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## Patterns of benzodiazepines use in primary care adults with anxiety disorders

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#### Abstract

**Background:** Benzodiazepines are among the most commonly prescribed drugs for anxiety disorders. While they are indicated as adjunctive treatment for shortterm use according to clinical practice guidelines, previous studies have shown patterns of long-term use of benzodiazepines, which is problematic due to side effects, dependence and potential of abuse. The aims of this study were to examine among a large sample of primary care adults suffering from anxiety disorders: 1) benzodiazepine use patterns; and 2) correlates of long-term benzodiazepine use.

**Methods:** Data were drawn from the "Dialogue" project, a large primary care study conducted in 64 primary care clinics in the province of Quebec, Canada. Following a mental health screening in waiting rooms, patients at risk of anxiety or depression completed the Composite International Diagnostic Interview-Simplified (CIDIS). A

sample of 740 adults meeting DSM-IV criteria for Generalized Anxiety Disorder, Panic Disorder or Social Anxiety Disorder in the past 12 months took part in this study.

**Results:** Benzodiazepines were used by 22.6% of participants with anxiety disorders in our primary care sample. A large majority of benzodiazepine users (88.4%) met our indicator of long-term use, as defined by utilization for more than 12 weeks including regular and as-needed use. Based on a logistic regression model, individual correlates associated with long-term benzodiazepine use included: being 30 years or older, having a comorbid physical illness, meeting criteria for comorbid agoraphobia, reporting the use of sleep-aids, and concurrent SSRI utilization.

**Limitation:** Data collection with self-reported questionnaires may be subject to information bias.

**Conclusions:** Despite knowledge of the risks of long-term use of benzodiazepines, this remains a pervasive problem. Clinicians need to be mindful of patterns and risk factors leading to long-term use of benzodiazepines in patients with anxiety disorders. Results of this study should raise awareness regarding appropriate prescription practices for benzodiazepines, including decision-making in initiation, duration of prescription, and use of strategies for discontinuation in current long-term benzodiazepine users.

Keywords: Medicine, Epidemiology, Health profession, Clinical psychology, Evidence-based medicine, Nursing, Psychiatry, Public health, Pharmaceutical science

#### 1. Introduction

Anxiety disorders are among the most prevalent mental disorders experienced in the general population [1, 2, 3]. Evidence-based treatment options for anxiety disorders comprise psychological and pharmacological treatments [1]. According to clinical practice guidelines (CPGs), selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine re-uptake inhibitors (SNRIs) are generally first-line pharmacological treatments for anxiety disorders since they present advantageous safety and tolerability profiles [1, 4, 5, 6]. While benzodiazepines (BZDs) have also demonstrated efficacy for some anxiety disorders, they are generally recommended in CPGs as adjunctive short-term options, preferably with regular dosing, either to help relieve patients with acute anxiety and agitation or pending a response to anti-depressants [1, 4, 6]. With their rapid anxiolytic and sedative/hypnotic effects, BZDs provide effective short-term relief for insomnia and anxiety [7].

Since their introduction in the late 1950's, BZDs have been among the most widely used medications in the community [8, 9, 10, 11, 12]. Despite their circumscribed

role in evidence-based practice and lack of first-line indication in anxiety disorders, about one in four patients suffering from an anxiety disorder could be using a BZD [13]. While maximal duration recommended in CPGs ranges from 2 to 8 weeks until the first-line antidepressant treatment takes effect - followed by slow tapering [1, 6, 14], previous studies have found long-term BZD use rates among users in the general population as high as 83%, and anxiety disorders often figure among risk factors [10, 15, 16, 17, 18]. Concerns have been raised for many years regarding long-term BZD use. Possible side effects of their long-term use include sedation, cognitive impairment and impaired psychomotor performance (e.g. risk of falls and fractures in the elderly, motor vehicle accidents) [1, 4, 7, 19, 20]. BZD dependence may develop among some users after only weeks of treatment, and discontinuation is complicated by a complex mix of withdrawal symptoms, rebound symptoms and recurrence of underlying anxiety [19]. These risks have to be taken into account when clinical situations warrant long-term BZD prescription, which is sometimes necessary to relieve severe symptoms or as part of a harm reduction strategy [21]. Nevertheless, long-term BZD use should remain exceptional in the population of anxiety disorders patients.

Few studies have examined patterns of BZD use among patients with anxiety disorders in primary care, which is the main point of care for patients with anxiety disorders [22]. In the present study, we aimed to examine BZD use patterns in a large sample of primary care patients suffering from anxiety disorders in the province of Quebec, Canada. A second aim of our study was to explore the correlates of long-term BZD use among individuals with anxiety disorders.

#### 2. Methods

#### 2.1. Study setting, participants and data collection

The "Dialogue" project is an observational study that examined mental health status, service utilization and experience of care of primary care patients with anxiety or depressive disorders (see detailed methodology) [23]. The study received the approval of all regional research ethics committees (Agence de santé de des services sociaux de Montréal; Centres de santé de des services sociaux de Chicoutimi, Sherbrooke, Gatineau, Laval, Saint Jérome, Jeanne-Mance, Lac-Saint-Jean-Est, Pointe-de-l'île, Bordeaux-Cartierville- Saint-Laurent, Therese-De-Blainville, Pierre Boucher, Haut-Richelieu-Rouville, Baie des Chaleurs, La Pommeraie; Hospital Notre-Dame and Hospital Sacré-Coeur). Study participants provided written informed consent.

Data for the current study were drawn from the waiting room screening questionnaire (T0) and the first telephone/web interview (T1). Participants were recruited in the waiting rooms of 64 primary care medical clinics (T0) in 2008 during

3 https://doi.org/10.1016/j.heliyon.2018.e00688 2405-8440/© 2018 Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/). randomly chosen periods. Patients were invited by a lay-interviewer to complete a brief self-administered screening questionnaire if they met the following inclusion criteria: 1) age 18 years or older; 2) consulting a GP for themselves; 3) able to complete a questionnaire in French or English. From the 22,600 eligible patients approached, 67.4% completed the questionnaire. The screening questionnaire included general questions about socio-demographic characteristics, overall health status, chronic conditions, consultations with health care providers and psychotropic medication, as well as the Hospital Anxiety and Depression scale (HADS) [24, 25] and the World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0; self-reported 12-item version) [26].

Patients were invited to participate in the T1 structured interview if their usual primary care source was one of the participating clinics and if they met any of the following inclusion criteria: i) current anxiety or depressive symptoms; ii) anxiety or depression medication in the past 12 months; iii) depression or anxiety disorder diagnosis made by a physician; iv) consulted for mental health issues in the past 12 months. Among eligible patients, 4 506 (59.9%) accepted to participate to the T1 follow-up telephone (70.8%) or web (29.1%) interview, 2-4 weeks after initial contact. In the first part of the interview, participants completed the Composite International Diagnostic Interview – Simplified (CIDIS [27]), a structured clinical interview administered by a lay-interviewer that aims at assessing symptoms of common mental disorders, according to DSM-IV criteria, that had been developed and validated as a shorter and simplified version of the CIDI [28]. After completing the CIDIS [27], the T1 interview then continued with the 1 956 people either: i) meeting DSM-IV criteria for generalized anxiety disorder, panic disorder, agoraphobia, social phobia or major depression in the past 12 months; ii) a high level of anxiety or depressive symptoms combined with any medication use, diagnosis by a health care professional, or meeting DSM-IV criteria for any anxiety or depressive disorders in the past 24 months. This second part of the interview included questions on experience of care, services utilization for emotional reasons, medication use for anxiety or depressive symptoms, perceived needs for care and socioeconomic data. The medication questionnaire was divided into two main sections. The first section included six questions oriented on the indication for medication use in the past 12 months, either prescription or over-the-counter, for the following reasons: 1- anxiety or nervousness; 2- sleep; 3- antidepressants; 4- mood stabilizer; 5- psychotic disorders; 6- stimulants. In the second section, a positive answer for anxiety or antidepressant medication was followed by: a) a subset of questions on the prescriber, number of follow-up, compliance, duration, dosage, and reason for discontinuation; b) a subset of questions on current anxiety or antidepressant medications: name of the medication, regular or as needed use, milligrams in each dose, doses per day, duration, and frequency of follow-up. For the present study, the final sample included 740 adults meeting the DSM-IV criteria for panic disorder,

https://doi.org/10.1016/j.heliyon.2018.e00688 2405-8440/© 2018 Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/). generalized anxiety disorder or social anxiety disorder during the 12 months preceding the survey.

### 2.2. Indicators for BZD use patterns

The indicator for BZD use in our sample was defined as reporting utilization of at least one BZD with evidence-based recommendations for any of the anxiety disorders under study as reported in the 2006 Canadian Psychiatric Association's *Clinical practice guidelines: Management of anxiety disorders* [14] (i.e. alprazolam, bromazepam, clonazepam, diazepam and lorazepam). The indicator of potentially non-therapeutic long-term use of BZDs was defined as using a BZD for more than 12 weeks, including regular and as-needed use [1, 6, 19]. While a recent systematic review identified 6 months and over as the most prevalent definition of long-term BZD use [29], this is a conservative definition adapted to drug claims data, whereas participants in the Dialogue study reported actual BZD use.

#### 2.3. Potential correlates of long-term BZD use

Patient characteristics included socio-demographic, clinical, medication and service use factors. **Socio-demographic factors** included sex, age group, educational attainment, marital status, perception of economic situation, and having private or collective insurance coverage for medication or complementary health services. **Clinical factors** included perception of mental health, degree of functional impairment (WHODAS 2.0), severity of anxiety and depressive symptoms (HADS), comorbid agoraphobia, comorbid major depression, as well as the count of comorbid chronic physical illnesses. **Medication factors** included reporting taking any drugs for sleep, as well as reporting use of specific psychotropic molecules with evidence-based recommendations for anxiety disorder when the survey was conducted [14]: SSRIs, atypical antipsychotic drugs, monoamine oxidase inhibitors, tricyclic antidepressants, anticonvulsive medication and others. **Service use factors** included consultation for mental health in the past 12 months of general practitioners and psychiatrists.

## 2.4. Statistical analysis

Descriptive analyses were conducted to examine socio-demographic and clinical characteristics of the sample, as well as service use and medication use. Patterns of BZD use were described for the sample. We calculated bivariate associations between aforementioned variables and long-term BZD use using logistic regressions, excluding short-term recent users due to unknown status regarding progression towards long-term use within the next 12 weeks. Variables integrated in the multiple regression models were based on the level of significance in the bivariate

models (p  $\leq$  .10). Missing data were excluded pairwise for bivariate analysis and listwise for multiple regression models. Analyses were conducted using SPSS, version 20.0.

#### 3. Results

#### **3.1. Descriptive analyses**

The sample was composed of 740 participants meeting DSM-IV criteria for at least one of three anxiety disorders: panic disorder (n = 373), generalized anxiety disorder (n = 373) or social anxiety disorder (n = 304). More than half of the participants also met DSM-IV criteria for major depressive episode in the previous year. The majority of the sample was female (76%), and the mean age of the sample was 42.6 (SD = 13.3). Over half of the sample was married or living with a partner, with a college or university education level (49%). Most participants reported having a family physician (83%), and most had access to private health insurance (66%) for reimbursement of medication and/or complementary health services. Over 30% of the sample considered their economic situation as being poor or very poor. The average score on the HADS-Anxiety and HADS-Depression subscales were respectively 11.3 (SD = 4.1) and 7.4 (SD = 4.6). More specifically, based on BZD use status, the average score on the HADS-Anxiety subscale for non-users, short-term users and long-term users were respectively 11.1 (SD = 3.9), 14.1 (SD = 4.3) and 12.0 (SD = 4.3). The average scores on the HADS-Depression subscale were respectively 7.2 (SD = 4.5), 11.8 (SD = 4.9) and 7.8 (SD = 4.6). Most participants also presented comorbid chronic physical illness, with more than a third (38.8%) reporting at least three conditions. Two thirds (67.0%) reached the WHODAS threshold for disability, with a mean score of 15.1 (SD = 9.9) on the scale.

During the 12 months preceding the survey, the majority of participants had consulted a family physician for mental health reasons (86.1%). The rates of current medication utilization by drug class were the following, for molecules with evidence-based recommendations in anxiety disorders: 27.4% for SSRI, 22.6% for benzodiazepines, 8.9% for atypical antipsychotic, 4.5% for monoamine oxidase inhibitors, less than 1% each for both tricyclic antidepressants and anticonvulsants, and 25% for other agents (i.e. venlafaxine, bupropion, hydroxyzine and mirtazapine).

#### 3.2. BZD use

Table 1 presents the patterns of BZD use among the 167 participants (22.6 %) reporting any use in the past 12 months. The majority of participants used only one BZD (96%), distributed evenly between regular and as-needed regimens. Over 88% of BZD users met the indicator of long-term use for at least one previously described

	n	%
Number of BZDs reported		
One	161	96.4
Two	6	3.6
BZD molecule		
Alprazolam	17	10.2
Bromazepam	4	2.3
Clonazepam	90	53.9
Diazepam	5	3.0
Lorazepam	53	31.7
Type of BZD		
Short acting $(t^{1/2} < 24h)$	70	41.9
Long acting $(t^{1/2} \ge 24h)$	99	59.3
Type of BZD prescription		
At least one regular	84	50.3
At least one as-needed	85	50.9
Treatment duration for at least one BZD		
0-84 days (0-12 weeks)	21	12.6
85-180 (up to 6 months)	15	9.0
Over 180 days	133	79.6

**Table 1.** Patterns of BZD use reported by participants in the past 12 months (n = 167).

BZD (i.e. use for more than 12 weeks); over half of those respondents reported a clonazepam prescription.

#### 3.3. Long-term BZD use

Table 2 presents the results of the bivariate and multivariate logistic regression analyses for long-term BZD use. Short-term users (n = 21) were excluded from the analysis. Factors associated with long-term BZD use in the multiple regression model included age group, comorbid agoraphobia, chronic physical illness, taking a medication for sleep problems and concurrent SSRI medication. When compared to participants of 18–29 years old, older participants were more likely to use BZDs: 30-44yrs [OR: 3.82, 95% CI: 1.56-9.33], 45-59yrs [OR: 7.88, 95% CI: 3.20-19.33], 60 years and more [OR: 7.08, 95% CI: 2.41-20.78]. Comorbid agoraphobia was also a correlate of long-term BZD use [OR: 2.01, 95% CI: 1.31-3.08]. Other correlates of long-term BZD use included reporting using a medication, prescribed or over the counter, for sleep-related problems [OR: 2.67, 95% CI: 1.71-4.16], having a concurrent SSRI [OR: 1.73, 95% CI: 1.11-2.70], and having a comorbid chronic illness [OR: 1.96, 95% CI: 1.12-3.43]. Other factors including sex, marital status, and perception of poor mental health were not significantly correlated to chronic BZD use in the multiple regression model.

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VARIABLE (Reference value)	Bivar (n =	Bivariate associations $(n = 715-721)^{a}$		Multivariate associations $(n = 700)$		
	OR	(95% CI)	<b>P</b> *	OR	(95% CI)	P†
Socio-demographic Sex (men) Women	0.97	(0.64-1.48)	0.896	1.10	(0.69 - 1.78)	0.687
Age group; years (18–29) 30–44	3.74	(1.63-8.57)	0.002	3.82	(1.56-9.33)	0.003
45-59	8.22	(3.68–18.4)	< 0.001	7.88	(3.20–19.3)	< 0.001
60 and above	7.18	(2.82-18.3)	< 0.001	7.08	(2.41-20.8)	< 0.001
Marital Status (Single) Married or living with	1.15	(0.74-1.78)	0.546	0.71	(0.42-1.20)	0.220
Separated/div./widow	2.34	(1.39-3.92)	0.001	0.99	(0.53-1.87)	0.994
Education (High school or less) College	) 0.67	(0.42-1.07)	0.092	0.73	(0.43-1.24)	0.241
University	1.02	(0.65-1.58)	0.948	1.20	(0.72-1.98)	0.489
Perception of economic situation Meets basic needs	on <sup>b</sup> (Poo 1.17	r/very poor) (0.65-2.12)	0.602			
Financially secure	0.88	(0.50-1.54)	0.653			
Private insurance coverage <sup>b</sup> (No Yes	o) 0.84	(0.57-1.22)	0.361			
Clinical Comorbid chronic illnesses (No One	one) 2.44	(1.48-4.01)	< 0.001	1.96	(1.12-3.43)	0.019
Two or more	2.13	(1.38-3.30)	0.001	1.33	(0.81-2.20)	0.262
Perception mental health (Good Poor or moderate	l) 1.75	(1.21-2.53)	0.003	1.25	(0.77-2.02)	0.367
Agoraphobia (No) Yes	1.91	(1.32-2.76)	0.001	2.01	(1.31-3.08)	0.001
Major depression episode (No) Yes	1.12	(0.77-1.63)	0.551			
Anxiety symptoms severity, HA Score 1–21	ADS [co 1.06	ontinuous] (1.01–1.11)	0.010	1.02	(0.96-1.08)	0.559
Depressive symptoms severity, Score 1–21	HADS 1.03	[continuous] (0.99-1.07)	.167			
Disability, WHODAS (<10) $\geq 10$	1.02	(1.00-1.04)	0.073	0.85	(0.52-1.49)	0.634
Medication Drug for sleep-related problems Yes	s (No) 3.22	(2.18-4.75)	< 0.001	2.67	(1.71-4.16)	<0.001
SSRIs (No)						
Yes	1.84	(1.25-2.69)	0.002	1.73	(1.11-2.70)	0.015
Atypical antipsychotics (No) Yes	2.52	(1.47-4.32)	0.001	1.49	(0.77-2.90)	0.237
					(continued on i	next page)

**Table 2.** Bivariate and multivariate logistic regression analyses for long-termBZD use compared to no use.

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Table	2.	(Continued)
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VARIABLE (Reference value)	Bivariate associations $(n = 715-721)^{a}$		Multivariate associations (n = 700)			
	OR	(95% CI)	<b>P</b> *	OR	(95% CI)	P†
Monoamine oxidase inhibitors Yes	(No) 2.07	(0.98-4.37)	0.057	1.07	(0.47-2.46)	0.870
Mental health professional consult General practitioner (No) Yes	tation 1.66	(1.06-2.60)	0.028	1.06	(0.62-1.80)	0.833
Psychiatrist consultation (No) Yes	1.42	(0.94-2.13)	0.095	0.87	(0.52-1.46)	0.603

\*Model includes variables p < 0.10 in bivariate analyses + sex.

 $\dagger$ Variables with p < 0.05 were considered as correlates of long-term BZD use.

<sup>a</sup> Tricyclic antidepressants or anticonvulsive medication were not included in the analysis (less than 1% of the sample), and neither were the "other agents" category.

<sup>b</sup> Missing data treated pairwise.

### 4. Discussion

This study examined BZD use patterns and the correlates of long-term BZD use in a large sample of primary care adults suffering from anxiety disorders. Almost one out of four (22.6%) participants reported BZD use; this result is within range of a Canadian general population study, which found BZD use prevalence of 16.9% in social phobia, 20.7% in generalized anxiety disorder, and 28.2% in panic disorder [15]. The most frequently used molecules were clonazepam and lorazepam, similarly to other outpatient samples in Canada, although not always in the same order [15, 17, 30]; however, availability, regulations and use of specific BZDs vary between countries [12, 16, 31]. BZD prescribing practices in our sample may be influenced by a preference for clonazepam, which is characterized by a longer half-life allowing for a more convenient dosing of once or twice a day, and potentially reduced withdrawal symptoms such as anxiety and insomnia [6]. Among BZD use patterns, we also noted similar rates of regular and as-needed utilization, which is a deviation from Canadian CPG recommendations [1, 14]. Patterns of BZD use were also characterized by infrequent use of combined BZD molecules compared to previous studies [16]. A possible explanation for this finding is that we focused on only five BZDs as possible treatments for anxiety disorders (i.e. alprazolam, bromazépam, clonazepam, diazepam and lorazepam); therefore, patients using another BZD (e.g. for sleep) would not have been identified as using more than one BZD.

Among patients with an anxiety disorder that were current BZD users, our study mostly found established long-term users (88.4%), and this pattern of potentially inadequate long-term use echoes previous studies that emphasize that long-term BZD use is much more prevalent than would be expected if CPGs were always complied with [15, 16, 18]. As discussed extensively in the BZD literature (e.g. Lader, 2011) [19], the passage from short-term use to potentially inadequate extended use is an unremitting public health concern - considering the dependence and abuse potential, aversive effects of withdrawal, rebound and recurrence symptoms associated with BZDs - that remains overlooked over time by many regulatory agencies and clinicians.

Our regression model identified a number of correlates of long-term BZD use in adults with anxiety disorders that are consistent with previous studies, which may help identify at-risk populations for potentially inappropriate use of BZD. Age was a significant predictor of a long-term BZD use [10, 18, 32, 33] that raises particular concern as BZDs are associated with falls and risk of fractures in the elderly [34, 35], as well as with mobility and activities of daily living disability [36]. Reporting taking a medication for sleep was also a correlate of long-term BZD use. Although specific motives for BZD use were not collected in our study, it is likely that these hypnotic drugs were often used to alleviate sleep problems, a common reason for BZD use in the general population [15]. Taking SSRIs was another correlate of long-term BZD use observed in our sample, and, among explanatory factors, it has been suggested that this association may be related to "help-seeking" behaviour leading to an indirect association of their usage, to the management of residual symptoms with an antidepressant medication or to dependence following an initial short-term prescription [17, 37, 38]. Since some SSRIs can cause agitation, insomnia, akathisia or restlessness as side effects, BZD are indicated as adjunctive therapy early in treatment to help patients in times of acute crises or while waiting for onset of adequate efficacy of antidepressants [14]. This might explain some of their association with BZD use. Not a consistent finding, the presence of comorbid chronic physical conditions was also a correlate of long term BZD use [13], and the association between chronic illness and BZD use could be related to our primary care sample. Also, the increasing prevalence of multiple chronic conditions with age might explain why comorbidities do not predict long-term BZD use after adjustment for age and other covariables in our regression models [39]. This association could also be attributable to an issue of power, or a possibility that general practitioners (GPs) might be more cautious in prescribing BZD when their patients have several chronic diseases, which often require multiple medications for optimal management. Due to high prevalence of chronic conditions among older adults, GPs may want to limit pharmacological interactions with BZD in presence of multiple medications. Finally, we also examined agoraphobia and depression as mental health correlates of BZD use. Unsurprisingly, agoraphobia was a correlate of long-term use, which could indicate a motivation of BZD use for the management of apprehension and avoidance behaviours, and for the prevention of panic attacks or the reduction of panic symptoms regarding feared situations. We expected that individuals with a comorbid major depressive episode would be less likely to be using a BZD in our sample, which was not the case. There is currently no evidence that BZDs are effective for depressive symptoms comorbid with anxiety disorders, especially in monotherapy [4, 6].

The findings of this study are based on a large sample of participants in different primary care settings and represent a population of interest to general practitioners in Canada and elsewhere. We included a wide range of variables in our study, namely socio-demographic data, clinical information, actual medication taken and some service use variables, some of which represent the patient perspective on their socioeconomic and mental health situations. However, data collection was based on selfreported questionnaires and may have been subject to information bias. Also, our results offer a partial view of BZD use as the participants could use them for problems we did not explore (e.g. alcohol use disorders), or could be prescribed other BZDs off-label for their anxiety disorder, and other important contributors to long-term BZD use might not have been assessed. Despite our hypotheses, the crosssectional research design of the Dialogue Study limits our capacity to draw some conclusions about causal relationships due to the simultaneous measurement of the presence of risk factors and outcomes. Thus, the impact of comorbidity on clinical decision-making regarding BZD prescription is an important topic, which might be interesting to investigate in a prospective study.

The high prevalence of long-term BZD use is a complex and pervasive problem, and a serious concern for many patients because of their wide range of well-documented adverse effects. BZD long-term use is likely related to tolerance and difficulty stopping the medication. When long term users of BZD attempt to withdraw this medication, they can suffer from severe discontinuation syndrome and rebound symptoms [40]. GPs should use strategies for discontinuing BZD, even more with all side effects of their long-term use including dependence and cognitive impairment. In clinical practice, BZDs can be very useful in providing timely relief of anxiety symptoms, but GPs should be able to identify those who are at higher risk of prolonged use and to take this information into account at the moment of prescription. In clinical practice, GPs should minimally [1, 6, 20]: 1) explain in detail the adverse effects, including the risks of motor vehicle accidents and of amplification of effects with alcohol use, as well as the risk of dependence and unwanted prolongation of use associated with BZD utilization; 2) inform that the BZD will be prescribed short-term only and when it should be discontinued; and 3) provide close follow-up for patients using a BZD whether acutely or when long-term use could not be avoided, and consider discontinuing BZDs at every follow-up visit. Among interventions to promote discontinuation, letters from clinicians or a single consultation with a GP to advise patients about the risk of long-term BZD use and the benefits of discontinuation can be effective [40, 41, 42, 43]. Some pharmacologic interventions are also considered effective: for example, the addition of pharmacologic therapies to facilitate BZD discontinuation, gradually reducing the dose, or substitution of a long-acting BZD [40, 44, 45]. A combination of cognitivebehaviour therapy with BZD dose-tapering or with supervised withdrawal is also considered an effective discontinuation strategy [46, 47]. Educational interventions should also be addressed: structured individualized education with dose-tapering and follow-up visits as well as using written instructions are both significantly associated with discontinuation success [43, 48, 49]. Finally, GPs should provide a supervised discontinuation plan to minimize adverse events linked to withdrawal and maximize rates of success notwithstanding the preferred discontinuation approach agreed with the patient. Improving awareness and competency on the rational use of BZD in primary care could be facilitated by clinicians education about BZD use evidence base, training in communication and negotiating skills for dealing with patients requesting BZDs, and access to appropriate psychological and psychosocial resources for their patients. Our study shows that there is a need to continue raising clinical awareness about this decades-long problem, and patients also need to be informed about the extensive prevalence of long-term BZD use in anxiety disorders to make an evidence-based decision when presented with the possibility of pharmacological treatment.

## Declarations

## Author contribution statement

Louise Fournier, Arnaud Duhoux: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data.

Marie-Michèle Tanguay Bernard, Mireille Luc: Analyzed and interpreted the data; Wrote the paper.

Pasquale Roberge: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data, Wrote the paper.

Élodie Côté, Olivier Lessard, Catherine Gibeault, Christian Bocti: Analyzed and interpreted the data.

Jean-Daniel Carrier: Analyzed and interpreted the data, Wrote the paper.

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## **Competing interest statement**

The authors declare no conflict of interest.

## Additional information

No additional information is available for this paper.

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