Developments in the management of benzodiazepine dependence: the views of Scottish addiction prescribers

Joe Schofield[1], Catriona Matheson[1], Seonaid Anderson[2], Michael Turner[2], Harriet Bloomfield[3]
1 University of Stirling; 2 NHS Grampian; 3 Drugs Research Network for Scotland

1 Introduction

Problematic use of diverted and illicit benzodiazepines and benzodiazepine-type drugs (BZDs) is a significant concern for addiction healthcare providers in Scotland. BZDs are frequently implicated in drug-related deaths, especially in combination with opioids and/or alcohol. BZD use is also considered a barrier to optimal engagement, retention and outcomes of addiction treatment and recovery. Local and national policies highlight the need to address problematic BZD use, but there is a lack of clinical consensus or guidance on the management of dependence.

The Drugs Research Network for Scotland established a BZD research group of addiction specialists, academics and people who use drugs to share information on evidence needs and opportunities to address these. This group includes Drs Seonaid Anderson and Michael Turner, NHS Grampian Addiction Psychiatrists Members who surveyed 61 (of 110) Scottish addiction medics in 2018 to understand their views and experiences of managing patients with BZD dependence. In 2020 this group developed a follow-on survey for Scottish addiction prescribers.

Summary results were presented to the Royal College of Psychiatrists (Scotland)'s 'Golden Lion group', to the BZD Steering Group of the Drug Deaths Taskforce's (DDTF) Medication Assisted Therapy group, and Scottish Drugs Forum/DDTF "Benzos - What can be done?" webinar. This report has been produced to inform development of clinical guidelines and consensus, and intervention development and testing research currently underway.

2 Methods

An online survey was developed to capture information on the characteristics of BZD-dependent patients, current service provision, and prescriber views on required service developments in service delivery. Using Anderson and Turner's 2019 survey as a starting point, questions were developed by members of the DRNS' BZD research group and the final version was designed using Jisc online surveys. Ethical approval was secured from the University of Stirling's General University Ethics Panel (ref. 2020-869) before recruitment commenced.

This survey was open to all prescribers working within Scottish addiction settings. Emails describing the project, inclusion criteria and a copy of the participant information sheet were circulated to prescribers via the chairs of relevant Scottish professional networks. The survey ran between May and July 2020, and a reminder email was sent to these networks at the start to July to encourage responses:

- The Royal College of Psychiatrists (Scotland).
- Specialist Pharmacists in Substance Misuse.

- Lead Psychologists in Addiction Services.

Descriptive summary statistics and charts were generated in Excel and R. As convenience sampling was used in this survey, no tests of statistical significance were applied.

3 Results

Respondent and service characteristics (Table 1)

Responses were received from 55 prescribers working in 10/14 of Scotland's geographical Health Boards representing a mix of professional disciplines, predominately Addiction Psychiatrists, Nurses and Specialist GPs but also including some pharmacist and other non-medical prescribers. Forty-nine worked in Specialist Addiction Services and 6 in Primary Care. Two worked across services including one who delivered care in both specialist addiction and prison settings.

The median (IQR) caseload of patients with an opiate problem was 90 (31.5-300). Respondents estimated that the median (IQR) proportion of these patients first presenting who reported a BZD problem was 20% (10%-52.5%), and the proportion with a current BZD problem was 30% (12.5%-60%).

Respondents were asked what conditions commonly associated with BZD use they routinely screen patients with problem opiate use for. Most reported screening for mental health problems including anxiety (96%), complex trauma / PTSD (95%), and depression (91%). In addition 85% reported assessing for sleep problems and 64% for pain. Free text responses indicated that other conditions patients are routinely screened for include: BZD dependence, blood borne viruses, stimulant use, bereavement and social stress, psychotic illness and other severe mental health disorders.

Prescribers estimated prevalence of comorbidities for which BZD are commonly prescribed among their BZD-dependent patients were anxiety (median 80%, IQR 30%), sleep problems (70%, 48%), trauma (60%, 50%) and depression (50%, 40%) (Figure 1).

Over half of respondents reported they use laboratory-based (65%) and/or point of care test (POCT) (76%) urine screens to monitor patients' drug use; less than half used oral fluid testing, POCT 47% and laboratory-based 40%.

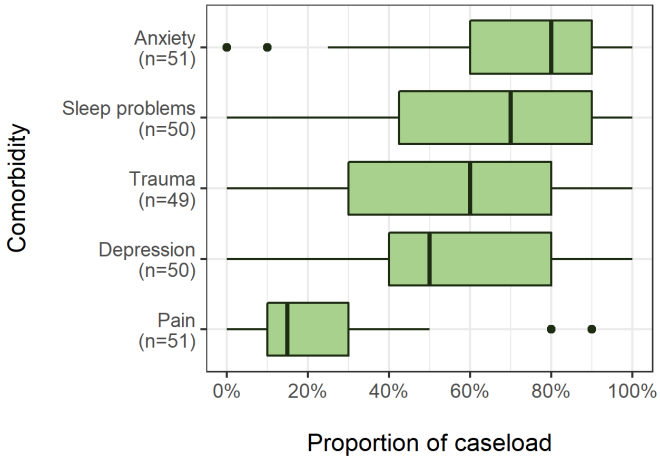

Figure 1 Estimated prevalence of comorbidities among current BZD-dependent patients

Three quarters (41/55) of prescribers reported that monitoring tests available to them were unable to differentiate between prescribable (e.g. diazepam) versus non-prescribable (e.g. etizolam) BZDs, 18% confirmed this information was available, 5% did not know, and of the two 'Other' responses one confirmed such testing was only available on a named patient basis rather than routinely available.

Table 1 Respondent and service characteristics

Question	Response	n	n/55
1. Health Board	**Ayrshire & Arran**	**8**	**15%**
	Borders	1	2%
	Fife	4	7%
	Forth Valley	3	5%
	Gtr. Glasgow & Clyde	6	11%
	Grampian	9	16%
	Highland	6	11%
	Lanarkshire	5	9%
	Lothian	6	11%
	Tayside	4	7%
	Missing	3	5%
	Total	**55**	**100%**
2. Professional discipline	Addiction Psychiatrist	24	44%
	Nurse	13	24%
	Specialist GP	10	18%
	Other addiction medic	3	5%
	Pharmacist	3	5%
	Missing	1	2%
	Other	1	2%
	Total	**55**	**100%**
3. What service(s) do you work in?	General Practice	6	11%
	Specialist Addictions	49	89%
	Other (Prison)	1	2%
	Total	**56**	*
4. What conditions associated with BZD use does your service routinely screen patients for?	Anxiety	53	96%
	Complex trauma / PTSD	52	95%
	Depression	50	91%
	Sleep problems	47	85%
	Pain	35	64%
	Other	13	24%
	Total	**250**	*
5. How does your service monitor cessation of unprescribed / illicit substances?	POCT Urine	42	76%
	Lab urine	36	65%
	POCT oral fluid	26	47%
	Lab oral fluid	22	40%
	Other	5	9%
	Total	**131**	*
6. Does patient monitoring allow differentiation between prescribable vs. non- prescribable BZDs?	No	41	75%
	Yes	8	15%
	Don't know	3	5%
	Other	2	4%
	Missing	1	2%
	Total	**55**	**100%**

* = Percentages not shown where respondents could select multiple responses and totals >55

POCT = Point of Care test. Rx = prescribe / prescribing / prescribable

BZD prescribing: current practice

Two-thirds (67%) of prescribers reported they currently prescribe BZDs for people who use opiates who have BZD dependence. Most of these (59%) were informed by two or more guidelines, usually referring to their local Health Board policy plus the Orange Book (Drug misuse and dependence: UK Guidelines on clinical management) (Table 2).

Table 2 Which guidelines inform your prescribing? (Ashton = Ashton Manual; Orange = Orange Book (Drug misuse and dependence: UK guidelines on clinical management); Local = Health Board policy / guideline; Royal College = Royal College of General Practitioners or Royal College of Physicians)

Number of guidelines	Guidelines	n	%
1	Ashton	1	3%
	Orange	4	11%
	Local	10	27%
2	Local + Ashton	1	3%
	Local + Orange	13	35%
3	Local + Orange + Ashton	3	8%
	Local + Orange + Royal College	4	11%
4	Local + Orange + Royal College + Ashton	1	3%

Just 19% (7/37) of those who prescribe BZDs have access to monitoring that allows them to detect use of non-prescribable street BZDs (Table 3).

Table 3 Crosstab of current BZD prescribing and patient monitoring information available.

		Does patient monitoring allow differentiation between prescribable vs. non-prescribable BZD use?					
		Yes	**No**	**Other**	**Don't know**	**Missing**	**Total**
Do you currently prescribe BZDs to people with opioid and BZD dependence?	**Yes**	7	27	2	1		**37**
	No	1	14		2		**17**
	Missing					1	**1**
	Total	**8**	**41**	**2**	**3**	**1**	**55**

Seventeen (31%) respondents said they did not currently prescribe BZD to people who use opiates who have BZD dependence. Reasons for this included:

- Lack of an adequate evidence base.
- Not permitted by local policy and practice.
- Service preference for supported patient self-detoxification.
- Available monitoring is unable to distinguish between prescribable and non-prescribable BZDs.
- No currently eligible patients.
- Problems for patients including drug-related death, escalating use including , and mood / cognitive / service engagement problems resulting from long-term use.
- Problems for service providers including demand from other patients and lower retention in care / engagement with psychosocial interventions.

BZD prescribing intentions (Table 5)

All 55 respondents were asked if they would be willing to prescribe BZDs to patients who use(d) opioids and are dependent on BZDs; 82% would and 16% would not, the latter group including 3 current BZD prescribers. Among the 17 who do not currently prescribe BZDs, 11 would be willing to do so in the future (Table 4).

Table 4 Crosstab of current vs. future BZD prescribing

		Would you prescribe BZDs to dependent patients in the future?			
		Yes	**No**	**Missing**	**Total**
Do you currently prescribe BZDs to people with opioid and BZD dependence?	**Yes**	34	3		**37**
	No	11	6		**17**
	Missing			1	**1**
	Total	**45**	**9**	**1**	**55**

Seven of the nine who would not prescribe BZDs gave reasons for this. The lack of robust evidence and lack of support for the practice in clinical guidelines was noted. Several stated a preference for other multiagency and multidisciplinary interventions to address the underlying reasons for BZD use. Some noted the complexity of BZD prescribing and risks of diversion, patients topping up with illicit BZDs, and contribution to drug-related deaths. Two reported they had prior experience of BZD prescribing and detoxes, noting "poor experience of this working for patients" and "none of them were successful. Attempting to integrate psychosocial intervention … didn't work either".

Forty-five respondents (82%) would consider BZD prescribing in the context of opiate and BZD dependence and many gave additional information in support of their response. Several current prescribers noted this is current practice in their service describing this as a pragmatic option with harm reduction benefits. This group noted that prescribing can help to stabilise patients, provide a safer alternative to street BZDs, and help to retain patients in treatment and increase engagement with other interventions.

Some who do not currently prescribe BZD said they would only consider doing so if there was clear and robust clinical evidence of benefit and reduction in harms.

Among the 45 respondents who would prescribe BZDs, most would use clinical history (98%), urine / oral fluid screens (93%), and information on other prescribed drugs (91%) to inform their decision to prescribe. Slightly lower numbers would consider the patients social / family / domestic situation (80%) or a patient diary of drug use (73%). 'Other' responses included:

- Service user treatment aims / goals.
- Evidence of patient motivation to engage in services.
- Evidence of patient emotional readiness and motivation to cease BZD and other substance use.
- Discussion and negotiation with the patient, informed by understanding of why they use BZDs (e.g. using Inventory of Drug-Taking Situations)
- Comorbid mental / physical illness.

Most (80%) would prescribe diazepam, 4% replied diazepam as their first choice, with the option of lorazepam or nitrazepam if indicated. Eleven participants did not answer this question of whom 8 do not currently prescribe BZDs in addiction care. Reasons for preferring diazepam included:

- Long half-life.
- Patient and clinician familiarity.

- “It’s what patients know and want.”
- Available as 2mg tablets which supports incremental dose reduction.
- Included in local Formularies, often as frontline treatment.
- Good / reasonable safety profile.

Almost half (49%) would use a maximum starting dose of 25-30mg a day, with equal numbers (8%) willing to consider slightly higher (35-40mg) or lower (25-30mg) doses.

Views on dispensing arrangements were sought based on whether patients were also being prescribed opiate substitution therapy (OST). For patients currently on OST, respondents expressed a preference for BZD dispending in line with that for OST (56%) or daily dispensing (36%). Similarly, for patients not receiving OST, prescribers would consider daily (64%) in preference to weekly (9%) dispensing. Free text responses provided additional views on BZD dispensing arrangements. Most commented that decisions would be made on a case-by-case basis considering individual circumstances, assessment of risk (including of diversion), clinical presentation and patient preference. For patients on OST, two prescribers said they would consider daily or three-times per week dispensing initially, one would only consider short term prescribing during opiate detox and one would only prescribe BZDs for patients also receiving OST.

When describing BZD treatment plans, respondents were generally willing consider prescribing with the aim of either short term treatment aiming for cessation within around 12 weeks (53%) or maintenance prescribing while patients stabilise on OST and/or address other physical/psychological issues (47%). Twenty-four percent replied ‘Other’ and provided additional information. Almost all indicated the aim of treatment, agreed with the patient from the outset, should be for reduction and cessation. One noted that they have never treated a patient who has actively worked to reduce a BZD prescription once initiated and that dose reduction is a process of negotiation and best compromise. Several suggested that 12 weeks is too short in most cases, and two proposed detoxification schedules over 30 weeks or 6 to 12 months. One noted that the duration of detox is longer for patients with a longer duration of dependence. Another reported some patients prefer a shorter duration whilst others can be on diazepam for over 1 year depending on their ability to cope with dose reductions and their stability. Two prescribers discussed a period of ‘maintenance’ prescribing to allow patients to make other changes or engage in other aspects of treatment, e.g. achieve abstinence from illicit BZDs, address underlying psychological issues, or become stable on OST.

Those willing to prescribe BZDs expressed support for a range of methods to monitor adherence including urine / oral fluid screens (87%), patient presentation (67%), and drug diaries (53%). Only 16% would include supervised consumption. Twenty-seven percent suggested ‘Other’, highlighting:

- Patient presentation for signs of progress or deterioration.
- Self-reporting of tolerance, ‘topping up’ with illicit valium, or “chaotic compliance”.
- Engagement with other components of treatment, e.g. psychosocial support.
- Involvement in recovery work, crime, therapeutic engagement.
- Pharmacy reports.
- Drug screens that allow differentiation to check for use of non-prescribed BZDs.
- Developing an open, honest therapeutic relationship.

Table 5 BZD prescribing assessment, drug, dose, dispensing, and treatment plans (among those who would prescribe BZD to dependent patients).

Question	Response	n	n/45
19. What info. would you use to inform prescribing decisions?	Clinical history	44	98%
	Urine / oral fluid screen	42	93%
	Patient diary of drug use	33	73%
	Social / family / domestic situation	36	80%
	Other prescribed drugs	41	91%
	Other	7	16%
	Total		*
20. Which BZD would you prescribe?	Diazepam	36	80%
	Other	2	4%
	Missing	7	16%
	Total	**45**	**100%**
Why this BZD?	Duration of action	14	31%
	Familiarity (prescriber)	8	18%
	Familiarity (patient)	6	13%
	Formulary / policy	10	22%
	Total		
21. Starting dose	<10 mg	5	11%
	15-20 mg	8	18%
	25-30 mg	22	49%
	35-40 mg	8	18%
	Missing	2	4%
	Total	**45**	100%
22. What dispensing arrangements would you consider for patients receiving OST?	Same as ORT	25	56%
	Daily dispense - supervised (part/full dose)	5	11%
	Daily dispense - take away	11	24%
	Weekly dispense	0	0%
	Monthly dispense	0	0%
	Other	2	4%
	Missing	2	4%
	Total	**45**	**100%**
23 What dispensing arrangements would you consider for patients not receiving OST?	Daily dispense – supervised (part/full dose)	5	11%
	Daily dispense – take away	24	53%
	Weekly dispense	4	9%
	Other	10	22%
	Missing	2	4%
	Total	**45**	**100%**
24. What BZD treatment plans would you consider?	Aim reduction & cessation within 12 weeks	24	53%
	Consider maintenance	21	47%
	Other	11	24%
	Total		*

Question	Response	n	n/45
25. How would you prefer to monitor adherence?	Urine / oral fluid screen	39	87%
	Patient drug use diary	24	53%
	Supervised consumption	7	16%
	Patient presentation	30	67%
	Other	12	27%
	Total		*

- * = Percentages not shown where respondents could select multiple responses and totals >45

BZD prescribing: managing destabilisation

Prescribers were presented with several patient destabilisation scenarios and asked how they would initially approach these. The preferred approach in each was to continue BZD prescribing and increase other intervention elements and supports.

Table 6 Responding to patient destabilisation

	Patient begins to:									
	Use excessive amounts of alcohol		Use street BZDs		Use stimulants		Use illicit opiates		Report significant deterioration in mental health	
Discontinue BZD over a short period	11	24%	12	27%	8	18%	7	16%	0	0%
Slow-down/halt the reduction plan for 2–4 weeks	5	11%	2	4%	3	7%	1	2%	11	24%
Continue BZD & increase other supports	19	42%	17	38%	26	58%	26	58%	22	49%
Increase dosage, review support & patient goals	0	0%	4	9%	6	13%	9	20%	2	4%
Other	8	18%	8	18%	0	0%			8	18%
Missing	2	4%	2	4%	2	4%	2	4%	2	4%
Total	**45**	**100%**	**45**	**100%**	**45**	**100%**	**45**	**100%**	**45**	**100%**

Supports and services for BZD dependent patients

All respondents, regardless of their BZD prescribing intentions, were asked which supports and services they currently offer, or would like to be able to offer, to patients dependent on BZDs (Figure 2). More than 75% are currently able to offer motivational interviewing, relapse prevention counselling and general psychological support, and around two-thirds said their patients could access anxiety management interventions.

Prescribers were most interested in being able to offer BZD-dependent patients a peer support service, either clinician/pharmacist-led (80%) or peer-led (73%). Fifty-eight percent are keen to offer an intervention to help patients manage pain, and 38% would like to offer support with complex trauma.

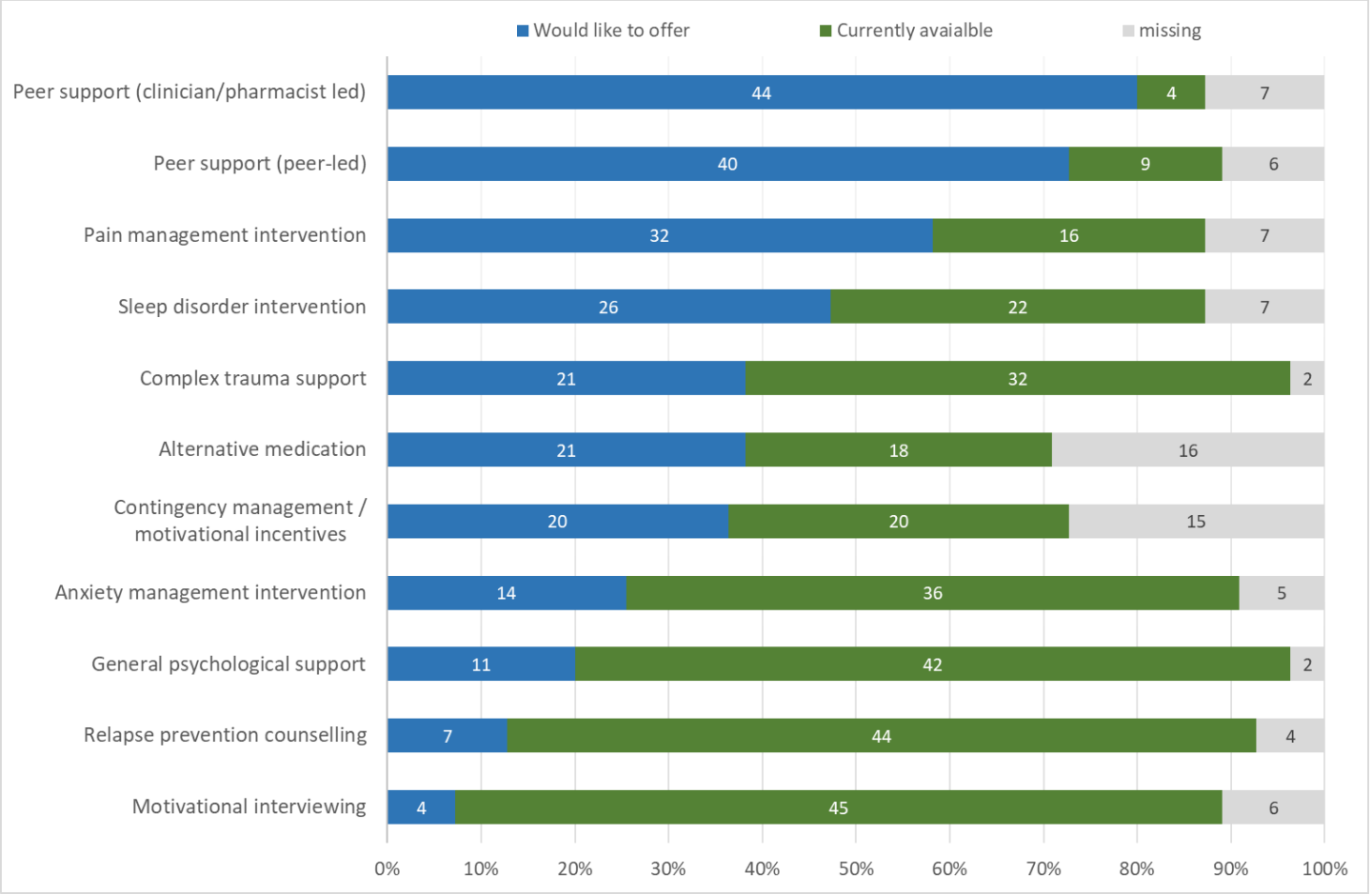

Figure 2 What other supports and services do you currently, or would you like to be able to, offer to BZD dependent patients?

4 Discussion

This survey engaged addiction prescribers from several disciplines and settings across most Health Boards. Results suggest that around 30% of patients receiving treatment for opiate addiction have a concurrent BZD problem, and this could be as high as 60% in some services.

Concurrent dependence on opiates and street BZDs is a significant issue among people presenting to addiction services and is reflected in patterns among Scottish drug-related deaths. There is geographical variance in approaches to the management of BZD dependence in addiction services, which is underpinned by the lack of robust evidence-informed clinical guidance and consensus. This is further complicated by the tension between clear evidence of harms, including death, resulting from BZD use among people with a drug problem, versus emerging experience of BZD prescribing as a harm reduction and treatment engagement strategy. This tension is clearly reflected in the views and practices of addiction prescribers identified in this survey.

It is also important to generate dialogue between prescribers, other health and social care professionals, and people with lived/living experience to identify a range of interventions and support – which may include, but is not limited to BZD prescribing – that are deemed to be acceptable, safe and effective. Ideally, these discussions should aim to develop a pragmatic consensus among addiction providers with involvement from current and potential patients. This should be seen as forming a starting point for Scottish practice, with the stated intent to revisit and review consensus in the light of emerging research and audit evidence.

There was a general consensus around the use of diazepam as the preferred treatment, due to the duration of effect, reasonable safety profile, and familiarity among prescribers and patients. This drug's availability in small dose tablets (2mg) was also seen as supporting dose reduction schedules. Prescribers generally agreed on considering a maximum starting dose of around 30mg per day. Dispensing would generally be aligned with OST pick-up or arranged for collection around three times per week.

There was also broad consensus that the ultimate goal of BZD prescribing should be gradual reduction and cessation of use. There was less agreement on a stated duration for this process and many comments recognised that the schedule should be informed by regular review of patient's experience of detoxification and evidence of stabilisation and engagement with other clinical and psychosocial supports. Most respondents highlighted the importance of increasing access to toxicology testing that provides more detailed information on the types of BZD consumed rather than basic "detected / not detected" results.

Prescribers generally preferred to be able to continue prescribing (including the option to slow or pause dose reductions) to patients who start to destabilise, and many wished to be able to offer additional supports to those experiencing difficulties. There was a strong call for the development of peer support groups for people with problem BZD use, and an appetite to offer interventions to help manage physical pain, anxiety, and trauma.

This survey builds on previous work to understand the views and experiences of prescribers and aligns with wider interest in developing responses to reduce risk of harm and improve outcomes for people with a BZD problem. A key limitation is the lack of a list of all Scottish addiction prescribers which would have provided a denominator for figures and supported a purposive sampling approach.

5 Conclusion

There is a pressing need to generate evidence of the harms and/or benefits of a range of interventions to help people who are dependent on BZDs, especially those also dependent on opiates such as heroin. If this is to inform clinical guidance and practice this information should result from robust and well-powered trials and wide scale clinical audit activities.

For a BZD prescribing intervention the following should be considered:

- Diazepam is first line treatment
- A period of stabilisation and maintenance would be advantageous before considering gradual dose reduction
- The move from maintenance to reduction should be a joint decision as part of an open and honest therapeutic relationship
- Urine or oral fluid testing that allows detection of prescribable vs. non-prescribable BZDs should be available
- Psychosocial interventions should include peer support and management of pain, anxiety and trauma.