

## Rational Deprescribing of Benzodiazepines and Newer Benzodiazepines in Psychiatric Outpatient and Inpatient Department of Tertiary Care Hospital

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### Abstract

**Background:** Despite the fact that clinical guidelines forbid this practice, BZDs and Z medications are still used for longer than the time of prescription in current clinical practice. This practice results in adverse effects. The purpose of this research was to determine whether or not it would be possible to stop giving BZDs and Z medicines to patients who had been misusing these medications for far longer than the allotted time frame. This study also looked into the Sleeping well (QoS) and financial savings that patients who were deprescribed experienced.

**Methods:** A prospective interventional study was conducted at the Psychiatric Department in both the inpatient and outpatient settings. Over the course of the study's Twelve -month recruitment period, 109 patients in all were enrolled, which was based on the inclusion criteria. Following a discussion with the prescribing psychiatrist, suggested that unsuitable BZD and Z-drugs users begin the process of deprescribing their medications. After they were taken off their medications, For the next 30 days, twice a month the patients were examined. To do the QoS analysis, the Pittsburg Sleep Quality Index (PSQI) was used as a measurement. Before and after the intervention, the total cost of medications that each patient had to pay each month was calculated and compared between the two groups.

**Results:** Following the intervention, 41 (37.61%) BZD users had their prescriptions for the drug revoked, which meant that their dose was either reduced 6 (5.5%), completely discontinued 28 (25.68%), or use a prescription for is opus sit (SOS) BZD 7 (6.4%). 43 patients (39.44.36%) continued BZDs as prescribed by the algorithm. The BZD that was deprescribed the most commonly was clonazepam 34 (82.92%). Patients' quality of life and the deprescription of BZDs were linked, according to p-value (<0.05). After deprescribing BZDs, a statistically significant cost reduction was seen (Z=5.6244, p=<0.001).

**Conclusion:** Deprescribing BZDs was linked to a decrease in consumption; applying deprescribing procedures to inappropriate BZD users is doable, enhances service quality, and has positive financial implications.

### Highlights

1. This is the study to investigate whether or not it would be possible to stop administering BZDs.
2. Patients who use BZDs (clonazepam, alprazolam, zolpidem) for an unnecessarily long period of time or for longer than the length that was prescribed are candidates for deprescribing.

**Keywords:** Deprescribing, Benzodiazepines, Polypharmacy, and Sleep Quality

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## Introduction

The practice of deprescribing that was established relatively recently to represent the practice of terminating or reducing the dosage of a drug or prescribing on an urgent basis when a patient is not obtaining benefit or is exposed unacceptably high dangers [1]. Concurrent observation and periodic evaluation based on patient- and drug-related data variables are required for deprescribing to be effective [2]. Hypnotic-sedative chemicals such as benzodiazepines (BZDs) and Z medicines have numerous medical uses, including the mitigation out of fear, sleeplessness, panic disorder and social anxiety, OCD, drug cessation or the adverse effects of antipsychotics and antidepressants. Used as an antiepileptic and muscle-relaxing drug [3].

Morbidity and death are both increased by inappropriate drug prescribing. Clinical guidelines state that for the most effective treatment of extreme phobia or sleeplessness, Use BZD and Z-drugs only as directed by your doctor., i.e. at conventional treatment dosages using just one BZD or Z-drug kind at a time, and for as short a term as possible [4]. When BZD and Z-drugs are used properly, side effects are uncommon [5].

Cognitive impairment, physical reliance (58–100%), as well as psychomotor dysfunctions like daytime drowsiness, ataxia, hip fractures, and car accidents caused by falls or postural instability (60%) are all common adverse drug reactions (ADRs) of BZDs and related medicines [6]. Lately, concerns about early (OR > 1 in 33 trials) Mortality and overdose

danger (29.4%) have been on the rise. The literature on this topic is extensive [7].

A study carried out in India indicated that, as a result of health ignorance, Patients take their prescriptions for a longer period of time than is necessary [8]. So, it is true to say that preventing chronic use (use for more than a month) is an essential part of prescription BZD and Z drugs, and that if strictly followed, dependence and withdrawal would only be a theoretical rather than a real issue [9]. Yet, a significant portion of patients continue to use BZDs and Z-drugs for an extended period of time, necessitating the careful planning of cessation programmes [10].

The current research is aimed at determining whether or not deprescribing methods can be implemented and studying the elements that affect deprescribing [11]. This is the first study to analyse the likelihood of deprescribing among India's unsuitable BZD users., which is surprising given the prevalence of the practise. So, the objective of the current investigation was to evaluate the practicability of BZDs deprescribing in the Psychiatric Service's patient population.

## Material and Methods

This is a prospective and interventional study was conducted in the Department of Psychiatry at a Tertiary care Teaching Hospital From August 2017 to August 2018. The project was green-lighted after a thorough assessment.

Patients were eligible if they were at least 18 years old and were currently using a BZD or Z-drug. Those having a history of alcoholism,

epilepsy, or other conditions that need Antiepileptic drug use was also excluded from the analysis.

According to the inclusion criteria, a total of 109 patients were enrolled. Researchers gathered information for the study by examining medical records, patient interviews, and prescription forms. Before beginning BZD and Z-drug deprescribing According to the BZRA Deprescribing protocol, the patient's and prescribing psychiatrist's agreement was obtained. We were able to collect this data from patients by using a specially designed data collection form.

The presence and severity of withdrawal symptoms following the discontinuation or the Benzodiazepine Withdrawal Symptom Questionnaire [BWSQ] was used to evaluate the reduction of BZDs and Z-drugs. Users of BZDs and Z-drugs had their sleep quality measured before and after using the Pittsburg Sleep Quality Index to stop prescribing (PSQI).

### Statistical Analysis

Statistics based on frequency and percentage were used to display the category variables. Quality-of-life differences between groups deprescribing BZDs and those continuing to use them, as well as between the two groups, were analysed using the Chi-square test. The average cost of BZDs and Z-drugs prescribed to each patient before and after the intervention

was determined. Median and interquartile range drug prices were compared between the two groups.

The statistical significance of the difference in cost reductions between the two groups was investigated using a Wilcoxon signed-rank test. P-values of less than 0.05 were considered to be indicative of significant results. The data was categorised and analysed using the IBM SPSS Statistics 21.0 for Windows application.

### Results

Sixty(55.04%) males and forty-nine(44.95%) females who used Z-drugs or BZD were included in the study. The highest prevalence of BZD use (54; 49.54%) was observed among individuals aged 18–35, followed by the lowest prevalence (43; 39.44%) in the age range of 36–55. The inpatient percentage was at 49(44.95%), with the outpatient rate at (55.04%) for 60patients.

Only 39(35.77%) were single adults, while 67(61.46%) were married. Out of 109 people, 45(41.28%) had jobs and 38 (34.86%) did not. The vast majority of BZD prescriptions were for clonazepam (76.14%), followed by lorazepam (13.76%). One (2.75%) alprazolam, one (2.75%) diazepam, and three (4.58%) zolpidem were prescribed to the remaining 5 patients. There were 12(11%), 34(31.19%), and 63 (68.67%) people who used BZDs for a period of 4 weeks or less, 3 months, or more, respectively.

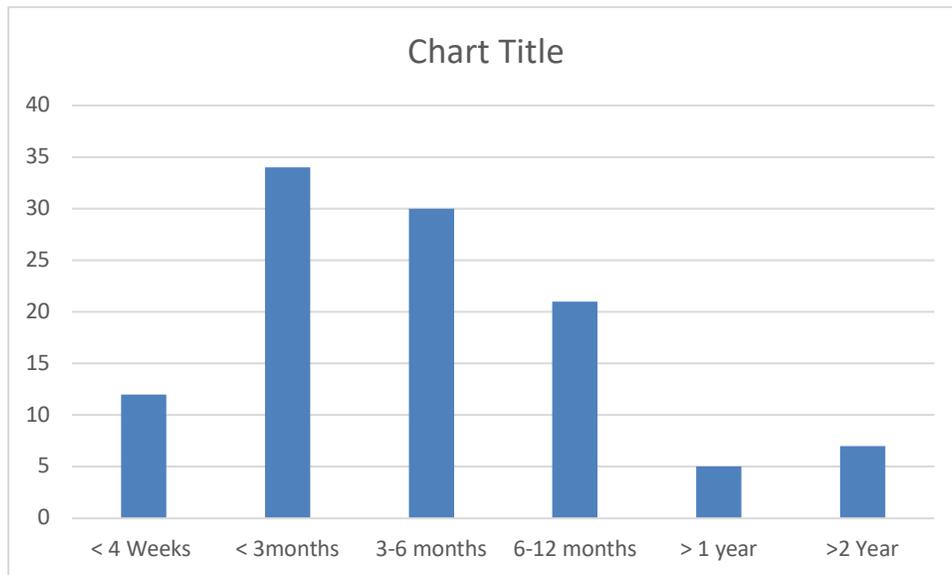
**Table 1: Demographic Detail of the Patients**

| Age            | N (%)      |
|----------------|------------|
| 18-35 Years    | 54(49.54%) |
| 36-55 Years    | 43(39.44%) |
| 56-65 Years    | 5(4.58%)   |
| 66-85 Years    | 7(6.42%)   |
| Sex            |            |
| Male           | 60(55.04%) |
| Female         | 49(44.95%) |
| Category       |            |
| Inpatient      | 49(44.95%) |
| Outpatient     | 60(55.04%) |
| Marital Status |            |

|                        |            |
|------------------------|------------|
| Married                | 67(61.46%) |
| Un Married             | 39(35.77%) |
| Other                  | 3(2.75%)   |
| Employment             |            |
| Employed               | 45(41.28%) |
| Unemployed             | 38(34.86%) |
| Self employed          | 26(23.85%) |
| Type of BZD prescribed |            |
| Clonazepam             | 83(76.14%) |
| Lorazepam              | 15(13.76%) |
| Alprazolam             | 3(2.75%)   |
| Diazepm                | 3(2.75%)   |
| Zolpidem               | 5(4.58%)   |
| Duration of use        |            |
| < 4 Weeks              | 12(11%)    |
| < 3months              | 34(31.19%) |
| 3-6 months             | 30(27.52%) |
| 6-12 months            | 21(19.26%) |
| > 1 year               | 5(4.58%)   |
| >2 Year                | 7(6.42%)   |

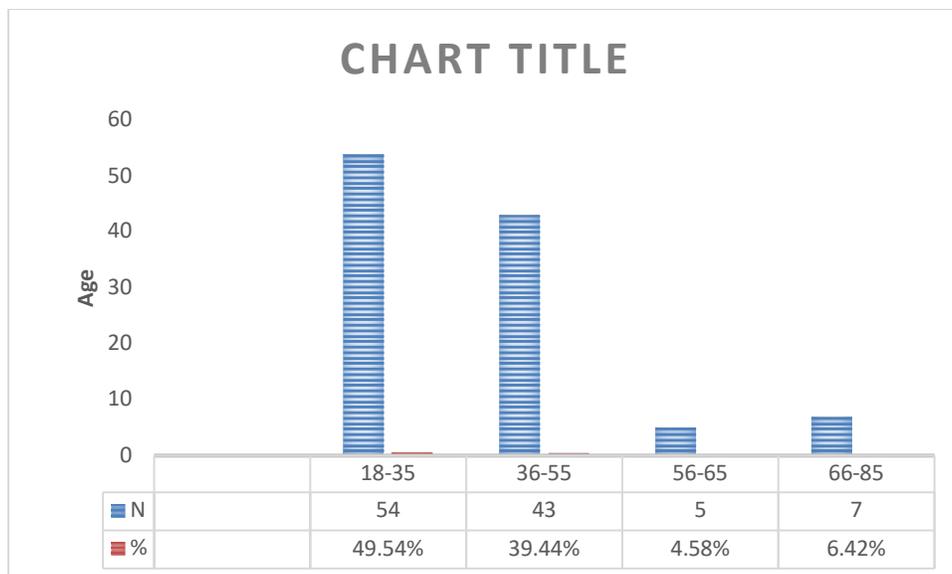
In all, 109 patients on BZDs were asked to participate in the study, and of those, the same number gave their approval to do so. Twelve patients were deemed to have rationally utilised (used BZDs for less than 4 weeks) according to our findings. Although the use of BZDs for less than three months in 34 patients and longer than three months in 63 patients was deemed to be unsuitable. These 99 BZD abusers may have been good candidates for detox. Just 44 of the initial 99 patients kept using BZD after 2 stopped taking it on their own, 10 were lost to follow-up, and 3 had a change of physicians.

Fifty-four patients kept using BZDs despite the algorithm's recommendation that they be discontinued. Thus far, 40 patients out of a total of 99 who were inappropriately prescribed BZD have agreed to be deprescribed. Three-thirty-three patients began dose reduction, and seven received SOS prescriptions. Among the 33 patients who began dose tapering, 27 were told to stop taking their medication altogether, and 6 were given instructions to keep reducing. The number of prescriptions for clonazepam decreased by 36 percent (32 percent for all BZDs) while for lorazepam it decreased by 4 percent (4%).



**Graph 1: The Age Distribution of Benzodiazepine Deprescribing**

Three(42%) BZD users between the ages of 66 and 85 were deprescribed, followed by 16(37.20%) users between the ages of 36 and 55, and 20 (37.03%) users between the ages of 18 and 35.

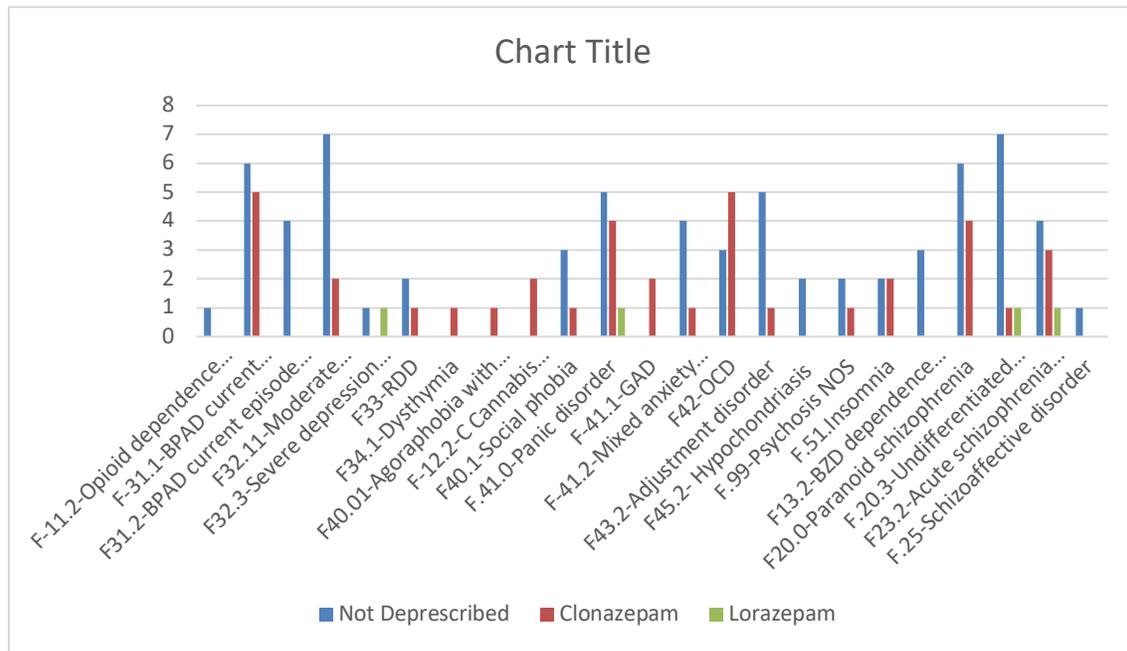


**Graph 2: Discontinued Benzodiazepine Prescriptions and Related Conditions**

ICD-10 data revealed that among the inappropriate users of BZDs, the most prevalent revocation of prescription was for patients diagnosed with panic disorder 5(4.58%) (F-41.0).

The quality of service was also evaluated using a questionnaire called the PSQI. Ten patients could not be tracked down because they moved, switched doctors, or simply stopped taking their prescription, and 10 were

reasonably deprescribed, 84 subjects were evaluated for quality of life. For the deprescribed group of 40, 38 (95%) experienced high-quality sleep whereas only 2 (5%) did not.



Graph 3

Table 2: Symptoms of Withdrawal from Prescription Drugs and Benzos

| The ICD-10 diagnosis                                                | Deprescribed Benzodiazepines Type |            |           | Total |
|---------------------------------------------------------------------|-----------------------------------|------------|-----------|-------|
|                                                                     | Not Deprescribed                  | Clonazepam | Lorazepam |       |
| F-11.2:Withdrawal symptoms and opioid dependency                    | 1                                 | 0          | 0         | 1     |
| Current episode of mania without psychotic symptoms, F-31.1-BPAD    | 6                                 | 5          | 0         | 11    |
| Current episode of mania with a psychotic manifestation, F31.2-BPAD | 4                                 | 0          | 0         | 4     |
| Mild depression with somatic symptoms, code F32.11                  | 7                                 | 2          | 0         | 9     |
| F32.3-Severe depression without indications of psychosis            | 1                                 | 0          | 1         | 2     |
| F33-RDD                                                             | 2                                 | 1          | 0         | 3     |
| F34.1-Dysthymia                                                     | 0                                 | 1          | 0         | 1     |
| F40.01-Panic disorder and agoraphobia                               | 0                                 | 1          | 0         | 1     |
| F-12.2-C symptoms of cannabis dependence                            | 0                                 | 2          | 0         | 2     |
| F40.1: Social anxiety                                               | 3                                 | 1          | 0         | 4     |
| Panic disorder, F.41.0                                              | 5                                 | 4          | 1         | 10    |
| F-41.1-GAD                                                          | 0                                 | 2          | 0         | 2     |
| F-41.2-Mixed Depression and Anxiety                                 | 4                                 | 1          | 0         | 5     |
| F42-OCD                                                             | 3                                 | 5          | 0         | 8     |
| Adjustment disorder, F43.2                                          | 5                                 | 1          | 0         | 6     |

|                                                            |    |    |   |     |
|------------------------------------------------------------|----|----|---|-----|
| Hypochondriasis, F45.2                                     | 2  | 0  | 0 | 2   |
| Psychosis F.99 NOS                                         | 2  | 1  | 0 | 3   |
| F.51.Insomnia                                              | 2  | 2  | 0 | 4   |
| Syndrome of F13.2-BZD dependency                           | 3  | 0  | 0 | 3   |
| Paranoid schizophrenia, code F20.0                         | 6  | 4  | 0 | 10  |
| Undifferentiated schizophrenia, code F.20.3                | 7  | 1  | 1 | 9   |
| F23.2-Acute psychotic illness that resembles schizophrenia | 4  | 3  | 1 | 8   |
| Schizoaffective disorder type 25                           | 1  | 0  | 0 | 1   |
| Total                                                      | 68 | 37 | 4 | 109 |

Patients who were deprescribed were also evaluated for withdrawal symptoms using the BWSQ. Two patients in the deprescribed group (50%) experienced no withdrawal symptoms, while 37 patients (100%) on lorazepam and 4 patients (100%) on clonazepam experienced mild to moderate withdrawal symptoms.

**Table 3: Benzodiazepine Withdrawal Symptoms and Deprescription Drugs**

| BZD Class  | Prescribed | Deprescribed | No withdrawal Symptoms | Moderate Withdrawal Symptoms | Severe Withdrawal Symptoms |
|------------|------------|--------------|------------------------|------------------------------|----------------------------|
| Clonazepam | 83(76.14%) | 37(33.94%)   | 37(100%)               | 0                            | 0                          |
| Lorazepam  | 15(13.76%) | 4(3.67%)     | 2(50%)                 | 2(50%)                       | 0                          |

Post intervention amongst the continuing group the median cost incurred was 242.809 (35.401606.60) and amongst the deprescribed group the median cost incurred was 238.69(0.00-1108.45). Statistically significant cost reduction was observed after deprescribing BZDs ( $Z=5.6244$ ,  $p<0.001$ ).

**Table 4: Cost analysis of Benzodiazepines continuation and deprescription**

| Category   | Continuing(N= 43) |                | Deprescribed (N= 41) |                |
|------------|-------------------|----------------|----------------------|----------------|
|            | Prev-Invention    | Post-Invention | Prev-Invention       | Post-Invention |
| Median     | 247.476           | 242.809        | 275.6                | 238.69         |
| Minimum    | 36.77             | 36.77          | 34.4                 | 1              |
| Maximum    | 2135.63           | 1568.63        | 1715.74              | 1108.45        |
| Percentile | 25                | 145.2          | 145.2                | 93.2           |
|            | 50                | 247.495        | 244.79               | 280.654        |
|            | 75                | 370.652        | 370.475              | 461.154        |

## Discussion

In this study, 109 BZD patients and their prescription histories were analysed. Of the participants in the study, men made up 60 (55.04%) and women made up 49 (44.95%) of the BZD users. In a study, similar outcomes

were discovered by Meagher *et al.*, which found that 88 (56% of) males utilised BZDs more frequently than females 70 (44%) [12]. The highest incidence of BZD use was found in those aged 18–35 (54; 49.54%), followed by

those aged 36–55 (43; 39.44%). The usage of BZD, however, was found to increase with age in both males (26% of those questioned) and women (74% of those surveyed), according to a study by Fourier *et al* [13]. Our data showed that 12 (11%) participants were considered to be appropriate BZD users (4 weeks), 34(31.19%), were categorised as short-term users (under 3 months), whereas 63 (57.79%) were categorised as long-term users (over 3 months).

12 (11%) of the 109 trial participants were lost to follow-up after the intervention. Forty people, or 30.69 percent, had their BZD prescriptions revoked. Six patients (5.5%), twenty-seven patients (24.8%), and seven patients (6.4%) had their drug consumption frequency changed to an SOS basis. According to the BZRA algorithm, 44 patients, or 40.36 percent, were told to keep taking benzodiazepines (BZDs) for a variety of reasons, including but not limited to: sleep disorders (e.g., restless legs syndrome), untreated anxiety, depression, BZDs that work for anxiety and a medical condition that may be causing or aggravating insomnia [9]. Only two patients (1.8%) quit using BZDs on their own (fearing dependency), three (2.8%) found a new physician, and ten (9.2%) were logically deprescribed less medication (i.e. within 4 weeks duration).

Naono-Nagatomo *et al.* discovered in another study that patients get BZDs for prolonged periods of time after trying to reduce their dosage but failing [14]. This research showed that patients with chronic insomnia might safely reduce their BZD doses while continuing ramelteon treatment. Patients' symptoms and quality of life improved once ramelteon-containing regimens were added to their treatment plans (Naono-Nagatomo *et al.*,2018) [14]. Three (42%) BZD users between the ages of 66 and 85 were deprescribed, followed by 16 (37.20%) users between the ages of 36 and 55, and 20 (37.03%) users between the ages of 18 and 35. This suggests that the rate of deprescription

among the elderly was greater than that among adults generally. Patients with panic disorder accounted for 5 (4.58%) of those de-prescribed, whereas those with BPAD with current episode mania without Journal Pre-proof 10 psychotic symptoms accounted for 4 (3.66%) and those with OCD accounted for 2 (1.5%) of those de-prescribed (OCD).

The majority of BZDs that were taken off the market were clonazepam (37, or 33.94%) and lorazepam (4, or 4%). Three BZD users aged 66–85 (42%) was deprescribed the drug, as were 16 users aged 36–55 (37.20%), and 20 users aged 18–35 (37.03%). This data suggests that deprescription was more common among the elderly than among individuals in general. Five patients (4.58%) were diagnosed with panic disorder, four were diagnosed with bipolar disorder with current episode mania without Journal Pre-proof 10 psychotic symptoms, and two were diagnosed with obsessive-compulsive disorder (1.5%). (OCD).

BZDs like clonazepam (37, or 33.94%) and lorazepam (4, or 3.67%) were the most often withdrawn types. Three (2.8% of patients) were found to be BZD-dependent. In a study of patients on BZDs, Lader (2011) found that 3-4% showed obvious evidence of dependence [15]. The Benzodiazepine Withdrawal Symptom Questionnaire (BWSQ) demonstrated that following deprescribing, 36 of 40 patients taking clonazepam (100%) had no withdrawal symptoms, but 2 of 4 patients using lorazepam (50%) had mild withdrawal symptoms (Tyrer *et al.*, 1990) [16]. Nevertheless, a different study by Lader (2011) found that when patients sought to stop taking BZDs, between 15 and 30 percent of them had withdrawal symptoms (Lader, 2011) [15].

## Conclusion

Deprescribing BZDs was linked to a decrease in consumption; applying deprescribing procedures to inappropriate BZD users is doable, enhances service quality, and has positive financial implications. Deprescribing

BZDs was associated with implementing deprescribing practice amongst the inappropriate BZD users is feasible, provides an improved QoS and an economic benefit.

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