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A Randomised Controlled Trial (RCT) of a Diazepam Maintenance Intervention versus Standard Care of Tapering Diazepam to Reduce Dependent Street Benzodiazepine Use in Adults Receiving Opioid Agonist Treatment (OAT)

Catriona Matheson

23rd April 2026 LJMU DRD conference

Funded by

NIHR | National Institute for
Health and Care Research

Study team



Chief Investigator - Prof Catriona Matheson

Co-Investigator Team

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- ▶ University of Aberdeen: Graeme MacLennan, Mary Kilonzo, Graham Scotland
- ▶ University of Bristol: Jenny Scott, Mat Hickman
- ▶ University of Edinburgh: Michael Eddleston, Roy Robertson
- ▶ University of Lancaster: Euan Lawson
- ▶ NHS Greater Glasgow and Clyde: Trina Ritchie
- ▶ NHS Lanarkshire: Duncan Hill
- ▶ NHS Tayside: Seonaid Anderson
- ▶ PPI Co-Investigator: Grant Brown, PPI Co-Investigator

Researchers:

- ▶ Christine Kennedy (trial manager), Esme Foxworthy-Bowers (surveillance)

Clinical Trials Unit - CHaRT, University of Aberdeen

Funding and Sponsorship

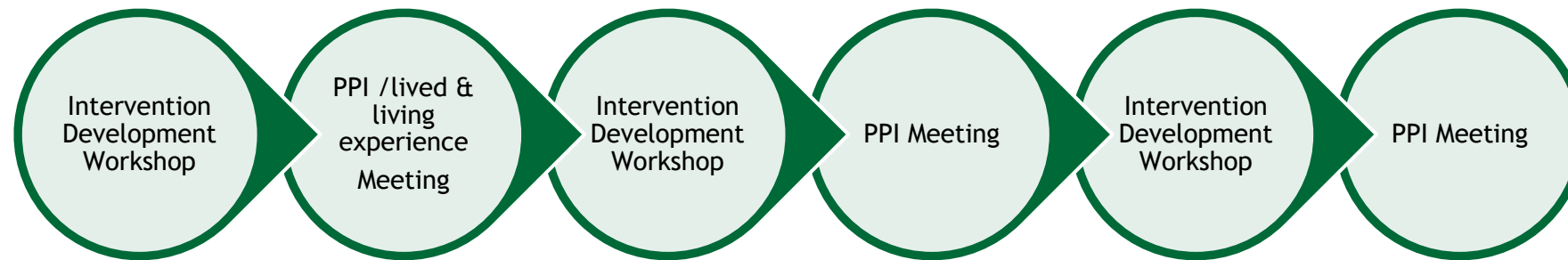
- ▶ **Funder:** National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme; NIHR Ref number: NIHR 163461
- ▶ **Sponsor:** University of Stirling
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- ▶ **ISRCTN:** 34696930
- ▶ **REC Reference:** 25-NI-0117
- ▶ **CTA Number:** 33885/0001/001-0001

Background

- ▶ Benzodiazepine use from non-prescription sources during Opioid Agonist Treatment is common.
- ▶ High-risk use in the form of bingeing, polydrug use and ‘mega-dosing’ which contribute to overdose and DRD.
 - ▶ e.g. 56% of DRD in Scotland include a benzodiazepine approx. 40% in England
- ▶ Control of non-prescribed benzodiazepines outside the NHS and in the hands of illicit suppliers, constantly distributing new synthetic variations.
- ▶ No randomised controlled trial (RCT) conducted to evaluate the possible intervention options and to support and provide a robust evidence base for prescribing guidelines.

Intervention Development and Feasibility 2022-2024 Study

funded by the Chief Scientist Office, Scottish Government



- ▶ Intervention was tested in 3 sites (Aberdeen, Edinburgh and Fife) 39 patients over 6 months

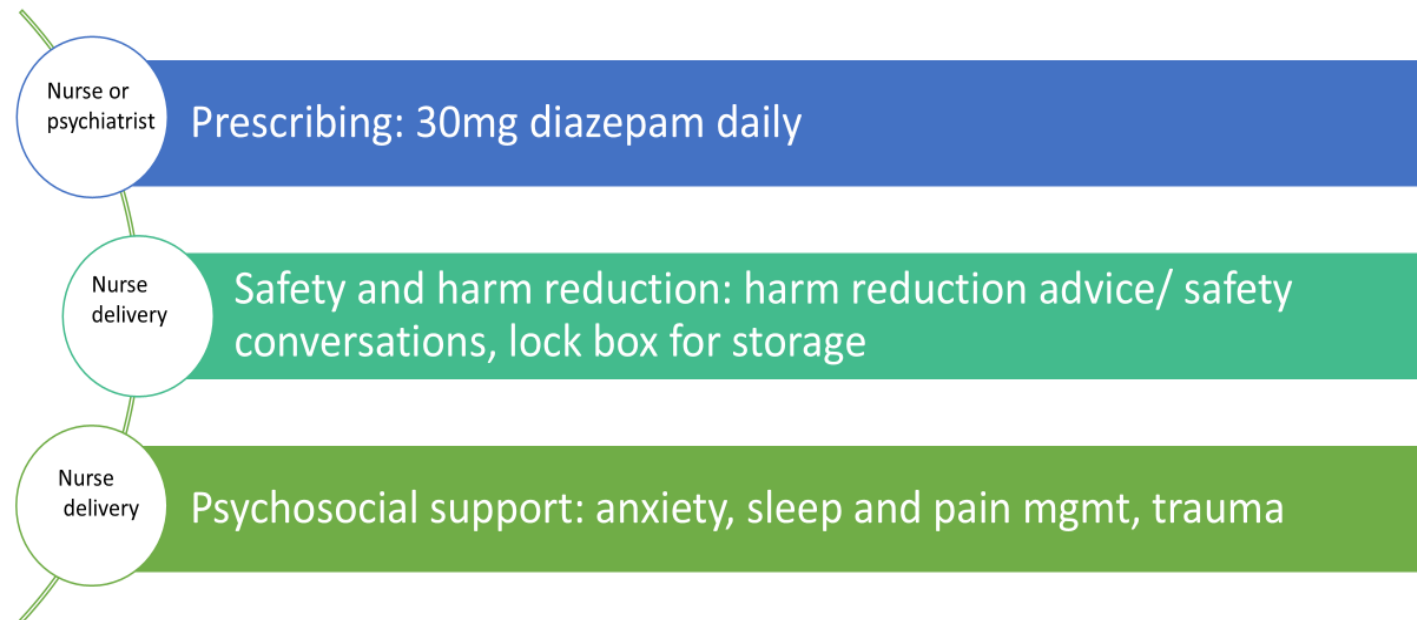
Publications: Matheson, C., Berry, K., Kilonzo, M. *et al.* A feasibility study of a co-designed intervention to manage benzodiazepine dependence and high-risk use in those receiving opioid agonist treatment. *Pilot Feasibility Stud* (2025).

<https://doi.org/10.1186/s40814-025-01743-0>

The Intervention

- Deliver in 1 hr fortnightly sessions

Bespoke training
for nurses on:
Anxiety mgmt,
pain,
sleep,
psychotrauma
education,
memory and
cognition risk



Reference: Berry, K., Matheson, C., Schofield, J. *et al.* 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. *BMC Health Serv Res* **23**, 1205 (2023). <https://doi.org/10.1186/s12913-023-10201-7>

Commissioned call from the NIHR's HTA Panel

Themed call for an RCT of maintenance diazepam versus tapered dose for people in Opioid agonist treatment

Full proposal submission July 2024

Awarded October 2024

Start Date: 1st May 2025

The brief asked for:

- A two-arm randomised controlled design
- Including sites in at least two UK countries
- Based in drug treatment services
- Maintenance prescribing of diazepam

£2.6 million

45 months

**RCT - CTIMP- Clinical Trial of a Medicinal Product
across at least 6 sites in Scotland and England**

Study Design

- ▶ Two arm, non blinded randomised controlled trial (RCT)
- ▶ Aim: To test the clinical effectiveness and cost effectiveness of a tailored diazepam maintenance intervention versus standard care (which is a tapering dose of diazepam).

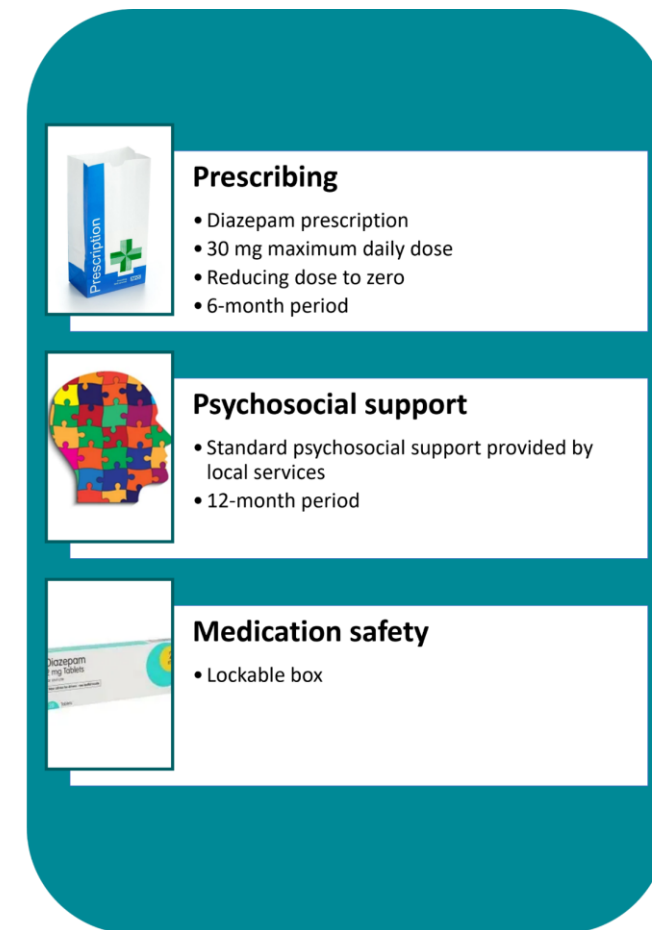
Intervention



The Intervention arm diagram is a vertical stack of four rounded rectangular boxes. Each box contains an icon on the left and text on the right. The icons are: a prescription box, a colorful puzzle head, a hand holding a heart, and a box of diazepam tablets.

- Prescribing**
 - Diazepam prescription
 - 30mg maximum daily dose
 - 15-month period
- Psychosocial support**
 - Trauma psychoeducation
 - Anxiety management
 - Sleep assessment
 - Pain management
 - 15- month period
- Harm reduction**
 - Harm reduction advice
 - Safety conversations
- Medication safety**
 - Lockable box

Control



The Control arm diagram is a vertical stack of four rounded rectangular boxes. Each box contains an icon on the left and text on the right. The icons are: a prescription box, a colorful puzzle head, and a box of diazepam tablets.

- Prescribing**
 - Diazepam prescription
 - 30 mg maximum daily dose
 - Reducing dose to zero
 - 6-month period
- Psychosocial support**
 - Standard psychosocial support provided by local services
 - 12-month period
- Medication safety**
 - Lockable box

Randomised Controlled Trial with Embedded:

Pilot Phase

6 month pilot phase with
Stop/go criteria

Toxicological Surveillance

To review emergence of new
street benzodiazepines
through toxicological
surveillance and adjust
screening accordingly

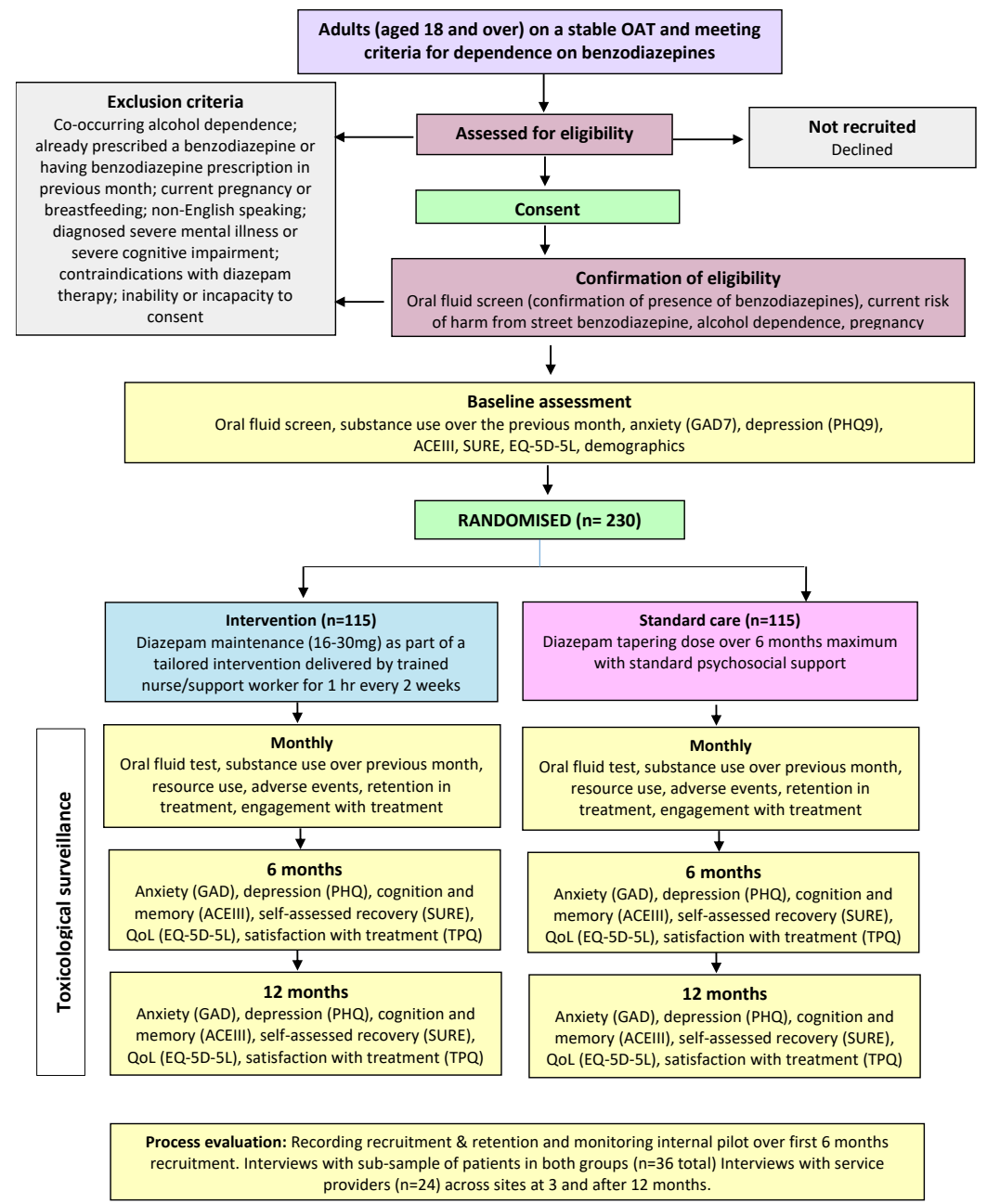
Economic Evaluation

To assess the cost
effectiveness of the
intervention compared to
standard care from a health
and social care perspective
and model long term cost
effectiveness if the trial was
implemented

Process Evaluation

To understand retention,
adherence to treatment, and
experiences of people in
each arm of the trial to
better understand the
success or otherwise of the
intervention

The In BOAT Trial



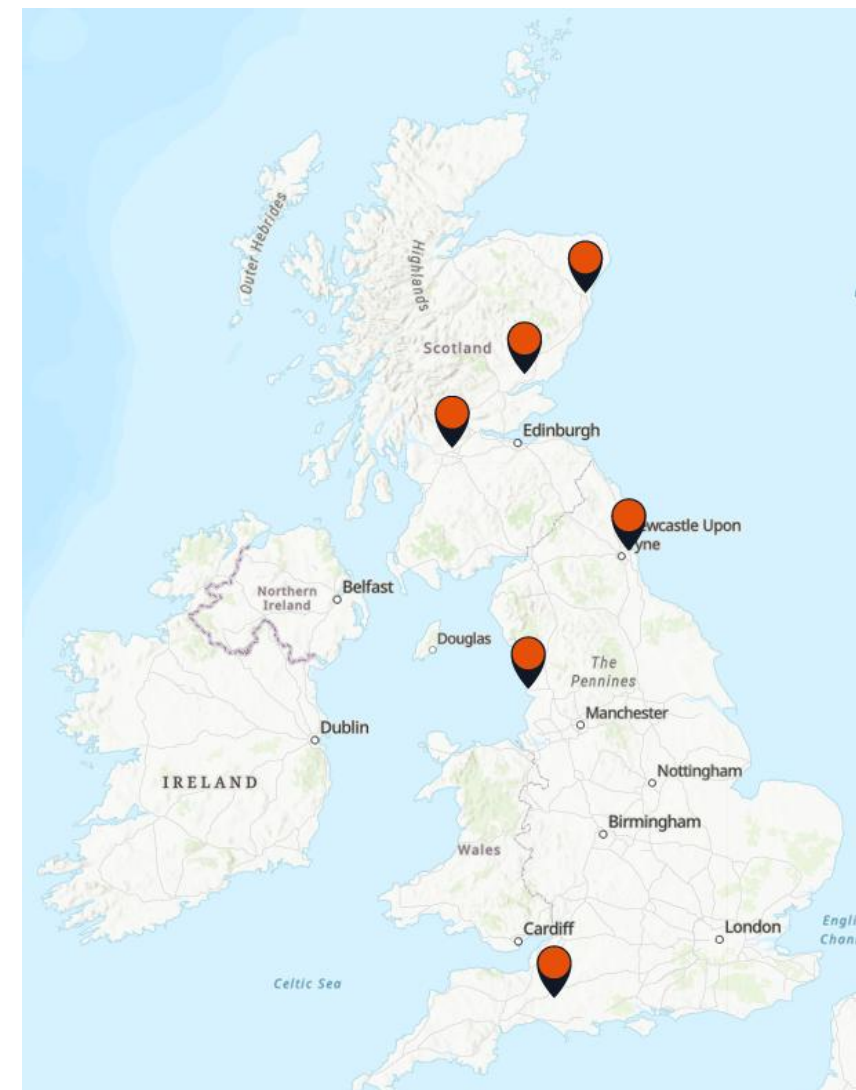
Economic cost effectiveness, cost consequence analysis using Unscheduled Care Datamart for Scottish sites and modelling including long term cost effectiveness.

Setting

- ▶ Recruitment target: 230 participants
- ▶ Participants will be recruited from 7 specialist drug treatment services in Scotland (NHS) and England (Third Sector Organisations)
- ▶ Scotland:
 - NHS Tayside
 - NHS Grampian
 - NHS Greater Glasgow and Clyde
 - tbc
- ▶ England:
 - Sunderland (CGL)
 - Somerset (Turning Point)
 - North Lancashire or Merseyside? (CGL)

In-BOAT

Intervention for Benzodiazepine
use in Opioid Agonist Treatment



Trial population

Inclusion Criteria

- ▶ Adult (18 years or over)
- ▶ Stable on opioid agonist treatment (methadone or buprenorphine)
- ▶ with toxicologically verified non-prescription benzodiazepine use in the previous month,
- ▶ With current DSM-5-diagnosed substance (benzodiazepine) use disorder, and
- ▶ at current risk of harm from street benzodiazepine use. Risk of harm is defined as regular use of unregulated street benzodiazepines

Exclusion Criteria

- ▶ Co-occurring alcohol dependence (requiring treatment)
- ▶ already being prescribed a benzodiazepine or having a benzodiazepine prescription in previous month
- ▶ Current pregnancy/ breastfeeding /women actively trying to become pregnant
- ▶ non-English speaking
- ▶ diagnosed severe mental illness such as active psychosis that clinical staff consider poses a risk to safety (of patient or staff)
- ▶ Contraindication with diazepam
- ▶ Inability or incapacity to consent

Primary outcome:

- ▶ Presence of ‘street’ benzodiazepines in toxicological testing - monthly - oral fluid swab

Secondary outcomes:

- ▶ Self reported substance use
- ▶ Anxiety
- ▶ Depression
- ▶ Quality of Life
- ▶ Memory and cognitive function
- ▶ Self-assessed substance use recovery
- ▶ Treatment satisfaction
- ▶ Drug related events: overdoses, drug related hospital admissions
- ▶ Resource use (ambulance calls, hospital admissions etc)

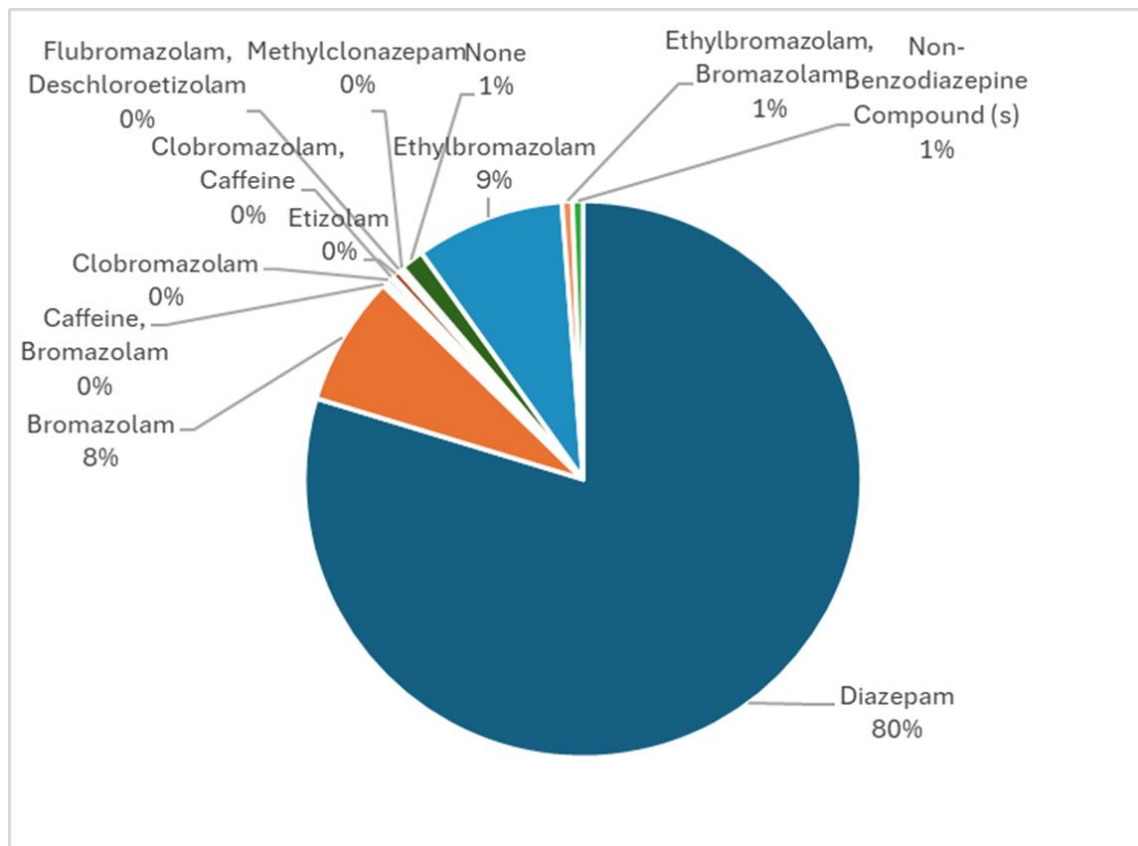
Pilot phase: 1st April - 1st October

- ▶ Testing the willingness to be recruited, randomised and retained

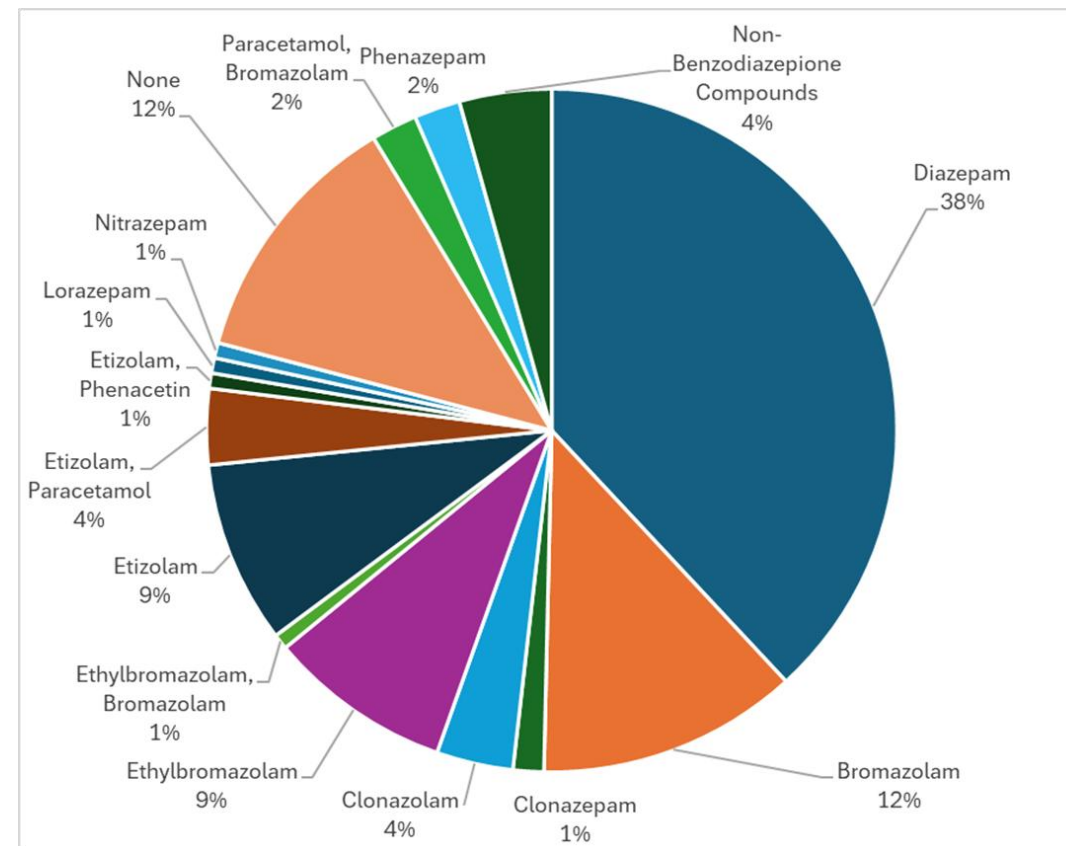
Progression criterion	Red (<60%)	Amber (60 to 100%)	Green (>100%)
1. Recruitment rate per centre-month	<3	3 to 5	>5
2. Number of centres opened during pilot	<3.6	3.6 to 6	>6
3. Total number of participants recruited during pilot	<54.6	54.6 to 91	>91
4 Retention across sites at 6 months	<50%	50-75%	>75%

Toxicology Surveillance: Wedinos Data Jan-Sept 2025

England: (Diazepam Purchase Intent, n = 694)



Scotland: (Diazepam Purchase Intent, n = 155)



Surveillance Scanning

- Periodic sample of 10% of participants over timescale
- Urine test for emerging substances
- ASI lab, St Georges, London

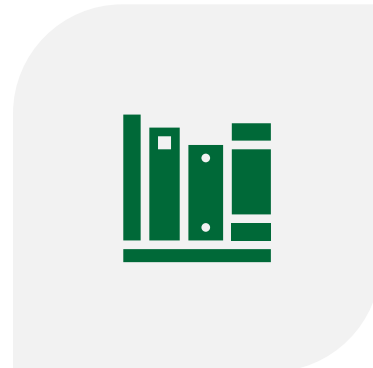
PPI Group (lived & living experience)



DEVELOPING A COMMON
QUESTIONS VIDEO



MAKING GOOD USE OF
LOCKABLE BOXES FOR STORAGE



SCANNING LITERATURE AND
INTERNET FOR EMERGING
SUBSTANCES!

Where are we now?

- ▶ One site active and recruiting first patients! (Angus in Tayside)
- ▶ Sunderland (CGL) site nurse starting in May
- ▶ Glasgow, Aberdeenshire, Somerset appointing site staff
- ▶ Re-recruiting a site in the North West



Thank you to site partners:
CGL, Turning Point, NHS Tayside, NHS Grampian, NHS
Greater Glasgow & Clyde
and
NHS Lothian toxicology
ASI, St Georges