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Original Research

Benzodiazepine and z-hypnotic prescribing from acute psychiatric inpatient discharge to long-term care in the community

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Abstract

Background: Benzodiazepine and z-hypnotic prescribing has slowly decreased over the past 20 years, however long-term chronic prescribing still occurs and is at odds with prescribing guidance.

Objectives: To identify the pattern of benzodiazepine and z-hypnotic prescribing in psychiatric inpatients at discharge and 12 months post-discharge.

Methods: Retrospective observational longitudinal cohort study of patients admitted to two adult psychiatric wards between June and November 2012 (inclusive) who were discharged with a prescription for a benzodiazepine or z-hypnotic drug. Routinely collected prescription data available from NHS Scotland Prescribing Information System was used to identify and follow community prescribing of benzodiazepine and z-hypnotics for a 12 month period post-discharge. Data were entered in Excel® and further analysed using SPSS 23. Ethical approval was not required for this service evaluation however Caldicott Guardian approval was sought and granted.

Results: Eighty patients were admitted during the study period however only those patients with a single admission were included for analysis (n=74). Thirty per cent (22/74) of patients were prescribed a benzodiazepine or z-hypnotics at discharge; 14 of whom received 'long-term' benzodiazepine and z-hypnotics i.e. continued use over the 12 month period. Seven patients received a combination of anxiolytics and hypnotics (e.g., diazepam plus temazepam or zopiclone). Long-term use was associated with a non-significant increase in median benzodiazepine or z-hypnotic dose, expressed as diazepam equivalents.

Conclusions: One in three patients were prescribed a benzodiazepine or z-hypnotics at discharge with 1 in 5 receiving continuous long-term treatment (prescriptions) for 12 months post-discharge. As chronic long-term B-Z prescribing and use still remains an issue, future strategies using routine patient-level prescribing data may support prescribers to review and minimise inappropriate long-term prescribing.

Keywords

Benzodiazepines; Patient Discharge; Practice Patterns, Physicians'; Psychiatric Department, Hospital; Psychiatry; Retrospective Studies; United Kingdom

INTRODUCTION

Benzodiazepine and z-hypnotic (B-Z) prescribing remains an issue across different care settings in North America, Australasia and Europe.[1-3] Whilst there has been some reduction in the use of specific benzodiazepines, it appears to be at the expense of z-hypnotics, whose usage has increased.[4] Much of the B-Z prescribing results in long-term chronic use[1,2] which is contrary to good practice, guidance, and terms of license.[5] B-Zs demonstrate marginal benefits for short-term relief of insomnia and some anxiety disorders[6] which are traits common in most psychiatric disorders and so may warrant short-term or 'as required' use in acute settings. However, issues with tolerance, dependence and adverse effects including cognitive impairment, depression and paradoxical effects i.e. disinhibition, anxiety and impulsivity, can limit their usefulness.[7] More recently, studies have reported increased mortality associated with B-Z use in various populations including those with psychiatric illness.[8,9]

Information regarding B-Z prescribing upon discharge from inpatient psychiatric services is limited, although a few studies have reported that 36%, 37% and 50% of patients in New Zealand[10] and the UK[11,12] received B-Zs on discharge. More importantly, information is lacking regarding their prescribing post-discharge which may contribute to potentially inappropriate long-term prescribing in primary care. At a practical level, routine patient-level prescribing information required to follow a patient's journey from hospital to community care is often lacking or incomplete in most health care systems. However, recent developments in Scotland in the collection and processing of routine patient-level primary care prescription dispensing data can now make this possible.[13] This paper reports on a study which set out to identify the pattern of B-Z prescribing in psychiatric inpatients at discharge and 12

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months post-discharge using routine patient-level prescribing and dispensing information.

METHODS

Ethical opinion was sought from the West of Scotland Research Ethics Service on the use of anonymised patient-level data for the study. The advice received was that the study was considered to be service evaluation and hence did not require research ethics approval. Nevertheless, Caldicott Guardian approval was sought and granted by the NHS Greater Glasgow and Clyde Prescription Data Governance Group.

A retrospective observational longitudinal cohort study design was applied. All patients admitted between June and November 2012, to two acute adult wards in the same psychiatric hospital, in the southwest region of the health board area were eligible for inclusion. Individual patient-level data including: Community Health Index (CHI) number; age; gender; residential postcode to allow mapping of Scottish Index of Multiple Deprivation (SIMD) codes[14]; primary psychiatric diagnosis and admission status (informal or detained) were collected using a standardised data collection form. Patients with multiple admissions during the study period were excluded, as it was assumed these individuals were 'more unwell/complicated' and so any B-Z prescribed would not necessarily be representative of 'routine practice'.

In Scotland, healthcare is delivered by a tax funded National Health Service (NHS) and service users are assigned a CHI number. The CHI number acts as a unique identifier containing details of gender and date of birth.[15] The CHI number enables linkage to other national datasets which use the CHI number as their point of reference such as the national Prescribing Information System (PIS). The PIS contains information pertaining to all NHS prescriptions that have been dispensed in the community i.e. primary care.[13] The overwhelming majority of which are prescribed by the patient's general practitioner (GP), with a minority of prescriptions being written by non-medical prescribers (e.g. nurses and pharmacists), Out of Hours and speciality outpatient services and dispensed in community. The CHI number was used to identify patients who had received a prescription, in primary care, for a B-Zs during within 12 months after discharge. The prescriptions included the patients CHI number and medication details: drug name, dosage form, strength, quantity dispensed, dosage instructions and date dispensed.

Patient-level admission data and B-Z prescribing data were matched for the 12 months following discharge. Details of any B-Z dispensed at months 1 to 12 post-discharge including the name of the medication and the total daily dose were collected from PIS. Where dosage instructions were unavailable or ambiguous e.g. 'as directed' or 'as required', the average daily dose was estimated by dividing the total prescription dose by 28 days e.g. 14 temazepam 10mg tablets (one as required) is 140mg/28 and would be recorded as a total daily dose of 5mg temazepam. As the majority of 'as required' and 'as directed' prescriptions were being dispensed monthly (e.g. zopiclone 7.5 mg tablets, 14 tablets, dispensed each month) and all regular prescriptions were supplied as 28 day prescriptions.

To enable comparison of individual patient-level total daily doses at various times post-discharge, diazepam dose equivalents were calculated for the different B-Zs in line with previous guidance.[16,17] Since most clinical guidelines and product licenses' recommend restricting B-Z use to 2-4 weeks[5,6], long-term or inappropriate use was defined as 'receiving the medication for more than 4 weeks'. All data was anonymised prior to analysis.

Data were entered in Excel and further analysed using SPSS v.23. Where appropriate, due to small cell sizes containing data counts <5, data were aggregated into 'quarters' for the 12 months post-discharge and were defined as: quarter 1=month 1, 2 and 3, quarter 2=month 4, 5 and 6, etc. Where appropriate the Chi-square test or Mann-Whtney U test were used. Since the diazepam dose equivalents did not exhibit normal distribution, the Mann-Whitney U test was used to assess statistical difference between discharge doses and quarter 4 doses for all patients prescribed B-Zs.

RESULTS

Eighty patients were admitted during the study period, six of whom had multiple admissions and were thus excluded. The remaining 74 patients had a mean age of 40 years (range 18-77 years), 45 of whom (61%) were male with just over half (54%, n=40), according to the SIMD score, living in the 20% most deprived areas of Scotland. The most

Table 1.Patient characteristics and demographics at discharge

Patient sample n=74	B-Z prescribed n=22 (30%)	B-Z not prescribed n=52 (70%)	
Gender			
Male n=45 (%)	14 (64)	31 (60)	
Female n=29 (%)	8 (36)	21 (40)	chi-sq=0, df 1, p=1
Median age years (range)	39 (26 to 62)	41 (18 to 77)	Mann-Whitney U test p=0.511
SIMD most deprived quintile (%)	12 (55)	52 (54)	chi-sq =0.04, df 1, p=0.814
Primary Psychiatric diagnosis			
Schizophrenia F20	7	18	
Mood disorder F30	5	11	
Personality disorder F60	5	9	chi-sq =0.4, df 3, p=0.940
Other: anxiety disorder, substance misuse, unknown	5	14	
Admission status (%)			
Informal	15 (68)	36 (69)	chi-sq =0.03, df 1, p=0.862
Detained	7 (32)	16 (31)	

B-Z: Benzodiazepine or z-hypnotic. Primary diagnosis grouped as per International Statistical Classification of Diseases and Related Health Problems 10th (ICD-10) Revision coding.[37]

common primary diagnosis was schizophrenia (n=25), followed by mood disorder (n=16), personality disorder (n=14), substance misuse (n=10) and anxiety disorder (n=7). Fourteen patients (19%) had multiple psychiatric co-morbidities. Twenty-three patients (31%) were detained under Mental Health Act legislation on admission.

Twenty-two patients (30%) were prescribed B-Z medication at discharge, five (7%) of whom received a combination of an anxiolytic and a hypnotic, e.g. diazepam plus temazepam or zopiclone, with males more commonly prescribed B-Zs (Odds Ratio 1.19, 95% CI 0.42 to 3.32). No significant differences in demographics were found between patients prescribed B-Zs and those not prescribed B-Zs at discharge (Table 1). The most commonly prescribed B-Zs were diazepam (n=11), zopiclone (n=8) and nitrazepam (n=3), with z-hypnotics more commonly prescribed than benzodiazepine-hypnotics. The median total daily dose expressed as diazepam equivalents was 8mg (range 2.5mg to 50mg). Four patients, not discharged on B-Zs, started treatment within three months of discharge and remained on long-term treatment.

B-Z prescribing for 12 months post-discharge

Of the 22 patients discharged on B-Zs, six patients did not receive any further B-Zs prescriptions. Of the remaining 16 patients (73%, 9 males and 7 females) who continued to receive repeat B-Z prescriptions post-discharge, 14 individuals received 'long-term' treatment including 9 patients receiving B-Zs continuously for 12 months; 3 patients for 12 months with a single 4 week break in their supply, 1 patient for 10 months and another for 7 months. Only two patients received less than a 4 weeks supply post-discharge. Three patients who were not originally discharged on B-Zs started and remained on long-term treatment: two for 12 months and one for 6 months continuously.

Seven of the 16 patients were dispensed diazepam in combination with either nitrazepam, temazepam or a z-hypnotic. Four of these individuals were prescribed these as 'regular' doses with the remainder using them on an 'as required' basis. Another 9 patients from the original cohort were found to have started a B-Z within the 12 months post-discharge period. Five of whom received short-term irregular treatment but 4 people received regular (long-term) prescriptions of a single B-Zs.

For all 25 patients who received B-Zs in the 12 months post-discharge, 275 B-Z prescriptions had been dispensed. The most frequent was diazepam (n=123, 45%, median total daily dose of 15mg, range 2mg to 50mg), followed by zopiclone (n=46, 17%, 7.5mg, 3.75mg to 15mg), nitrazepam (n=39, 14%, 10mg, 2.5mg to 20mg), zolpidem (n=28, 10%, 10mg, 5mg to 10mg), temazepam (n=21, 8%, 20mg, 20mg to 60mg) and lorazepam/lormetazepam (n=18, 7%). The most common primary diagnosis amongst this cohort was schizophrenia (n=7), personality disorder (n=5) and mood disorders (n=5). The remainder were diagnosed with either an anxiety disorder, substance misuse or had an 'unknown' diagnosis.

B-Z long-term use

Of the 14 patients discharged on B-Zs who subsequently received long-term regular prescriptions there was a statistically non-significant (Mann-Whitney U test, p=0.519) increase in median doses (expressed as diazepam equivalents) from 10mg at discharge to 15.8mg at 12 months, Figure 1. For all patients (n=18) who received long-

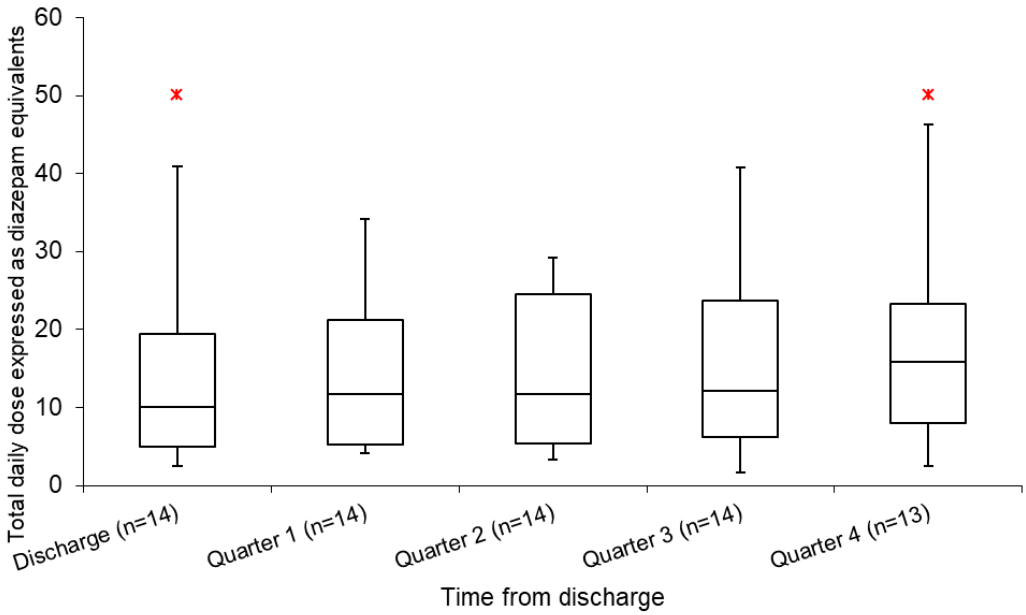

Figure 1, Box plot of total daily doses (expressed as diazepam equivalents) for patients prescribed Benzodiazepines or z-hypnotics at discharged and long-trem.
Quarter 4, n=13 patients as one patient did not receive Benzodiazepines after 7 months of continuous treatment. Mann-Whitney U test p=0.519 discharge versus quarter 4.

term B-Zs including those not prescribed at discharged, the most common primary diagnoses were schizophrenia (33%) followed by depression (22%) and personality disorder (22%). While the median dose for this group increased from 10mg at discharge to 14.6mg at 12 months, Figure 2.

DISCUSSION

One in three patients in this cohort were prescribed B-Zs at discharge. This is comparable to other studies[10,12], but significantly lower than a previous UK study.[11] One in five patients were also found to receive continuous, long-term, B-Zs prescriptions 12 months post-discharge. Most clinicians are aware of the problems associated with chronic B-Z use, and that courses should be limited to a maximum of 2-4 weeks[5], stopping or reducing chronic prescribing in this instance may be more challenging. This may be partly due to patient or carer expectations of continuing treatment, or GPs having reservations in reducing or stopping B-Zs as they were initiated by specialist mental health services. GPs may also lack training or the psychiatrists support in managing the reduction and withdrawal of long-term B-Zs.[18]

B-Z tolerance can develop quickly, particularly if there is dose escalation, and our study is the first to our knowledge to demonstrate small escalations in median doses over time. One factor acknowledged by others as contributing to dose escalation is concomitant use of 2 or more B-Zs. This was observed in a small proportion of our patients and was higher than that reported amongst a Spanish sample.[19] Diazepam was the most commonly prescribed B-Z, with one patient's dose being above the licensed maximum daily dose of 30mg at discharge and at three months post-discharge.[5] The median discharge B-Z dose, expressed as diazepam equivalents, of 10 mg daily is nearly half that previously reported[12] although the dose range was similar to that reported by Summers and Brown.[11] Some differences will be due to patient characteristics including severity and nature of illness or prescriber characteristics which can be influenced by local practice and policy[20], such as z-hypnotic use in preference to benzodiazepine-hypnotics, e.g. temazepam, due to the potential for misuse and drug-related deaths.[21,22]

The majority of those prescribed B-Zs had a diagnosis of schizophrenia, followed by mood disorders and personality disorder, as with other studies[10-12], although Summers and Brown more commonly reported alcohol dependence as the main indication.[11] The long-term use of B-Zs in people with schizophrenia may be to address suboptimal antipsychotic response or an attempt to achieve an antipsychotic sparing effect.[23] However, the evidence supporting such strategies is lacking[24], and more worryingly, B-Z use is associated with increased mortality for people with schizophrenia.[9] For those with mood disorders, selective serotonin reuptake inhibitors (SSRIs) use has been associated with greater longer-term B-Z use, and in part may be due to SSRIs exacerbating insomnia and agitation, especially at higher doses.[25,26] A possible reason for long-term B-Z use in personality disorder could be the challenging nature of the patients who present with a range of behaviours. Nevertheless, B-Zs can provoke aggressive behaviour and increase the risk of suicide

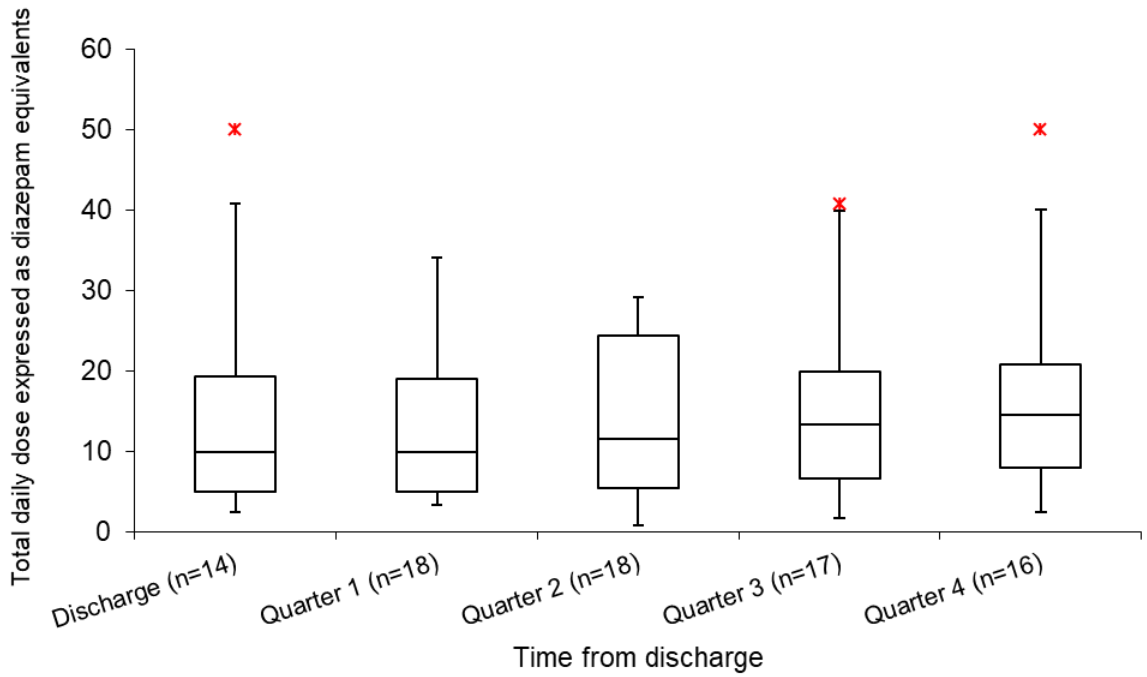

Figure 2. Box plot of total daily doses (expressed as diazepam equivalents) for all patients receiving long-term Benzodiazepines or z-hypnotics post-discharge.
Number of patients receiving long-term Benzodiazepine or z-hypnotics varied during the 12 months. Mann-Whitney U test p=0.498, discharge versus quarter 4.

amongst people with personality disorder.[27] Another problem is that concomitant B-Z use can reduce the efficacy of some psychological therapies, particularly for anxiety.[28] Alternatives such as sedating antipsychotics are not without their own substantial cardiometabolic risks and require more intensive physical health monitoring.[29,30]

The main strength of this study is that it uses routine patient-level primary care prescribing data for dispensed prescriptions containing the CHI number, allowing primary and secondary care data to be 'linked'. This enables relatively easy longitudinal assessment of long-term routine prescribing, without the demands of significant resource implications which previously made this work very challenging and prohibitive prior to PIS data being available. Another strength was that we did not solely rely on the manual collection of prescribing data and the inherent problems associated with that type of data collection.

The main limitations, as with other studies, is that we were unable to assess concordance and compliance with the prescription directions and actual drug use, including possible self-medication with non-prescribed B-Zs[31,32], as well as patient, carer, ward staffing, and prescriber factors which are known to be associated with variations in B-Z prescribing. The lack of post-discharge information such as: if prescribers discussed, attempted or supported patients with B-Z reductions; or if patients' experienced crises which did not require admission but did require extra 'as required' doses which may have inadvertently continued, all contribute to potential limitations affecting the depth and totality of the analysis. Finally, some may consider findings to be limited in their generalisablity; however, this study's findings may be of interest to those working in primary and secondary care serving populations with similar demographics.

As already acknowledged, a challenge for practice is ensuring good communication between specialist services and general practice[33,34] to help minimise inappropriate long-term B-Z prescribing and avoidable drug-related harms. In recent years, pharmacists working within general practices have been supporting GPs to review patients receiving B-Zs; including those attending mental health services, and where appropriate support joined up working.[35] This study demonstrates the utility of routine patient-level PIS prescribing data and 'linked data' in identifying such prescribing issues within specific patient groups at a local level. The use of PIS data will enable national, regional, and local services to target resources to achieve reductions in inappropriate prescribing of various medicines, including psychotropics in line with clinical guidance and policies. It can also be used to enable clinicians to identify high-priority patients for regular medication review in line with national polypharmacy guidance supporting the reduction in inappropriate medicines and associated avoidable drug risks, as well as assessing the impact of regional and national prescribing strategies and interventions.[36] The ability to 'link' PIS patient-level data with other datasets at local, regional and national levels opens up significant potential for pharmacists and non-pharmacist led pharmacovigilance and pharmacoepidemolgical studies, as well as evaluating changes in routine practice at a local, regional or national level. However, patient-level PIS data could also be used to support and enable secondary care specialists to review and reflect on prescribing as general practitioners and practice pharmacists currently do.

CONCLUSIONS

One in three patients were prescribed B-Zs at discharge with 1 in 5 receiving continuous long-term B-Z prescriptions 12 months post-discharge. For those receiving regular long-term benzodiazepine and z-hypnotics prescriptions there was a small non-statistically significant increase in median prescribed dose during the 12 months post-discharge. As chronic long-term B-Z prescribing and use still remains an issue, future strategies using routine patient-level prescribing data may support prescribers to review and minimise inappropriate long-term prescribing.

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CONFLICT OF INTEREST

None.

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