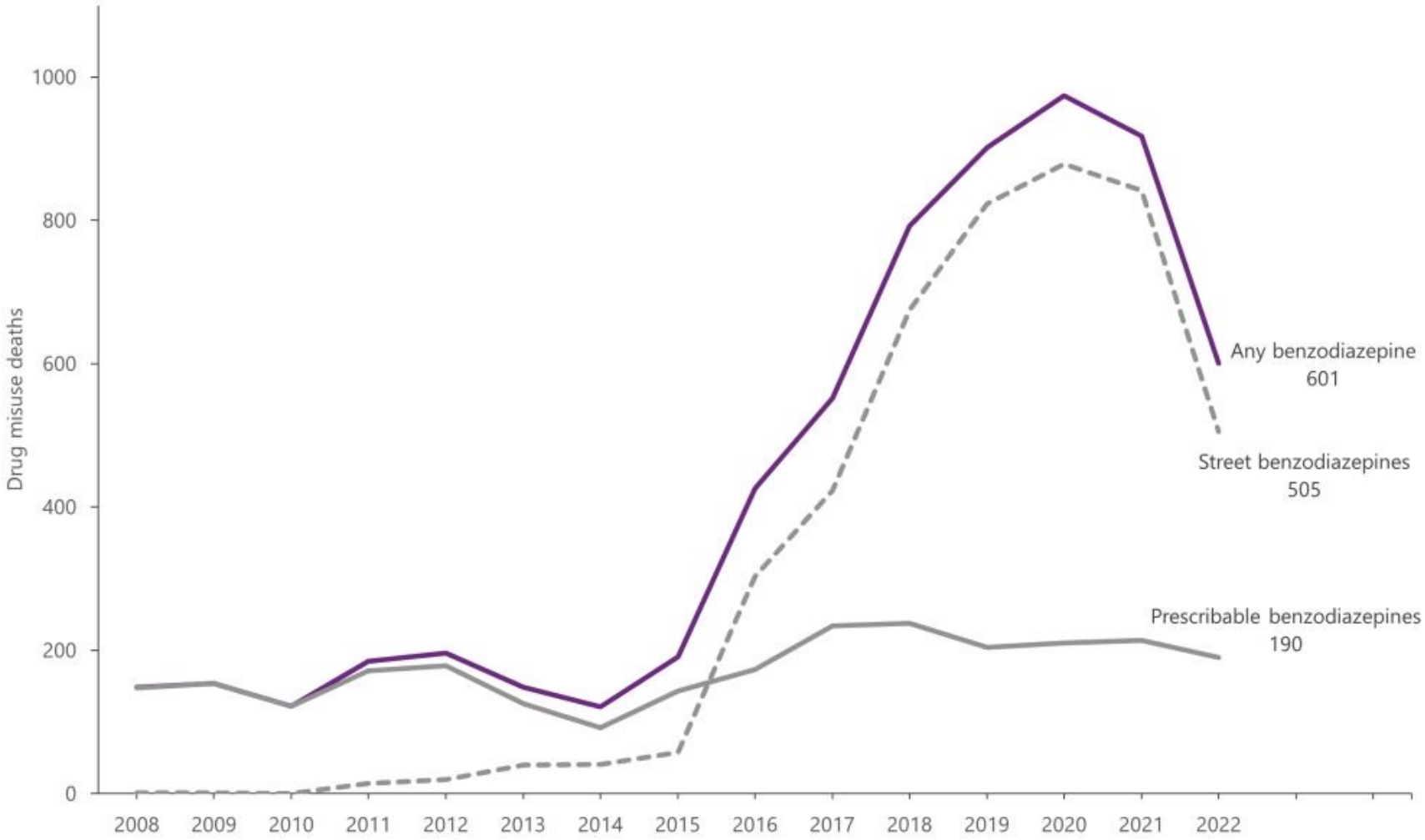


- **4.10.1 Benzodiazepines and z-drugs**
- Good assessment, care planning and adherence to local protocols
- Diazepam 30mg daily maximum dose
- OST dose should remain steady
- Most people should manage stepped detox reductions
- Consider maintenance prescribing in exceptional risk
- Ensure regular review of treatment goals and milestones

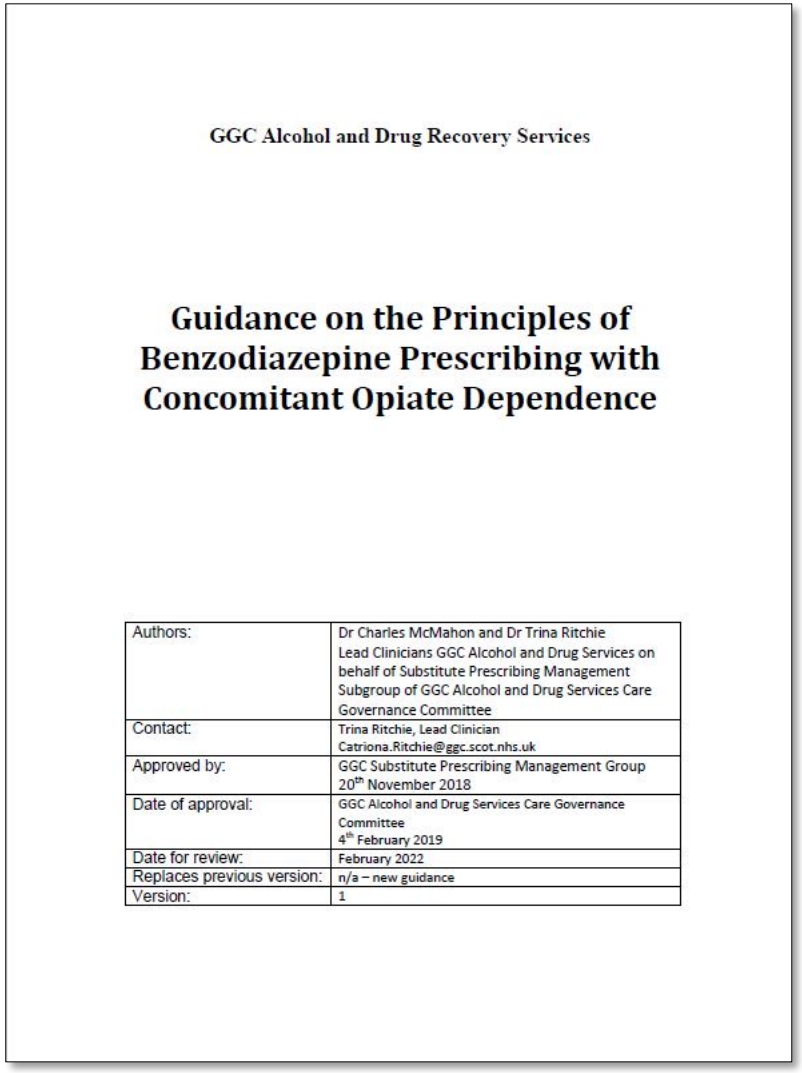
Glasgow City HSCP
Health and Social Care Partnership

NRS Drug-related deaths in Scotland 2022





2018 GGC Concomitant Prescribing



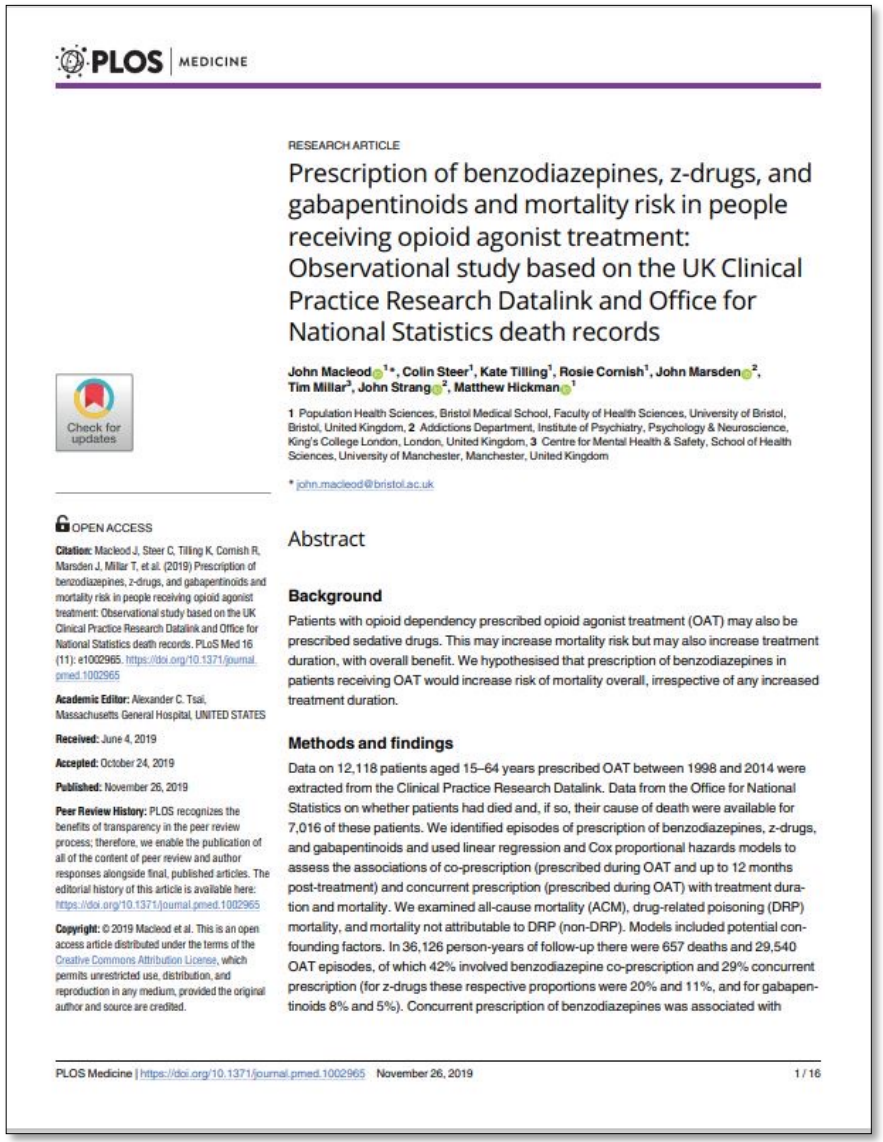
GGC Alcohol and Drug Recovery Services

Guidance on the Principles of Benzodiazepine Prescribing with Concomitant Opiate Dependence

Authors:	Dr Charles McMahon and Dr Trina Ritchie Lead Clinicians GGC Alcohol and Drug Services on behalf of Substitute Prescribing Management Subgroup of GGC Alcohol and Drug Services Care Governance Committee
Contact:	Trina Ritchie, Lead Clinician Catriona.Ritchie@ggc.scot.nhs.uk
Approved by:	GGC Substitute Prescribing Management Group 20th November 2018
Date of approval:	GGC Alcohol and Drug Services Care Governance Committee 4th February 2019
Date for review:	February 2022
Replaces previous version:	n/a – new guidance
Version:	1

1. Continuation of an existing long term prescription
2. Therapeutic agent for coexistent psychiatric conditions
3. Detox where the individual is focussed on abstinence
4. To stabilise benzodiazepine use that is causing risk or harm

2019 BMJ Prescribed benzo mortality risk paper



PLOS | MEDICINE

RESEARCH ARTICLE

Prescription of benzodiazepines, z-drugs, and gabapentinoids and mortality risk in people receiving opioid agonist treatment: Observational study based on the UK Clinical Practice Research Datalink and Office for National Statistics death records

John Macleod[1]*, Colin Steer[1], Kate Tilling[1], Rosie Cornish[1], John Marsden[2], Tim Millar[3], John Strang[2], Matthew Hickman[1]

1 Population Health Sciences, Bristol Medical School, Faculty of Health Sciences, University of Bristol, Bristol, United Kingdom, 2 Addictions Department, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, United Kingdom, 3 Centre for Mental Health & Safety, School of Health Sciences, University of Manchester, Manchester, United Kingdom

* john.macleod@bristol.ac.uk

OPEN ACCESS

Citation: Macleod J, Steer C, Tilling K, Cornish R, Marsden J, Millar T, et al. (2019) Prescription of benzodiazepines, z-drugs, and gabapentinoids and mortality risk in people receiving opioid agonist treatment: Observational study based on the UK Clinical Practice Research Datalink and Office for National Statistics death records. PLoS Med 16 (11): e1002965. https://doi.org/10.1371/journal.pmed.1002965

Academic Editor: Alexander C. Tsai, Massachusetts General Hospital, UNITED STATES

Received: June 4, 2019

Accepted: October 24, 2019

Published: November 26, 2019

Peer Review History: PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: https://doi.org/10.1371/journal.pmed.1002965

Abstract

Background

Patients with opioid dependency prescribed opioid agonist treatment (OAT) may also be prescribed sedative drugs. This may increase mortality risk but may also increase treatment duration, with overall benefit. We hypothesised that prescription of benzodiazepines in patients receiving OAT would increase risk of mortality overall, irrespective of any increased treatment duration.

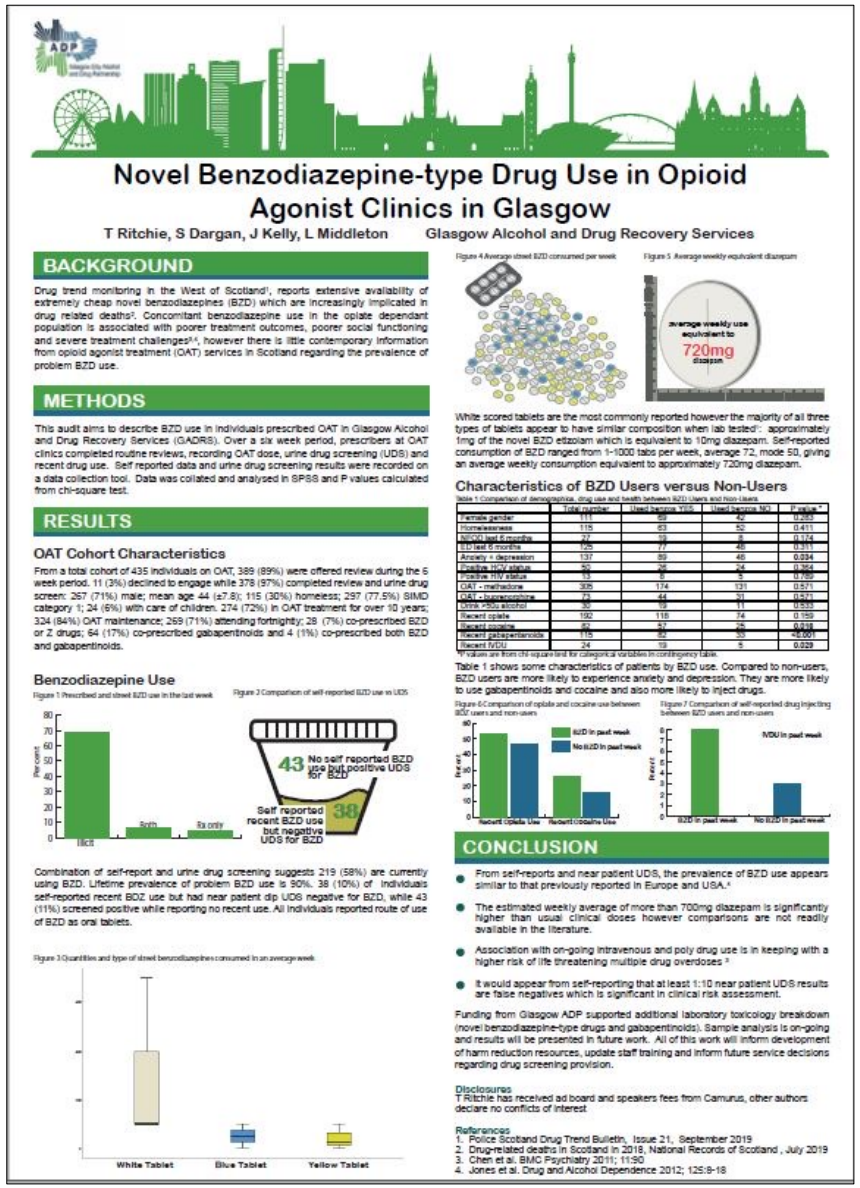
Methods and findings

Data on 12,118 patients aged 15–64 years prescribed OAT between 1998 and 2014 were extracted from the Clinical Practice Research Datalink. Data from the Office for National Statistics on whether patients had died and, if so, their cause of death were available for 7,016 of these patients. We identified episodes of prescription of benzodiazepines, z-drugs, and gabapentinoids and used linear regression and Cox proportional hazards models to assess the associations of co-prescription (prescribed during OAT and up to 12 months post-treatment) and concurrent prescription (prescribed during OAT) with treatment duration and mortality. We examined all-cause mortality (ACM), drug-related poisoning (DRP) mortality, and mortality not attributable to DRP (non-DRP). Models included potential confounding factors. In 36,126 person-years of follow-up there were 657 deaths and 29,540 OAT episodes, of which 42% involved benzodiazepine co-prescription and 29% concurrent prescription (for z-drugs these respective proportions were 20% and 11%, and for gabapentinoids 8% and 5%). Concurrent prescription of benzodiazepines was associated with

- UK data 1998 to 2014
- 12,118 patients prescribed OST
- Co-prescription benzos hazard ratio 2.96 for drug-related poisoning
- Associated with retention in OST treatment but increased risk of overall mortality

Glasgow City HSCP
Health and Social Care Partnership

2019 Glasgow Service Audit



Novel Benzodiazepine-type Drug Use in Opioid Agonist Clinics in Glasgow

T Ritchie, S Dargan, J Kelly, L Middleton Glasgow Alcohol and Drug Recovery Services

BACKGROUND

Drug trend monitoring in the West of Scotland[1], reports extensive availability of extremely cheap novel benzodiazepines (BZD) which are increasingly implicated in drug related deaths[2]. Concomitant benzodiazepine use in the opiate dependant population is associated with poorer treatment outcomes, poorer social functioning and severe treatment challenges[3,4], however there is little contemporary information from opioid agonist treatment (OAT) services in Scotland regarding the prevalence of problem BZD use.

METHODS

This audit aims to describe BZD use in individuals prescribed OAT in Glasgow Alcohol and Drug Recovery Services (GADRS). Over a six week period, prescribers at OAT clinics completed routine reviews, recording OAT dose, urine drug screening (UDS) and recent drug use. Self reported data and urine drug screening results were recorded on a data collection tool. Data was collated and analysed in SPSS and P values calculated from chi-square test.

RESULTS

OAT Cohort Characteristics

From a total cohort of 435 individuals on OAT, 389 (89%) were offered review during the 6 week period. 11 (3%) declined to engage while 378 (97%) completed review and urine drug screen: 267 (71%) male; mean age 44 (±7.8); 115 (30%) homeless; 297 (77.5%) SIMD category 1; 24 (6%) with care of children. 274 (72%) in OAT treatment for over 10 years; 324 (84%) OAT maintenance; 269 (71%) attending fortnightly; 28 (7%) co-prescribed BZD or Z drugs; 64 (17%) co-prescribed gabapentinoids and 4 (1%) co-prescribed both BZD and gabapentinoids.

Benzodiazepine Use

Figure 1 Prescribed and street BZD use in the last week

Figure 2 Comparison of self-reported BZD use vs UDS

Combination of self-report and urine drug screening suggests 219 (58%) are currently using BZD. Lifetime prevalence of problem BZD use is 90%. 38 (10%) of individuals self-reported recent BDZ use but had near patient dip UDS negative for BZD, while 43 (11%) screened positive while reporting no recent use. All individuals reported route of use of BZD as oral tablets.

Figure 3 Quantities and type of street benzodiazepines consumed in an average week

Figure 4 Average street BZD consumed per week

Figure 5 Average weekly equivalent diazepam

White scored tablets are the most commonly reported however the majority of all three types of tablets appear to have similar composition when lab tested[3]; approximately 1mg of the novel BZD etizolam which is equivalent to 10mg diazepam. Self-reported consumption of BZD ranged from 1-1000 tabs per week, average 72, mode 50, giving an average weekly consumption equivalent to approximately 720mg diazepam.

Characteristics of BZD Users versus Non-Users

Table 1 Comparison of demographics, drug use and health between BZD Users and Non-Users

	Total number	Used benzos YES	Used benzos NO	P value*
Female gender	111	69	42	0.283
Homelessness	115	63	52	0.411
NHDO last 6 months	27	19	8	0.174
ED last 6 months	125	77	48	0.311
Anxiety + depression	137	89	48	0.034
Positive HCV status	50	26	24	0.364
Positive HIV status	13	8	5	0.789
OAT - methadone	305	174	131	0.571
OAT - buprenorphine	73	44	31	0.571
Drink >50u alcohol	30	19	11	0.533
Recent opiate	192	118	74	0.159
Recent cocaine	82	57	25	0.018
Recent gabapentinoids	115	82	33	<0.001
Recent IVDU	24	19	5	0.029

*P values are from chi-square test for categorical variables in contingency table.

Table 1 shows some characteristics of patients by BZD use. Compared to non-users, BZD users are more likely to experience anxiety and depression. They are more likely to use gabapentinoids and cocaine and also more likely to inject drugs.

Figure 6 Comparison of opiate and cocaine use between BDZ users and non-users

Figure 7 Comparison of self-reported drug injecting between BZD users and non-users

CONCLUSION

- From self-reports and near patient UDS, the prevalence of BZD use appears similar to that previously reported in Europe and USA.[4]
- The estimated weekly average of more than 700mg diazepam is significantly higher than usual clinical doses however comparisons are not readily available in the literature.
- Association with on-going intravenous and poly drug use is in keeping with a higher risk of life threatening multiple drug overdoses [3]
- It would appear from self-reporting that at least 1:10 near patient UDS results are false negatives which is significant in clinical risk assessment.

Funding from Glasgow ADP supported additional laboratory toxicology breakdown (novel benzodiazepine-type drugs and gabapentinoids). Sample analysis is on-going and results will be presented in future work. All of this work will inform development of harm reduction resources, update staff training and inform future service decisions regarding drug screening provision.

Disclosures
T Ritchie has received ad board and speakers fees from Camurus, other authors declare no conflicts of interest

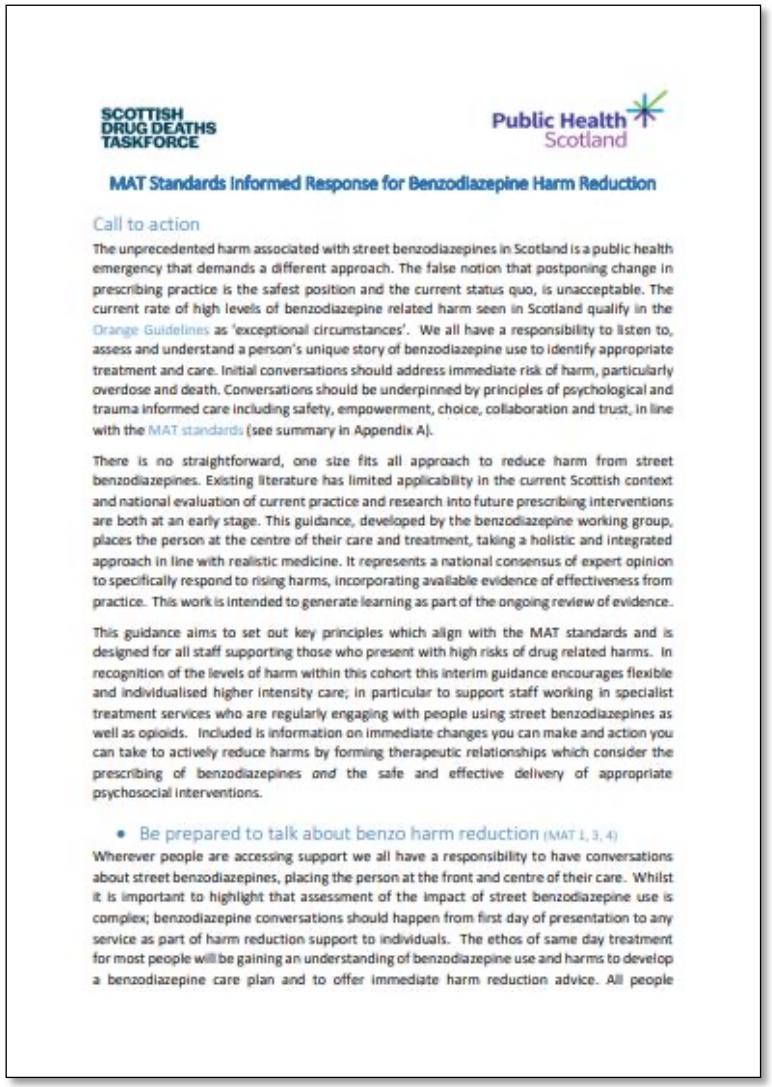
References
1. Police Scotland Drug Trend Bulletin, Issue 21, September 2019
2. Drug-related deaths in Scotland in 2018, National Records of Scotland , July 2019
3. Chen et al. BMC Psychiatry 2011; 11:90
4. Jones et al. Drug and Alcohol Dependence 2012; 125:8-18

- 378 people in OST treatment
- 7% also co-prescribed benzos
- Life time street benzo use 90%
- Current street benzo use 58%
- Range 1- 1000 tabs per week, av 72 tabs
- Associated with recent IVDU

NHS Greater Glasgow and Clyde

Glasgow CITY COUNCIL

2020 MAT Standards Interim Benzo Response



SCOTTISH DRUG DEATHS TASKFORCE

Public Health Scotland

MAT Standards Informed Response for Benzodiazepine Harm Reduction

Call to action

The unprecedented harm associated with street benzodiazepines in Scotland is a public health emergency that demands a different approach. The false notion that postponing change in prescribing practice is the safest position and the current status quo, is unacceptable. The current rate of high levels of benzodiazepine related harm seen in Scotland qualify in the Orange Guidelines as 'exceptional circumstances'. We all have a responsibility to listen to, assess and understand a person's unique story of benzodiazepine use to identify appropriate treatment and care. Initial conversations should address immediate risk of harm, particularly overdose and death. Conversations should be underpinned by principles of psychological and trauma informed care including safety, empowerment, choice, collaboration and trust, in line with the MAT standards (see summary in Appendix A).

There is no straightforward, one size fits all approach to reduce harm from street benzodiazepines. Existing literature has limited applicability in the current Scottish context and national evaluation of current practice and research into future prescribing interventions are both at an early stage. This guidance, developed by the benzodiazepine working group, places the person at the centre of their care and treatment, taking a holistic and integrated approach in line with realistic medicine. It represents a national consensus of expert opinion to specifically respond to rising harms, incorporating available evidence of effectiveness from practice. This work is intended to generate learning as part of the ongoing review of evidence.

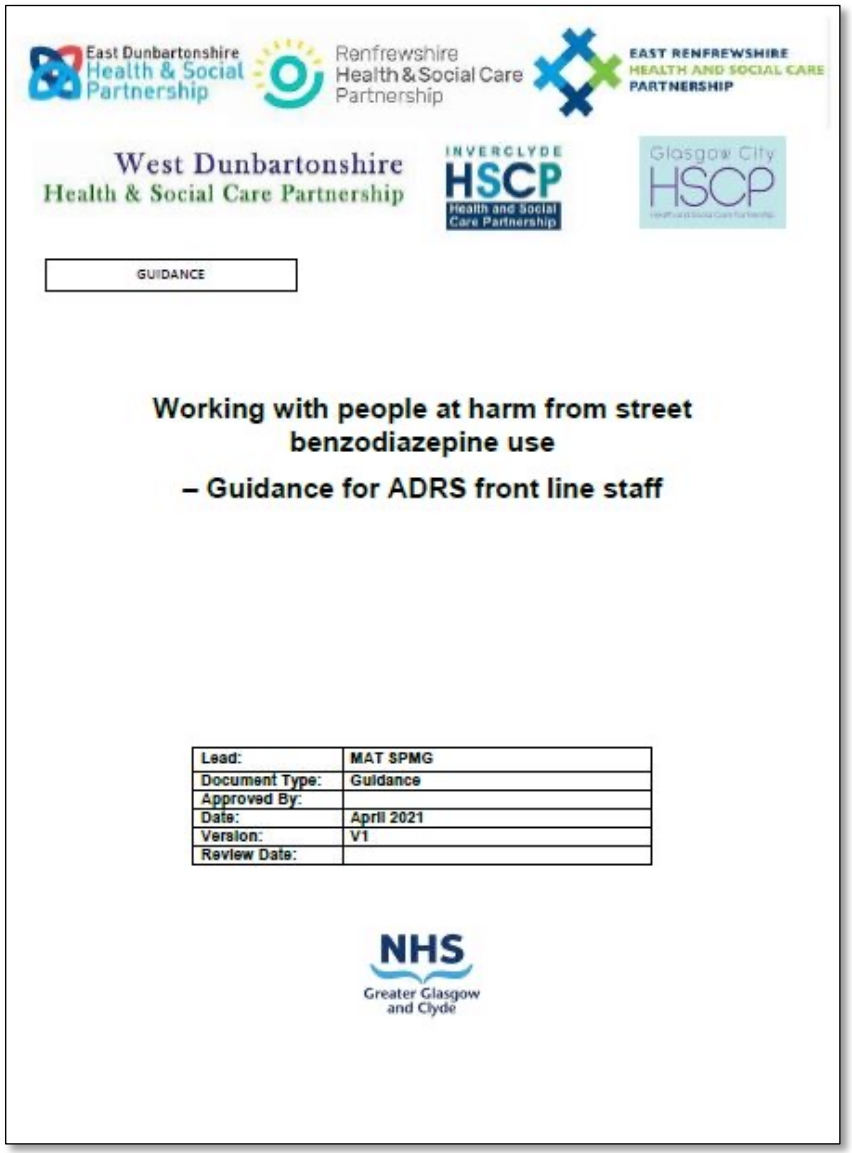
This guidance aims to set out key principles which align with the MAT standards and is designed for all staff supporting those who present with high risks of drug related harms. In recognition of the levels of harm within this cohort this interim guidance encourages flexible and individualised higher intensity care; in particular to support staff working in specialist treatment services who are regularly engaging with people using street benzodiazepines as well as opioids. Included is information on immediate changes you can make and action you can take to actively reduce harms by forming therapeutic relationships which consider the prescribing of benzodiazepines *and* the safe and effective delivery of appropriate psychosocial interventions.

- Be prepared to talk about benzo harm reduction (MAT 1, 3, 4)

Wherever people are accessing support we all have a responsibility to have conversations about street benzodiazepines, placing the person at the front and centre of their care. Whilst it is important to highlight that assessment of the impact of street benzodiazepine use is complex; benzodiazepine conversations should happen from first day of presentation to any service as part of harm reduction support to individuals. The ethos of same day treatment for most people will be gaining an understanding of benzodiazepine use and harms to develop a benzodiazepine care plan and to offer immediate harm reduction advice. All people

- **B**e prepared to talk about benzo related harm
- **E**mpathic listening – seek to understand
- **N**eeds Based Assessment
- **Z**one of Tolerance – collaborative risk taking
- **O**ffer benzodiazepine harm reduction
- **S**afe as possible – regular review

2021 GGC ADRS Guidance for Staff



East Dunbartonshire Health & Social Partnership
Renfrewshire Health & Social Care Partnership
EAST RENFREWSHIRE HEALTH AND SOCIAL CARE PARTNERSHIP
West Dunbartonshire Health & Social Care Partnership
INVERCLYDE HSCP Health and Social Care Partnership
Glasgow City HSCP

GUIDANCE

Working with people at harm from street benzodiazepine use

– Guidance for ADRS front line staff

Lead:	MAT SPMG
Document Type:	Guidance
Approved By:	
Date:	April 2021
Version:	V1
Review Date:	

NHS Greater Glasgow and Clyde

- Establish a picture of harms
- Agree a benzo care plan
- Deliver core skills interventions
- Self managed step down
- Importance of psychosocial interventions – not a prescription alone

NHS Greater Glasgow and Clyde

Glasgow City Council

Glasgow City HSCP
Health and Social Care Partnership

BENZOS

INFORMATION GUIDE ON USE, EFFECTS, SAFETY AND HELP

V1.0 11/20

Information Sheet
Etizolam

Version: 1.0
Original version: 17/06/2014

SDF Scottish Drugs Forum
DrugWatch

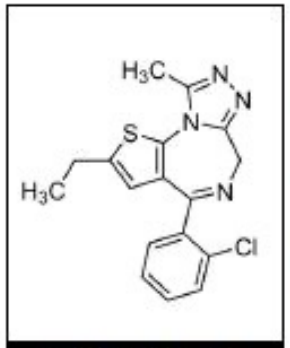


Image: Wikimedia commons

Drug overview: Etizolam is a benzodiazepine analogue, a thienodiazepene[1]. It has gathered some popularity on the new psychoactive substance (NPS) market in the UK and Europe.

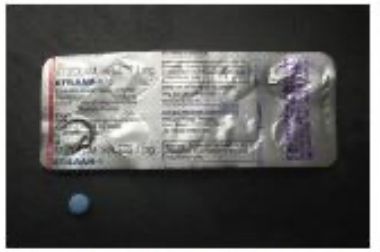
Chemical name(s): 4-(2-chlorophenyl)-2-ethyl-9-methyl-6H-thieno[3,2- f][1,2,4]triazolo[4,3-a][1,4]diazepine[2]

Brand Names[3]: Etilasm, Etizest, Etizola, Sedekopan, Depas, Pasaden.

Classification: Depressant.

Background: Etizolam is unlicensed in the UK although used as a prescribed medication in other countries such as India[4], Italy[5] and Japan[6]. A 1mg tablet is equivalent to a 10mg diazepam (Valium) tablet[7].

Appearance[8]: Etizolam typically comes in 1mg and 2mg tablets which are often described as 'pellets'. Its appearance can vary depending on the source of purchase. A popular brand name Etilasm sold online is found in a foil strip packet with 1mg dark blue 'sugar pill'-sized coated tablets. There are other tablets in circulation which are lighter blue (similar to blue diazepam colour) and can display the markings EZ. The 2mg are often small dark pink coated tablets. Tablets from other vendors may simply come loose in a zip-seal plastic bag.

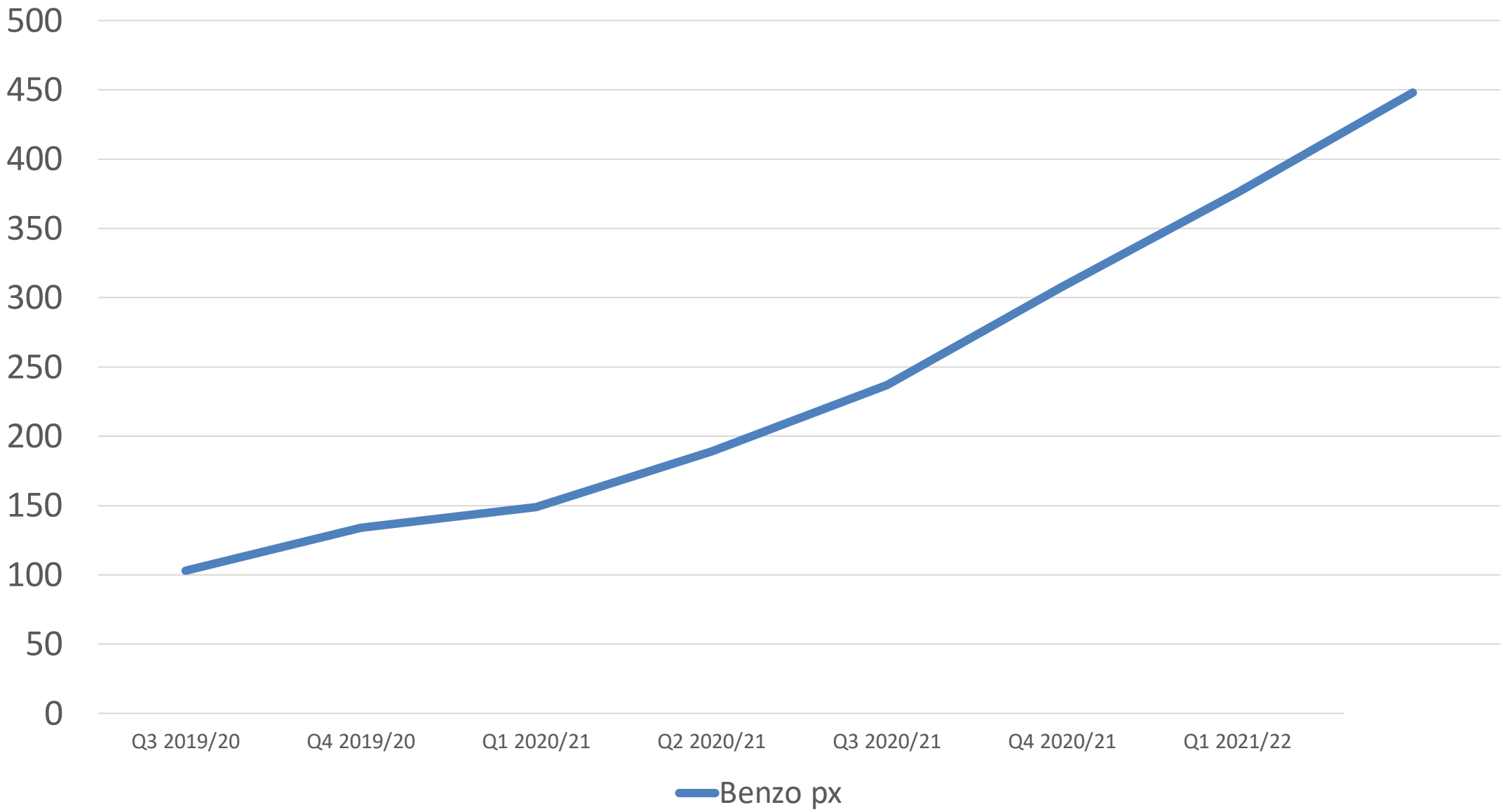


It is also possible to purchase in powder form, which is often white. Anecdotal reports suggest that it is rare for users to purchase the powder form in the UK.

Cost: Etizolam varies in cost, depending on the form and quantity purchased. They can range from £1 for single tablets (or in quantities less than 10), to as low as 5p per tablet at larger quantities. 100 tablets typically cost around £40. The powder form ranges from approximately £10 for 50mg, to £950 for 20 grams.

Glasgow City HSCP
Health and Social Care Partnership

2019 to 2021 trend in co benzo prescribing in GADRS



Glasgow City HSCP
Health and Social Care Partnership

2022 Current Trends Evidence Review

- Wide ranging reasons for using benzos
- Etizolam prescribed safely in Italy, Japan, India
- Harms from illicit manufacture, availability, affordability
- National variation in prescribable benzodiazepine harms
  - 2% DRD in GGC; 42% Lothian and 40% Grampian
- 2.1 million benzo tablets seized in 2018/19
- 5.3 million benzo tablets seized in 2019/20 (94% etizolam)

NHS Greater Glasgow and Clyde

Glasgow City Council

2023 Large Scottish population based cohort study

Open access Original research

BMJ Open

Association between benzodiazepine coprescription and mortality in people on opioid replacement therapy: a population-based cohort study

Catherine Susan Best ,[1] Catriona Matheson,[2] James Robertson,[3,4] Trina Ritchie ,[5] Fiona Cowden,[6] Josh Dumbrell,[2] Clare Duncan,[7] Karthigayan Kessavalou,[7] Caroline Woolston,[7] Joe Schofield [8]

To cite: Best CS, Matheson C, Robertson J, *et al*. Association between benzodiazepine coprescription and mortality in people on opioid replacement therapy: a population-based cohort study. *BMJ Open* 2024;**14**:e074668. doi:10.1136/bmjopen-2023-074668

► Prepublication history for this paper is available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2023-074668).

Received 14 April 2023
Accepted 09 February 2024

For numbered affiliations see end of article.

Correspondence to
Catherine Susan Best;
catherine.best2@stir.ac.uk

ABSTRACT

Objective To investigate the association between opioid replacement therapy (ORT) and benzodiazepine (BZD) coprescription and all-cause mortality compared with the prescription of ORT alone.

Design Population-based cohort study.

Setting Scotland, UK.

Participants Participants were people prescribed ORT between January 2010 and end of December 2020 aged 18 years or above.

Main outcome measures All-cause mortality, drug-related deaths and non-drug related deaths.

Secondary outcome ORT continuous treatment duration.

Analysis Cox regression with time-varying covariates.

Results During follow-up, 5776 of 46 899 participants died: 1398 while on coprescription and 4378 while on ORT only. The mortality per 100 person years was 3.11 during coprescription and 2.34 on ORT only. The adjusted HR for all-cause mortality was 1.17 (1.10 to 1.24). The adjusted HR for drug-related death was 1.14 (95% CI, 1.04 to 1.24) and the hazard for death not classified as drug-related was 1.19 (95% CI, 1.09 to 1.30).

Conclusion Coprescription of BZDs in ORT was associated with an increased risk of all-cause mortality, although with a small effect size than the international literature. Coprescribing was also associated with longer retention in treatment. Risk from BZD coprescription needs to be balanced against the risk from illicit BZDs and unplanned treatment discontinuation. A randomised controlled trial is urgently needed to provide a clear clinical direction.

Trial registration number NCT04622995.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ A strength of this analysis is the population-based analysis that included the whole opioid replacement therapy treatment population in Scotland.
- ⇒ A strength of this analysis is that follow-up took place over 10 years.
- ⇒ A weakness of this study is that the analysis has not considered dose of opioid replacement therapy, or benzodiazepine (BZD), which will be variable within individuals over time.
- ⇒ A weakness of the study is that there is potential residual unmeasured confounding that means that the relationship between BZD coprescription and mortality cannot be assumed to be causal.

INTRODUCTION

We have an ongoing challenge in the UK and abroad on how to address the risks associated with illicit drug use. Opioid replacement treatment (ORT) is a well-evidenced treatment which has provided a safe and effective treatment to reduce the risks of illicit opiate use.[1] Despite this, in recent years, there have been remarkably high numbers of deaths reported in Scotland, with increasing numbers recorded in England and Wales and Northern Ireland. The opioid crisis of north America is also well documented.[2] A strong feature associated with increasing deaths in the UK is that of concurrent use of benzodiazepines (BZDs) alongside opiate drugs.[3] This does not occur in isolation and may be compounded by use of alcohol, cocaine and gabapentinoids.[3 4]

Nowhere is the issue more apparent than in Scotland where the rise of the use of non-prescription BZDs is clear. In 2008, BZDs were implicated in 26% (n=149) of drug-related deaths (DRDs) and were mainly drugs licensed for prescription such as diazepam. By 2018, BZDs and BZD-type drugs were implicated in 67% (792) of DRDs, reducing slightly to 57% in 2022.[3] BZDs identified are predominately substances not licensed for prescription in the UK such as etizolam (a thenodiazepine), but there is an ongoing trend of novel BZDs emerging.[5]

People who use non-prescription BZDs, of unknown constituents and potency, can consume 'megadoses' of BZDs many times in excess of safe therapeutic doses, often with

- Large study – 46,899 Scottish participants
- January 2010 – December 2020
- Mortality per 100 person years 2.34 on ORT only and 3.11 if co-prescribed benzos
- Hazard ratio 1.17
- Increased risk of All Cause Mortaility if co-prescribed

2024 Development of an intervention to reduce harm

CHIEF SCIENTIST OFFICE

HIPS 20/09

RESEARCH INFORMATION EDUCATION EXPERIMENT DATA SCAN ASK PROBE LINK BOOK PROOF

Developing an Intervention to Manage Benzodiazepine Dependence and High-Risk Use in the Context of Escalating Drug Related Deaths: A feasibility study

AIMS

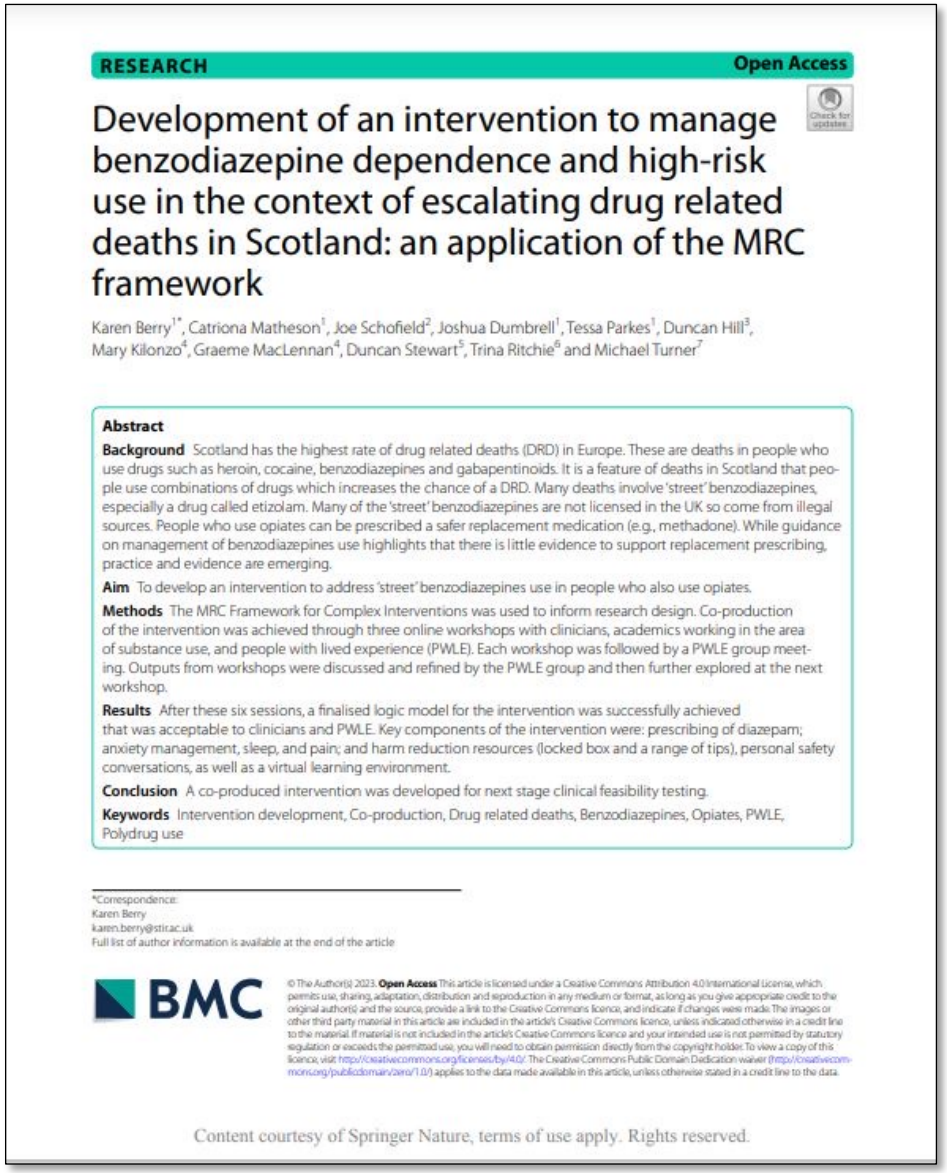
The study aimed to develop a new intervention to address 'street' benzodiazepine use in people who are in opiate replacement treatment and, to conduct a single arm feasibility trial (no control) of the new intervention, in three test sites (Grampian, Lothian, Fife), in preparation for a full randomised trial.

KEY FINDINGS

- A targeted intervention was successfully developed which was acceptable to all stakeholders. (people with experience of benzodiazepine use, clinical doctors, nurses, pharmacists, psychologists and academics). It included prescribed diazepam (up to 30mg daily) and support for anxiety, sleep, pain as well as addressing past trauma and providing harm reduction advice.
- 39 patients were recruited to the receive the intervention in three sites. Of these, 30 completed the study (77%).
- There were general indications of improvements in level of anxiety, quality of life, substance use recovery and depression. Cognitive function remained stable.
- Changes in some 'street' drug use were reported by patients but oral fluid testing data was incomplete and inconclusive. This would need addressed in a larger trial.
- Recruitment was facilitated by positive and proactive research nurses, ideally working closely with the local clinical lead which helped them address concerns about inclusion criteria. This needs addressed in a larger trial with a control group.
- Fidelity to the prescribing component of the intervention was mixed.
- Interviews with patients and clinicians found general satisfaction with the intervention. The increased nursing time and strong therapeutic alliance to help address problems like anxiety was important, as was the diazepam prescription.
- Patients appreciated the prescription as a safer, regular supply compared to street drugs. Others noted the importance of being ready to make meaningful change that reduced drug use.

Chief Scientist Office, St Andrews House, Regent Road, Edinburgh, EH1 3DG

www.cso.scot.nhs.uk @CSO_Scotland



RESEARCH Open Access

Development of an intervention to manage benzodiazepine dependence and high-risk use in the context of escalating drug related deaths in Scotland: an application of the MRC framework

Karen Berry[1*], Catriona Matheson[1], Joe Schofield[2], Joshua Dumbrell[1], Tessa Parkes[1], Duncan Hill[3], Mary Kilonzo[4], Graeme MacLennan[4], Duncan Stewart[5], Trina Ritchie[6] and Michael Turner[7]

Abstract

Background Scotland has the highest rate of drug related deaths (DRD) in Europe. These are deaths in people who use drugs such as heroin, cocaine, benzodiazepines and gabapentinoids. It is a feature of deaths in Scotland that people use combinations of drugs which increases the chance of a DRD. Many deaths involve 'street' benzodiazepines, especially a drug called etizolam. Many of the 'street' benzodiazepines are not licensed in the UK so come from illegal sources. People who use opiates can be prescribed a safer replacement medication (e.g., methadone). While guidance on management of benzodiazepines use highlights that there is little evidence to support replacement prescribing, practice and evidence are emerging.

Aim To develop an intervention to address 'street' benzodiazepines use in people who also use opiates.

Methods The MRC Framework for Complex Interventions was used to inform research design. Co-production of the intervention was achieved through three online workshops with clinicians, academics working in the area of substance use, and people with lived experience (PWLE). Each workshop was followed by a PWLE group meeting. Outputs from workshops were discussed and refined by the PWLE group and then further explored at the next workshop.

Results After these six sessions, a finalised logic model for the intervention was successfully achieved that was acceptable to clinicians and PWLE. Key components of the intervention were: prescribing of diazepam; anxiety management, sleep, and pain; and harm reduction resources (locked box and a range of tips), personal safety conversations, as well as a virtual learning environment.

Conclusion A co-produced intervention was developed for next stage clinical feasibility testing.

Keywords Intervention development, Co-production, Drug related deaths, Benzodiazepines, Opiates, PWLE, Polydrug use

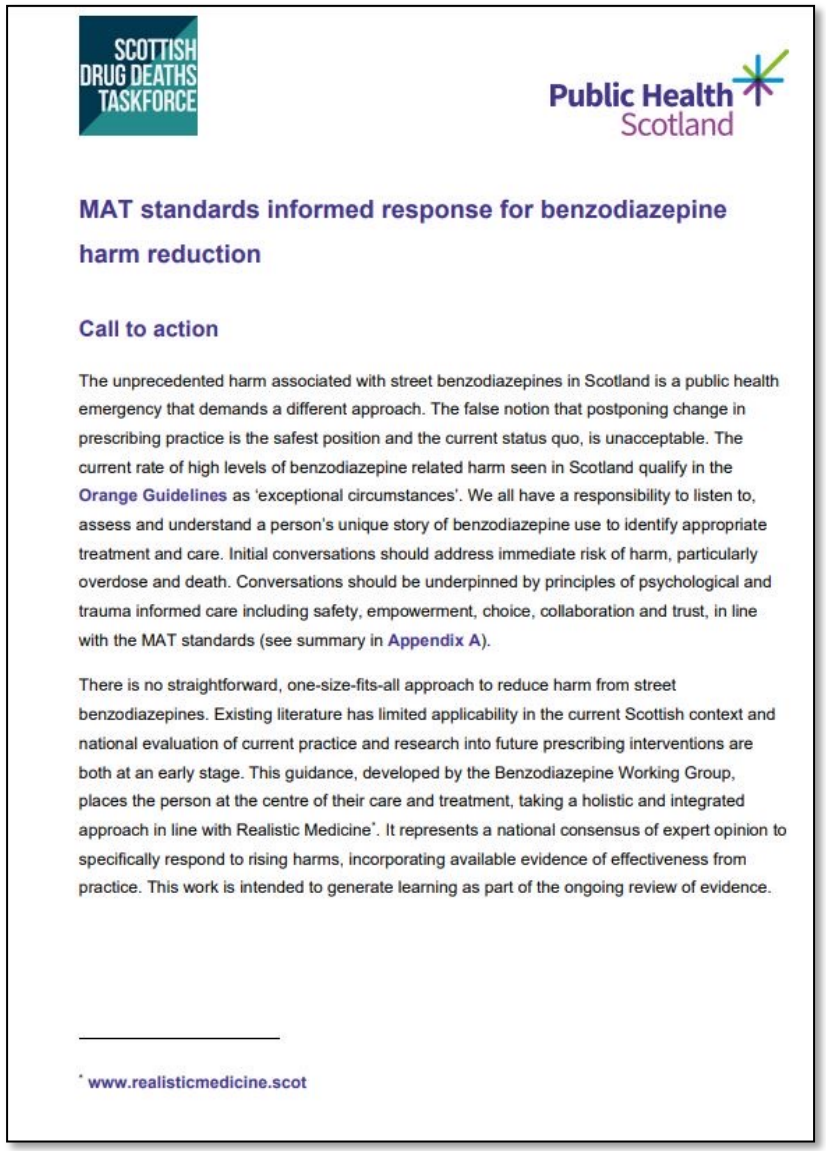
*Correspondence:
Karen Berry
karen.berry@strath.ac.uk
Full list of author information is available at the end of the article

NHS Greater Glasgow and Clyde

Glasgow City Council

Glasgow City HSCP
Health and Social Care Partnership

2024 PHS vignettes sharing prescribing cases



SCOTTISH DRUG DEATHS TASKFORCE

Public Health Scotland

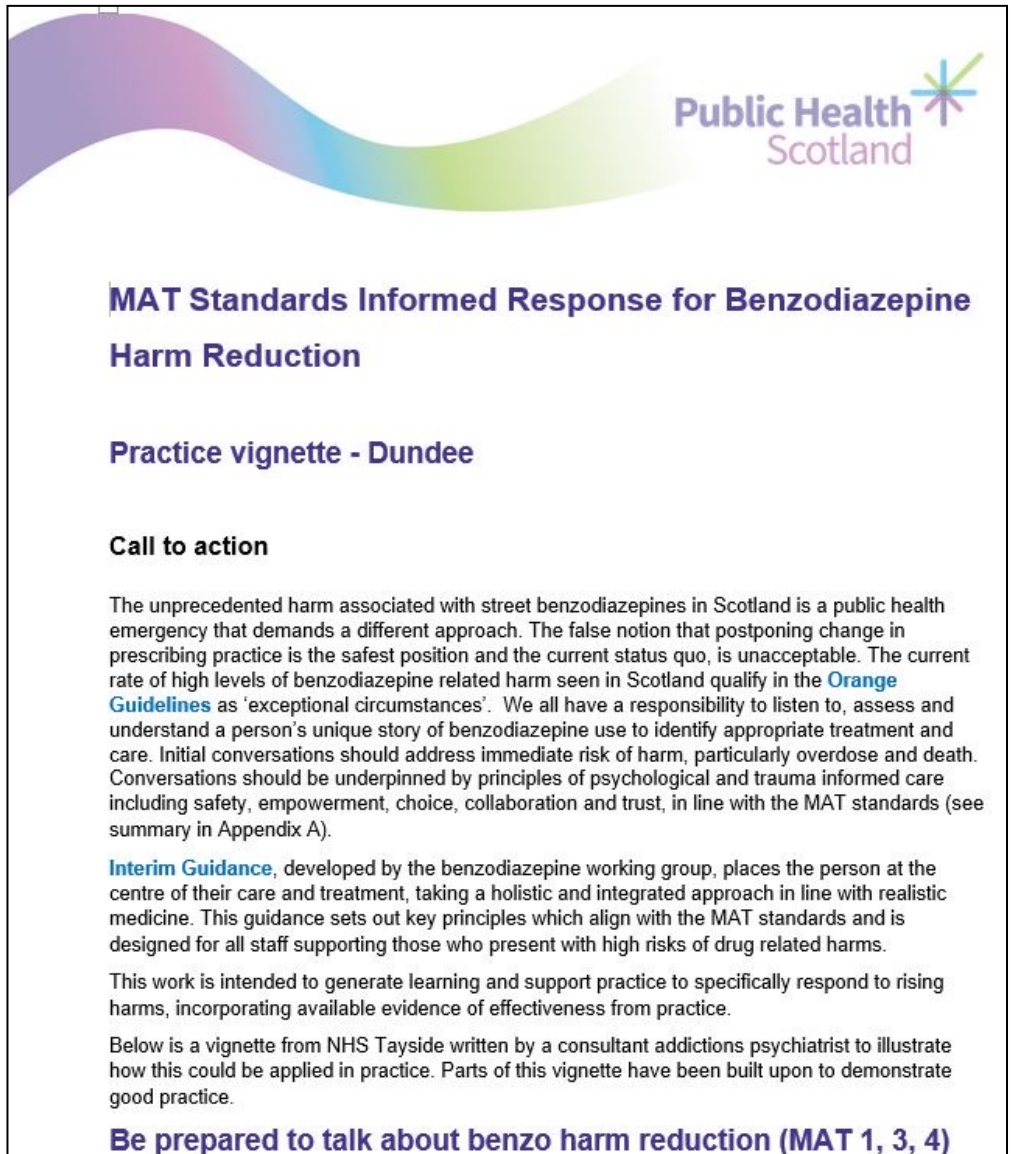
MAT standards informed response for benzodiazepine harm reduction

Call to action

The unprecedented harm associated with street benzodiazepines in Scotland is a public health emergency that demands a different approach. The false notion that postponing change in prescribing practice is the safest position and the current status quo, is unacceptable. The current rate of high levels of benzodiazepine related harm seen in Scotland qualify in the Orange Guidelines as 'exceptional circumstances'. We all have a responsibility to listen to, assess and understand a person's unique story of benzodiazepine use to identify appropriate treatment and care. Initial conversations should address immediate risk of harm, particularly overdose and death. Conversations should be underpinned by principles of psychological and trauma informed care including safety, empowerment, choice, collaboration and trust, in line with the MAT standards (see summary in Appendix A).

There is no straightforward, one-size-fits-all approach to reduce harm from street benzodiazepines. Existing literature has limited applicability in the current Scottish context and national evaluation of current practice and research into future prescribing interventions are both at an early stage. This guidance, developed by the Benzodiazepine Working Group, places the person at the centre of their care and treatment, taking a holistic and integrated approach in line with Realistic Medicine*. It represents a national consensus of expert opinion to specifically respond to rising harms, incorporating available evidence of effectiveness from practice. This work is intended to generate learning as part of the ongoing review of evidence.

* www.realisticmedicine.scot



Public Health Scotland

MAT Standards Informed Response for Benzodiazepine Harm Reduction

Practice vignette - Dundee

Call to action

The unprecedented harm associated with street benzodiazepines in Scotland is a public health emergency that demands a different approach. The false notion that postponing change in prescribing practice is the safest position and the current status quo, is unacceptable. The current rate of high levels of benzodiazepine related harm seen in Scotland qualify in the Orange Guidelines as 'exceptional circumstances'. We all have a responsibility to listen to, assess and understand a person's unique story of benzodiazepine use to identify appropriate treatment and care. Initial conversations should address immediate risk of harm, particularly overdose and death. Conversations should be underpinned by principles of psychological and trauma informed care including safety, empowerment, choice, collaboration and trust, in line with the MAT standards (see summary in Appendix A).

Interim Guidance, developed by the benzodiazepine working group, places the person at the centre of their care and treatment, taking a holistic and integrated approach in line with realistic medicine. This guidance sets out key principles which align with the MAT standards and is designed for all staff supporting those who present with high risks of drug related harms.

This work is intended to generate learning and support practice to specifically respond to rising harms, incorporating available evidence of effectiveness from practice.

Below is a vignette from NHS Tayside written by a consultant addictions psychiatrist to illustrate how this could be applied in practice. Parts of this vignette have been built upon to demonstrate good practice.

Be prepared to talk about benzo harm reduction (MAT 1, 3, 4)

NHS Greater Glasgow and Clyde

Glasgow City Council

Standard 1: All people accessing services have the option to start MAT from the same day of presentation.

Standard 2: All people are supported to make an informed choice on what medication to use for MAT, and the appropriate dose.

Standard 3: All people at high risk of drug-related harm are proactively identified and offered support to commence or continue MAT.

Standard 4: All people are offered evidence based harm reduction at the point of MAT delivery.

Standard 5: All people will receive support to remain in treatment for as long as requested.

Standard 6: The system that provides MAT is psychologically informed (tier 1); routinely delivers evidence-based low intensity psychosocial interventions (tier 2); and supports individuals to grow social networks.

Standard 7: All people have the option of MAT shared with Primary Care.

Standard 8: All people have access to independent advocacy and support for housing, welfare and income needs.

Standard 9: All people with co-occurring drug use and mental health difficulties can receive mental health care at the point of MAT delivery.

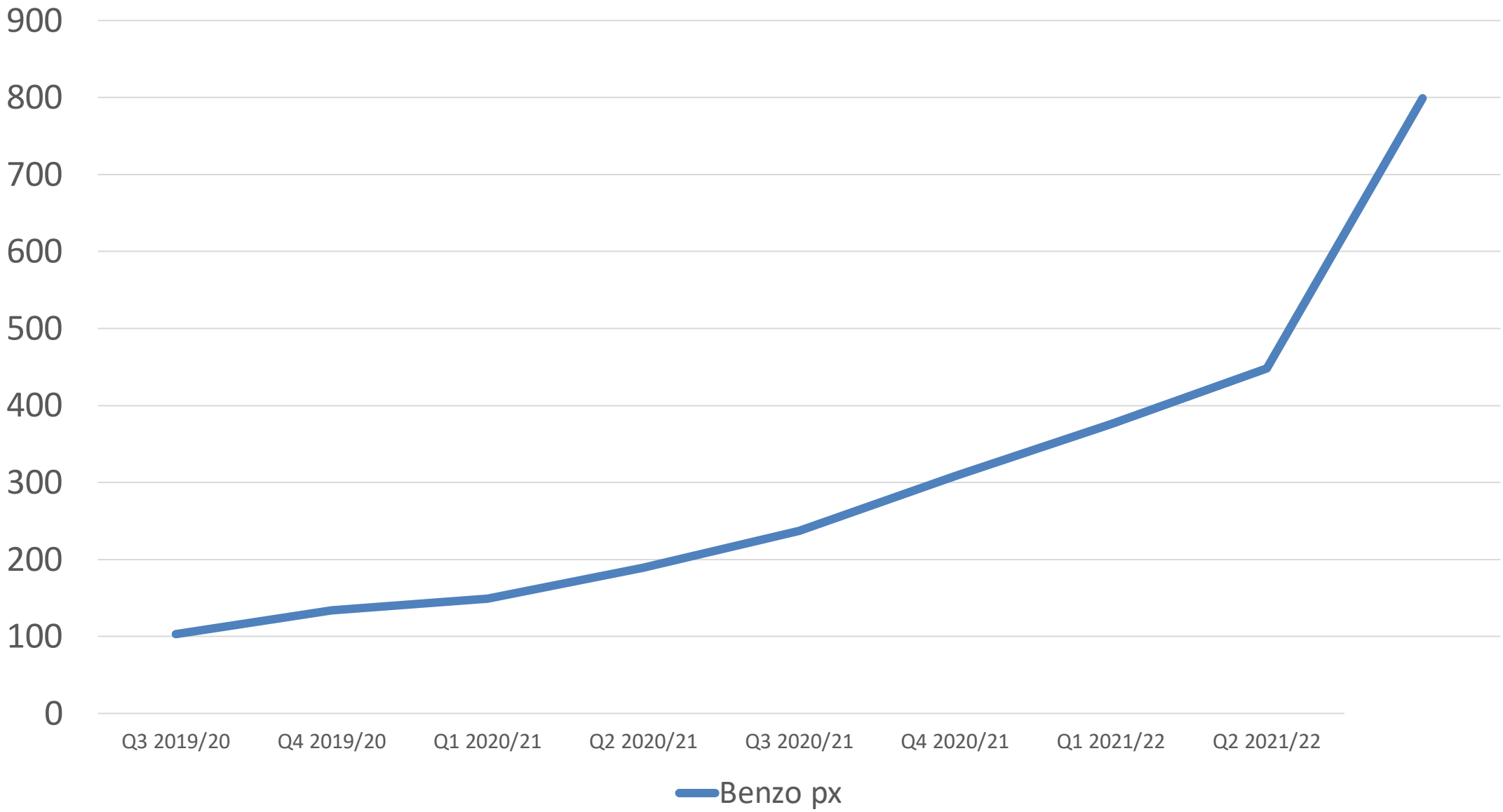
Standard 10: All people receive trauma informed care.

Medication Assisted Treatment

- evidence-based complex intervention
- substitute medication plus behavioural and psychological therapies
- aim - reduction of harms from alcohol/drug use
- aim - reduction or cessation of alcohol/drug use
- framework includes - initiation, maintenance, detoxification

Glasgow City HSCP
Health and Social Care Partnership

2019 to 2024 trend in co benzo prescribing in GADRS



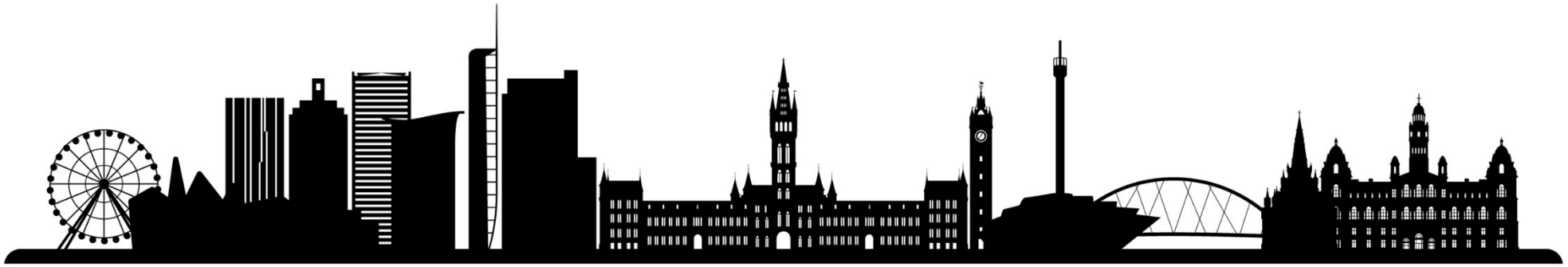
Challenges in Benzodiazepine Prescribing

1. Only concomitant prescribing with OST
2. Adequate assessment and picture of harms
3. Making shared decisions and gaining informed consent
   - Anterograde amnesia (issue consolidating new memory)
   - May appear to be functioning “normally”
   - Use of unique strategies, repetition, non-verbal reminders
4. Set realistic benzo harm reduction goals
5. Ensure shared understanding of plans if harms don’t reduce

Glasgow City HSCP
Health and Social Care Partnership

Trends in Treatment – Providing MAT for people with Benzodiazepine Dependency

Trina Ritchie, Lead Clinician
NHS GGC Alcohol and Drug Recovery Services



NHS Greater Glasgow and Clyde

Glasgow City Council