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Discontinuation of chronic benzodiazepine use in primary care: a nonrandomized intervention

Milene Fernandes[1], Inês Neves[1], Joana Oliveira[1,2], Osvaldo Santos[1,3], Pedro Aguiar[4], Paula Atalaia[2], Fátima Matos[2], Maria Carina Freitas[2], António Alvim[2], Vasco Maria[1,2,*]

[1]Instituto de Medicina Preventiva e Saúde Pública, Faculdade de Medicina—Universidade de Lisboa, Av. Prof. Egas Moniz, Lisboa 1649-028, Portugal, [2]ACES Lisboa Norte, Administração Regional de Saúde de Lisboa e Vale do Tejo, Largo Professor Arnaldo Sampaio, Lisboa 1549-010, Portugal, [3]Instituto de Saúde Ambiental, Faculdade de Medicina—Universidade de Lisboa, Av. Prof. Egas Moniz, Lisboa 1649-028, Portugal, [4]Public Health Research Center, Escola Nacional de Saúde Pública—Universidade Nova de Lisboa, Av. Padre Cruz, Lisboa 1600-560, Portugal

*Corresponding author: Instituto de Medicina Preventiva e Saúde Pública, Faculdade de Medicina, Av. Prof. Egas Moniz, Lisboa 1649-028, Portugal. Email: vasco.a.maria@gmail.com

Abstract

Background: Chronic benzodiazepine use is a challenge in primary care practice. Protocols to support safe discontinuation are still needed, especially in countries with high utilization rates.
Objectives: To evaluate the feasibility, effectiveness, and safety of a benzodiazepine discontinuation protocol in primary care setting.
Methods: Nonrandomized, single-arm interventional study, at primary care units. Family physicians (FPs) recruited patients (18–85 years-old) with benzodiazepine dependence and chronic daily use ≥3 months. Patients with daily dosages ≥30 mg diazepam-equivalent, taking zolpidem, with a history of other substance abuse or major psychiatric disease were excluded. After the switch to diazepam, the dosage was gradually tapered according to a standardized protocol. Primary endpoint was the percentage of patients who stopped benzodiazepine at the intervention last visit. Dosage reduction, withdrawal symptoms, patients' and FPs' satisfaction with the protocol were evaluated.
Results: From 66 enrolled patients (74% female; 66.7% aged >64 years; median time of benzodiazepine use was 120 months), 2 withdrew due to medical reasons and 3 presented protocol deviations. Overall, 59.4% of participants successfully stopped benzodiazepine (60.7% when excluding protocol deviations). Men had higher probability of success (relative risk = 0.51, $P = 0.001$). A total of 31 patients reported at least 1 withdrawal symptom, most frequently insomnia and anxiety. Most of participating FP considered the clinical protocol useful and feasible in daily practice. Among patients completing the protocol, 77% were satisfied. For the patients who reduced dosage, 85% kept without benzodiazepines after 12 months.
Conclusion: The discontinuation protocol with standardized dosage reduction was feasible at primary care and showed long-term effectiveness.

Key words: benzodiazepines, deprescribing, discontinuation protocol, primary healthcare, substance use, withdrawal symptoms

Key Messages

- Chronic benzodiazepine use is associated with poorer health conditions.
- Benzodiazepine deprescribing protocols are sought after by family physicians.
- With this standardized protocol, 60% of patients discontinued benzodiazepines.
- After 12 months, 85% of patients continued with no benzodiazepine use.

Introduction

Benzodiazepines are widely used for the treatment of anxiety and insomnia symptoms.[1] Short-term treatment is usually safe and effective whereas its chronic use poses several safety concerns.[1,2] Tolerance and physical dependence may develop within weeks, and withdrawal symptoms following abrupt discontinuation can be serious and life threatening, especially for higher doses.[1,3] Benzodiazepine long-term use was also linked with depression, cognitive impairment, stroke, and cancer, mainly among older patients at nursing home residencies.[4,5] Furthermore, benzodiazepine users seem to have more medical appointments, emergency events, and hospitalizations.[6]

International and national guidelines establish that treatment should not exceed 8–12 weeks for anxiety and 2–4 weeks for insomnia[7] and urge physicians to support long-term users on ceasing benzodiazepine consumption. However, benzodiazepine's rapid relief of symptoms, perceived safety, and easy access contribute to its over-prescription and chronic use.[8,9] In Europe, Portugal is one of the countries with the highest benzodiazepine consumption, particularly among the elderly population.[10]

A slow and gradual reduction of the dose, under the supervision of a qualified healthcare professional, has been advocated as the best strategy for benzodiazepine discontinuation while preventing withdrawal symptoms.[9] Nevertheless, effective interventions are not commonly available or seem difficult to implement at the outpatient level, namely in a primary care setting, and consensus about the most appropriate clinical protocol and the best tapering schedule is still lacking.[11–13]

Although consumption of benzodiazepines may be initiated by other specialists, family physicians (FPs) are responsible for most prescription refills.[14] In the United States, benzodiazepine prescription at outpatient level has increased substantially, mostly due to FPs prescriptions.[15] At a Portuguese primary care centre, 23% of adults were taking at least 1 benzodiazepine, from which 72% were using it for longer than 12 months.[16]

This exploratory study aimed to evaluate the effectiveness and safety of a structured intervention for benzodiazepine discontinuation in a population of long-term users attending primary care centres in the Lisbon urban area. The feasibility and satisfaction of participating FPs and patients regarding the intervention were also evaluated.

Methods

Study design and participants

A nonrandomized, single-arm, interventional study was carried out in a primary care setting. In Portugal, primary care units (PCUs) are part of the public healthcare services, organized by groups (ACES) and supervised by regional health administrations, and differentiated into conventional Primary Health Care Centers vs Family Health Units (smaller autonomous multiprofessional teams, providing closer and regular care). All units (n = 14) from a PCU group in Lisbon city (*ACES Lisboa Norte*), following a total of 225,038 patients, were invited to participate in the study. Six PCUs—corresponding to 114,574 patients and from which 5 were Family Health Units—accepted to collaborate. A presential session was scheduled at each participating PCU for the training of FPs on the discontinuation protocol and study procedures. Overall, 92.3% (n = 24) of a total of 26 FPs entered the study. One team member, external to the PCUs, was responsible for study monitoring. The study protocol was approved by the competent ethics committee and the Portuguese Data Protection Authority. All participants provided their written informed consent.

Eligible subjects were aged 18–85 years, daily benzodiazepine users, with a diagnosis of benzodiazepine dependence defined as presenting long-term chronic benzodiazepine use (≥3 months), regardless of indication, and coded *P18-Abuse of Medication* according to the International Classification of Primary Care (ICPC-2). Subjects with use of benzodiazepines above the maximum therapeutic dose (e.g. ≥30mg diazepam-equivalent daily dosage), receiving zolpidem, with other substance abuse disorder, dementia, epilepsy, major and recurrent psychiatric disorder (*P72-Schizophrenia*, *P73-Affective Psychosis*, *P76-Depressive Disorder*) were excluded. Subjects with suicidal ideation, terminal disease, depending on others for medication intake, unable to read, understand, or fully comply with the intervention were also excluded. All eligible subjects who were already scheduled in regular medical appointments, were consecutively invited to participate by their FP. Recruitment took place for up to 2 months in each centre, from May until November 2016.

Intervention

The intervention included a screening/first appointment, follow-up visits during dose-tapering and final evaluation (Fig. 1) while promoting the interaction with the patient and use of motivational interview techniques. At the screening visit, the FP evaluated eligibility and, for all eligible patients who provided informed consent, the following variables were collected from medical records and patient questionnaire: sociodemographic characteristics (including marital status, employment, smoking status, regular alcohol consumption, and comorbidities), history of benzodiazepine use and current dosage, and patient motivation for discontinuation. Benzodiazepines were classified in short ($t_{½}$ <12 h), intermediate (12 ≤ $t_{½}$ < 24 h), or long-acting ($t_{½}$ ≥24 h) duration of action.[1,16] Benzodiazepine daily dosages were converted and switched to diazepam-equivalents (supplemental information).[1,17] Tapering plans were established with each patient, according to the plans shown in Supplementary Table 2. Participants received a diary that included educational contents about benzodiazepines (to be reviewed with the patient during the first visit), the calendar of in-office appointments, a graph where the FP draws the planned decrease of benzodiazepine dose and any changes during the protocol, daily registries for benzodiazepine intake (hour and diazepam dosage), perceived health status (Likert scale), and a registry of any withdrawal symptoms (date and description). If withdrawal symptoms occur, patients were advised to inform their FP and could continue with the previous dosage until the next face-to-face appointment. Face-to-face appointments, at weeks 2 and 4 and every 4 weeks afterward, were interspersed with

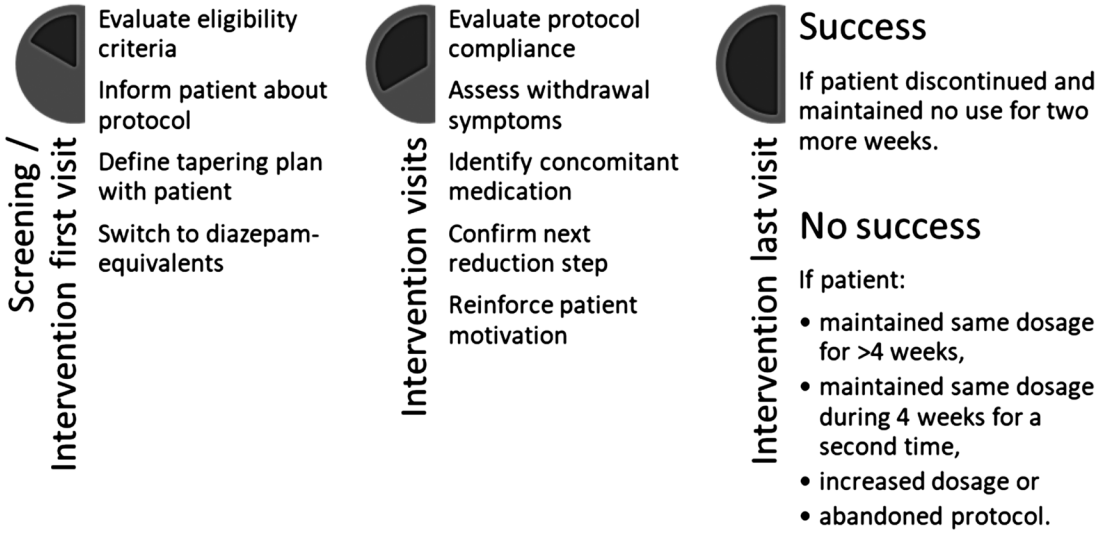

Fig. 1. Overall description of study procedures.

phone contacts by a study member (psychologist) at week 6 and every 4 weeks afterward. The follow-up visits and phone calls comprehended an evaluation of withdrawal symptoms, protocol compliance, and joint decision-making and counselling about the next step of the intervention. The intervention could take up to 30 weeks, for maximum dosages up to 30 mg diazepam. A brief questionnaire was completed at each visit.

The intervention was successful in case of discontinuation of benzodiazepines for 2 weeks or longer, observed by the FP at a face-to-face medical appointment and documented in clinical records. The intervention was concluded without success when the patient kept using the same dosage for more than 4 weeks, when using the same dosage during 4 weeks for a second occasion, increased dosage or abandoned the protocol, confirmed at a face-to-face medical appointment.

The psychologist contacted, by phone, patients that reduced at least 80% of initial benzodiazepine dosage, 6 and 12 months after the final evaluation visit, to verify if benzodiazepine use, withdrawal symptoms, patient motivation, concomitant treatments, and perceived health status. At the end of the study, a questionnaire was sent by email to all participating FPs, to evaluate their satisfaction and experience with the discontinuation protocol.

Study endpoints and other variables

The primary endpoint was the percentage of patients with successful discontinuation. Secondary endpoints included the percentage of patients who reduced the daily dosage by at least 80%, the mean reduction of daily dosage, the percentage with withdrawal symptoms, and the satisfaction of patients and FPs with the intervention. Scores of quality of life, self-perceived general health status, Hospital Anxiety and Depression Scale (HADS),[18] and sleepiness (Epworth scale)[19] were compared before and after the intervention.

Perceived general health status was evaluated with the question "*In general, how do you consider your state of health?*" (1—*very good*, 2—*good*, 3—*reasonable*, 4—*bad*, and 5—*very bad*).[20] Health-related quality of life was assessed with the EQ-5D-5L dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.[21]

Withdrawal symptoms reported by the patient in the diary or during the in-office or phone contacts were validated by the FP during in-office appointments. In addition, causality was evaluated by the study members with expertise in pharmacovigilance, using the global introspection method and with results expressed as 1 of 4 classes of probability: certain; probable; possible; unlikely.[22]

Statistical analysis

As this was an exploratory study, a minimum sample size of 55 evaluable patients was selected without formal power considerations, based on similar studies (with discontinuation rates between 25% and 100%) and according to the recruitment capacity of the centres during 1 month.[23–25] A response rate (i.e. the proportion of patients with benzodiazepines reduction ≥80%) of at least 25% was considered clinically relevant (*P0*). For a significance level of 5% and according to the binomial distribution, the inclusion of 55 patients would enable comparisons between threshold efficacy and response rates ≥50% (*P1*) with at least 90% power. The proportions of patients with benzodiazepine discontinuation were determined for all included patients (full analysis set, FAS) and for those without protocol deviations (per-protocol subset). We compared patients achieving discontinuation vs no discontinuation through Chi-square or Fisher's exact tests, and Student's *t*-test or Mann–Whitney test and developed a logistic multivariate regression model (with manual backward deletion; *P* value <0.05) to identify baseline variables independently associated with the successful intervention. The variables included in the initial model were selected if unadjusted *P* value <0.15 and based on clinical relevancy. We compared baseline and final evaluation of HADS anxiety and depression scores, EQ-5D dimensions and total score, Epworth score, or perceived general health status with paired Wilcoxon and McNemar tests. The analysis was performed in IBM/SPSS version 21, with a 2-tailed significance of 5%.

Results

FPs' and patients' characteristics

Participating FPs (n = 24) had a mean ± SD age of 38.1 ± 10.8 years, and 62.5% were female. The average time of clinical experience was 12.9 ± 11.7 years, with 45.8% having <10 years. A total of 66 patients were enrolled in the study. Two patients subsequently received a recommendation from their specialist physicians to maintain

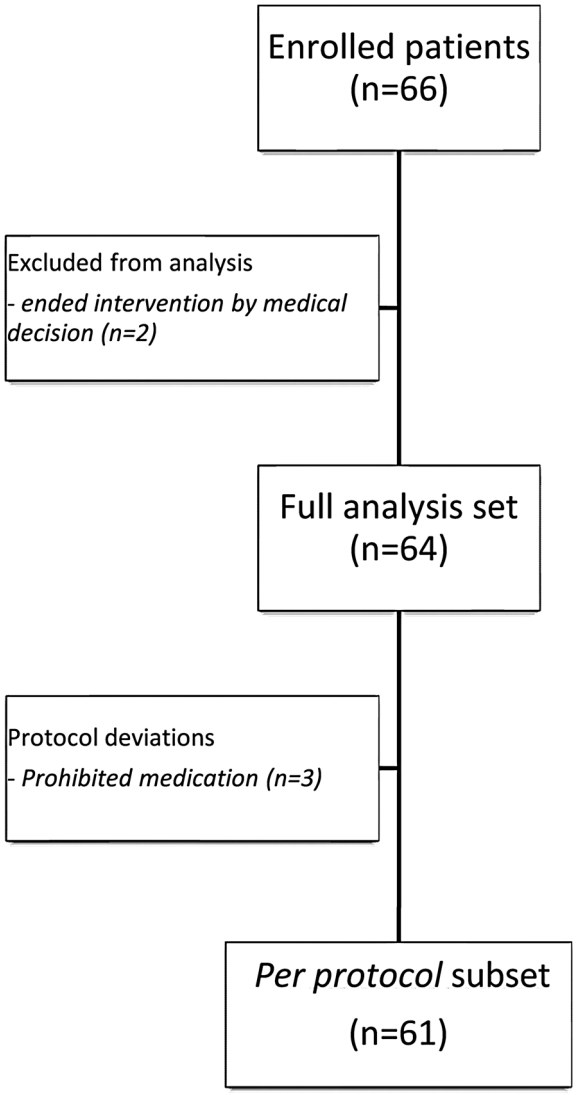

Fig. 2. Study flowchart.

benzodiazepine and were excluded from the analysis (Fig. 2). Three patients with protocol deviations have initiated zolpidem (n = 2) and antidepressants (n = 1).

Included patients (FAS, n = 64) were, on average, 67.4 ± 11.1 years-old, 75.0% were female, 62.5% were married or living together, and 9.4% were current smokers (Table 1). Regarding the professional situation, 71.9% were retired, 21.9% were employed, and 6.3% were unemployed.

Median time since benzodiazepine initiation was 120 months. The self-reported reason for benzodiazepine current use was anxiety (37.1%), insomnia (35.5%), both conditions (25.8%), and other (1.6%). Benzodiazepine was initiated by a FP in 68.8% of the cases, 10.9% by a psychiatrist, 17.2% by another specialist, and 3.2% by self-medication (e.g. from family members or other related individuals). Among patients taking only 1 benzodiazepine (n = 63), 7.9% were using short-acting, 68.3% intermediate-acting, and 23.8% long-acting benzodiazepines. The median dosage was 5 mg/day [percentile 25–percentile 75: 2.5–10.0 mg/day].

Almost half (45.3%) of the patients reported at least 1 previous attempt to discontinue benzodiazepine (range, 1–12 attempts; median, 2), 65.8% had already considered stopping it, 60.9% were worried about its chronic use, and 81.3% felt prepared to discontinue, with a perceived self-efficacy median score of 7.0 [min–max: 2–10] (in a 0–10 scale).

Success of the intervention

A total of 38 participants discontinued benzodiazepine successfully, representing 59.4% (95% confidence interval [CI] 46.4%–71.5%) of included patients (FAS, n = 64). For the per-protocol subset (n = 61), success rate was 60.7% (n = 37; 95% CI 47.3%–72.9%). Among patients without discontinuation (n = 26), 34.6% have maintained the same dosage for more than 4 weeks (Fig. 3).

The proportion of patients who reduced benzodiazepine for at least 80% of the initial dosage was 62.5% (n = 40; 95% CI 49.5%–74.3%) among included patients (FAS) and 63.9% (n = 39; 95% CI 50.6%–75.8%) for the per-protocol subset. The mean reduction of dosage was 4.13 ± 3.89 mg of diazepam, ranging from 0 to 15 mg of diazepam (median, 3.125 mg).

Gender and marital status at baseline were associated with successful discontinuation. Women had a lower probability of success (47.9% female patients with success vs 93.8% male patients; relative risk [RR] = 0.51, 95% CI 0.37–0.70). Married/living together patients had a statistically higher probability of success compared with widowed subjects (70.0% married/living together patients with success vs 25.0% widowed patients; RR = 2.80, 95% CI 1.03–7.62). After adjusting for gender, age, marital status, education level, professional status, initial diazepam-equivalent dosage, time since benzodiazepine initiation, being worried about taking a benzodiazepine for so long, and self-efficacy to discontinue (Supplementary Table 3), only gender remained associated with success (adjusted odds ratio = 0.07, 95% CI 0.01–0.54; P value = 0.011). Gender was also the only baseline characteristic significantly associated with dosage reduction, with women having a lower probability of reducing dosage at least 80% (RR = 0.66, 95% CI 0.41–0.75).

Withdrawal symptoms

A total of 31 (48.4%) patients reported at least 1 withdrawal symptom during the intervention. A total of 20 withdrawal symptoms were confirmed by the physician in 13 (20.3%) patients, most frequently new episodes/worsening of anxiety (n = 8) or insomnia (n = 8), 2 cases of irritability and one case of nightmares and another of myalgia. Causality was assessed as probable in 4 cases (new-onset symptoms) and possible in 9 (worsening of previous conditions). No withdrawal symptoms were considered serious, although a patient sought medical attention at an emergency department because of anxiety aggravation.

Evolution of secondary outcomes

The intervention had no negative impact on HADS anxiety and depression scores, quality of sleep (Epworth score), or quality of life (both EQ-5D total score and its dimensions) (Table 2). Patients who discontinued reported an improvement of perceived general health status, with the proportion reporting a *very good or good health status* increasing from 34.2% at baseline to 73.7% at the last protocol visit.

Satisfaction of patients and FPs

Overall, 49 (77.8%) patients were satisfied with the intervention, 10 (15.9%) were neither satisfied nor unsatisfied, and 4 (6.3%) were unsatisfied [missing information of 1 patient]. All patients with successful discontinuation (n = 38) were satisfied with the intervention.

Table 1. Baseline characteristics of successful vs unsuccessful intervention.

	Included subjects (n = 64)	Successful intervention (n = 38)	Unsuccessful intervention (n = 26)	P value
Female gender	48 (75.0%)	23 (60.5%)	25 (96.2%)	0.001[a]
Age (years), median [range]	69.5 [30–85]	68.5 [38–85]	72.0 [30–81]	0.45[b]
Elementary education (≤9 years)	35 (55.6%)	18 (48.6%)	17 (65.4%)	0.19[a]
Marital status				0.02[a]
Married/living together	40 (62.5%)	28 (73.7%)	12 (46.2%)	
Single/divorced	12 (18.8%)	7 (18.4%)	5 (19.2%)	
Widowed	12 (18.8%)	3 (7.9%)	9 (34.6%)	
Employed	14 (21.9%)	10 (26.3%)	4 (15.4%)	0.30[a]
Regular alcohol consumption	15 (23.4%)	9 (23.7%)	6 (23.1%)	0.96[a]
Perceived good general health	21 (32.8%)	13 (34.2%)	8 (30.8%)	0.77[a]
EQ-5D score, median [range]	0.53 [–0.02; –0.65]	0.55 [0.32; –0.65]	0.53 [–0.02; –0.65]	0.36[b]
HADS anxiety score, median [range]	13.0 [7–21]	13.0 [7–16]	13.0 [8–21]	0.56[b]
HADS depression score, median [range]	9.0 [5–15]	9.0 [5–12]	9.0 [5–15]	0.29[b]
Epworth score, median [range]	3.0 [0–10]	4.0 [0–10]	3.0 [0–8]	0.22[b]
BZD by duration of action (n = 63)[e]				0.81[a]
Short acting	5 (7.9%)	3 (7.9%)	2 (8.0%)	
Intermediate	43 (68.3%)	27 (71.1%)	16 (64.0%)	
Long acting	15 (23.8%)	8 (21.1%)	7 (28.0%)	
BZD by type (n = 63)[e]				0.57[a,d]
Alprazolam	20 (31.7%)	12 (31.6%)	8 (32.0%)	
Bromazepam	11 (17.5%)	8 (21.1%)	3 (12.0%)	
Estazolam	6 (9.5%)	3 (7.9%)	3 (12.0%)	
Lorazepam	6 (9.5%)	4 (10.5%)	2 (8.0%)	
Other	20 (31.6%)	11 (28.8%)	9 (36.0%)	
Daily dosage of BZD (mg of diazepam), median [range]	5.00 [1.25–20.00]	5.00 [1.25–12.50]	5.00 [1.25–20.00]	0.99[b]
Time since BZD initiation (months), median [range]	120.0 [5–492]	120.0 [5–480]	168.0 [5–492]	0.26[b]
BZD prescribed for anxiety (n = 62)	23 (37.1%)	16 (44.4%)	7 (26.9%)	0.16[a]
BZD initiated by a general physician	44 (68.8%)	24 (63.2%)	20 (76.9%)	0.24[a]
Ever tried to discontinue BZD	29 (45.3%)	17 (44.7%)	12 (46.2%)	0.91[a]
Worried about taking BZD for so long	39 (60.9%)	26 (68.4%)	13 (50.0%)	0.14[a]
Ever thought about stopping BZD	44 (65.8%)	27 (71.1%)	17 (65.4%)	0.63[a]
Feeling prepared to discontinue BZD	52 (81.3%)	31 (81.6%)	21 (80.8%)	0.94[c]
Self-efficacy to discontinue BZD (score), median [range]	7.0 [2–10]	7.0 [2–10]	7.5 [3–10]	0.76[b]

BZD, benzodiazepine; RR, relative risk for successful intervention. Values are no. (%), except otherwise mentioned. Percentages shown are within groups (columns).

[a]Chi-square test.

[b]Mann–Whitney test.

[c]Fisher's exact test.

[d]P value for the comparison of distribution of alprazolam, bromazepam, and remaining benzodiazepine.

[e]One subject taking both alprazolam (intermediate) and diazepam (long acting) was excluded from the analysis.

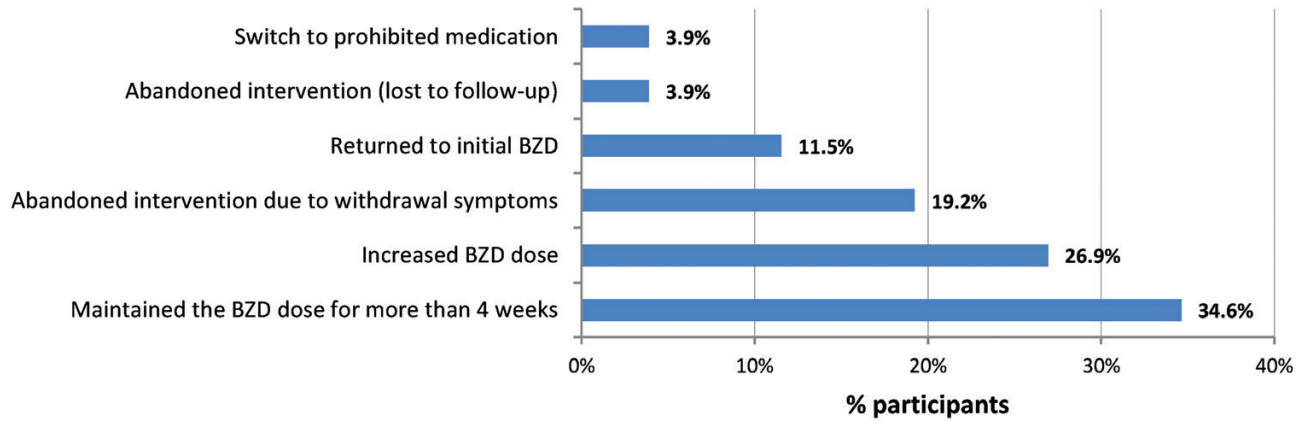

Fig. 3. Reasons for unsuccessful discontinuation of benzodiazepines.

Table 2. Patient-reported outcomes at baseline and last visit, by successful vs unsuccessful intervention.

	Successful intervention (n = 38)			Unsuccessful intervention (n = 25)[c]		
	At baseline	Last visit	P value	At baseline	Last visit	P value
Perceived general health status			<0.001[a]			1.00[a]
Very good/good	13 (34.2%)	28 (73.7%)		8 (32.0%)	8 (32.0%)	
Reasonable/bad/very bad	25 (65.8%)	10 (26.3%)		17 (68.0%)	17 (68.0%)	
EQ-5D (score), median [range]	0.55 [0.32 - 0.65]	0.53 [0.32 - 0.65]	0.97[b]	0.53 [–0.02 - 0.65]	0.53 [0.03 - 0.65]	0.98[b]
Having some problems with						
Mobility	12 (31.6%)	9 (23.7%)	0.25[a]	4 (16.0%)	5 (20.0%)	1.00[a]
Daily activities	2 (5.3%)	3 (7.9%)	>0.99[a]	3 (12.0%)	2 (8.0%)	1.00[a]
Pain	20 (52.6%)	16 (42.1%)	0.39[a]	11 (44.0%)	12 (48.0%)	1.00[b]
Anxiety/depression	18 (47.4%)	12 (31.6%)	0.15[a]	14 (56.0%)	15 (60.0%)	1.00[b]
HADS anxiety (score), median [range]	13.0 (7 - 16)	14.0 (9 - 15)	0.05[b]	13.0 (8 - 21)	13.0 (5 - 16)	0.78[b]
HADS depression (score), median [range]	9.0 (5 - 12)	9.0 (5 - 13)	0.71[b]	9.0 (5 - 15)	9.0 (6 - 16)	0.73[b]
Epworth (score), median [range]	4.0 [0 - 10]	3.5 [0 - 8]	0.48[b]	3.0 [0 - 8]	2.0 [0 - 9]	0.55[b]

Values are no. (%), except otherwise mentioned.

[a]*P* value of difference between baseline and last intervention visit (McNemar test).

[b]*P* value of difference between baseline and last intervention visit (Wilcoxon signed-rank test).

[c]One participant had missing information for these secondary outcomes.

Among FPs who responded to the questionnaire (n = 19), 47% considered the intervention *useful* and 53% *very useful*. In addition, 89% agreed that intervention is feasible in daily practice. The majority (89%) classified the protocol as simple, and 53% agreed that the protocol length was *adequate*. Time spent on study visits and final evaluation was considered *adequate/very adequate* by 79%, while time spent on patient recruitment was considered *adequate/very adequate* by 47%. The reported recruitment rate per FP (i.e. the number of patients admitted to the study over the number of eligible patients) ranged from 20% to 100%, being on average 51%.

Follow-up evaluation at 6 and 12 months

Patients that reduced at least 80% of initial benzodiazepine dosage (n = 40) were followed up for 6 and 12 months after the final evaluation visit, with information available for 39 (97.5%) patients. At the end of follow-up, 84.6% (n = 33) maintained abstinence, while 3 patients relapsed at 6 months and 3 others relapsed at 12 months. Overall, 5 patients restarted benzodiazepine at ≤50% of the baseline dosage by medical decision, and 1 patient decided to return to the baseline dosage. Among included patients (FAS, n = 64), 51.6% remained without any benzodiazepine use after 12 months.

Discussion

Our structured protocol, with stepped-dosage reduction of benzodiazepines, promoted successful discontinuation among 60% of chronic users. About 52% discontinued benzodiazepines and remained without any use 12 months later. Women were less likely to achieve successful discontinuation. Most of the confirmed withdrawal events were due to the worsening of anxiety or insomnia and were classified as possibly related. However, the intervention did not negatively impact anxiety, depression, sleepiness, nor the quality of life. In fact, patients with successful discontinuation reported a better general health status at the end of the intervention. Both FPs and patients were satisfied with the intervention. FPs considered the discontinuation protocol useful and feasible in daily practice.

Making comparisons between studies should be done cautiously, as discontinuation protocols, their endpoints and timelines often differ.[23,25,26] Nevertheless, our result is similar to the 62% success rate observed in other studies that assessed systematic discontinuation alone[24] and higher than the 24%–58% success observed in studies comparing dose-tapering vs other more complex interventions, such as psychotherapy or the use of pregabalin.[25] Patients receiving simple interventions seem to be twice as likely to discontinue benzodiazepines compared with usual care (RR = 2.04, 95% CI 1.5–2.8).[13] Furthermore, there is evidence that combining dose-tapering with structured patient education and follow-up visits, as proposed in our protocol, results in higher discontinuation rates.[9,25] Compared with usual care provided by FPs, patients that undergone a dose-tapering strategy, with written instructions or follow-up visits, had a 3 times higher probability of discontinuation 12 months after baseline, with 45% patients not using benzodiazepines at this time point.[23] Another study observed that 28% (n = 446) of patients who received a discontinuation letter followed by a FP evaluation consultation had no benzodiazepine prescription 3 months after receiving the letter, from whom 52% remained with no prescriptions of benzodiazepine at 21 months.[27]

Results regarding gender and age as determinants of benzodiazepine discontinuation have been inconsistent.[28] However, women tend to use these drugs more frequently, and the female gender has been described as a risk factor for long-term use.[28] This difference may be related to a prescription decision since women seem more likely to be prescribed benzodiazepines during stressful life events, such as grief or life changes, even in the absence of a medical diagnosis.[29,30] Of notice, we did not observe any statistical association between the likelihood of success and benzodiazepine characteristics as described by others, namely, treatment duration, elimination half-life, and baseline dosage.[27,28]

The protocol was feasible at the primary care level, despite some limitations. Since the experimental protocol could be eased when applied in daily practice by changing the face-to-face appointments to phone contacts and by reducing the burden of data collection, adherence to intervention by FPs and patients can be further improved.

To facilitate the reduction of small benzodiazepine dosages and to ease the implementation of the protocol, we switched all benzodiazepines into diazepam prior to initiate tapering. Despite the benefit of this approach lacks evidence,[1,31] it promoted the standardization of procedures with no reported problems by the patients.

Our study was a nonrandomized interventional study in a real-world setting. The ethical constraints of not offering all patients an intervention with expected benefits and the high risk of contamination between groups outweigh the advantages of a controlled study design in the context of an exploratory study. We cannot exclude that a selection bias may have occurred at FPs' level (since the mean age was somewhat lower than the 50 years-old mean age of medical doctors in Portugal) and patient level (despite the instructions given to FPs to consecutively invite all eligible patients). Nevertheless, in the daily practice, FPs would also invite those patients that could complete the reduction protocol and benefit most from the intervention. We also acknowledge that this protocol results could not be generalized to patients with underlying conditions besides anxiety and insomnia since patients with other psychiatric disorders for which benzodiazepines are prescribed (e.g. acute treatment of depression) were excluded. Even so, anxiety and insomnia are the most frequent users at a primary care level in Portugal. Another limitation is some related to the lack of pill counts or drug screens to confirm benzodiazepine use, which was evaluated ongoing at each clinician–patient interaction. Finally, the sample size enabled the evaluation of protocol feasibility and effectiveness but, most probably, was insufficient when identifying factors associated with a successful intervention.

Despite the nonrandomized design of our study, we demonstrated that simple interventions with a structured reduction of benzodiazepine dosage are a strong support to both physicians and patients trying to discontinue chronic use. Others have shown this in the context of randomized interventional studies. We present a real-world perspective of what to expect with the implementation of a standardized discontinuation protocol. Furthermore, based on our results, we strongly suggest that most in-office appointments can be replaced by phone contacts provided by nurses and/or psychologists, so that the intervention could be more efficient.

Conclusion

Chronic benzodiazepine use is a demanding clinical and public health issue worldwide. The primary care setting plays a key role in preventing inadequate use of medicines, especially in a postpandemic setting where access to healthcare suffered several constraints and mental health disorders are of utmost relevance. However, FPs express concerns about their skills to motivate patients engaging in withdrawal programs in addition to the lack of time to support them during the process.[8] Our standardized discontinuation protocol was feasible in this setting, with short- and long-term success and improving patients perceived health status and can support FPs when deprescribing benzodiazepines.

Supplementary material

Supplementary material is available at *Family Practice* online.

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Ethical approval

The study protocol was approved by the competent Ethics Committee of Lisbon and Tagus Valley Health Region.

Conflict of interest

The authors declare that they do not have any conflicts of interest. I. Neves received a research grant from Calouste Gulbenkian Foundation.

Data availability

The data underlying this article cannot be shared publicly for the privacy of individuals that participated in the study. The data will be shared on reasonable request to the corresponding author.

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