Craving for benzodiazepines : the development of the benzodiazepine craving questionnaire

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Chapter 4

The absence of benzodiazepine craving in a general practice benzodiazepine discontinuation trial

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ABSTRACT

Aim – This study aimed to assess benzodiazepine craving longitudinally and to describe its time course by means of the Benzodiazepine Craving Questionnaire (BCQ).
Setting and participants – Subjects were long-term benzodiazepine users participating in a two-part treatment intervention aimed to reduce long-term benzodiazepine use in general practice in the Netherlands.
Measurements – Four repeated measurements of benzodiazepine craving were taken over a 21-month follow-up period.
Findings – Results indicated that (1) benzodiazepine craving severity decreased over time, (2) patients still using benzodiazepines experienced significantly more severe craving than patients who had quit their use after one of the two interventions, and (3) the way in which patients had attempted to quit did not influence the experienced craving severity over time, however, (4) patients who had received additional tapering off, on average, reported significantly more severe craving than patients who had only received a letter as an incentive to quit.
Conclusions – Although benzodiazepine craving is prevalent among (former) long-term benzodiazepine users during and after discontinuation, craving severity decreases over time to negligible proportions. Self-reported craving can be longitudinally monitored and quantified by means of the BCQ.

INTRODUCTION

'Craving' is often regarded as a central phenomenon related to substance dependence. In ICD-10, but not in DSM-IV, a 'strong desire or compulsion' to use a drug is one of the diagnostic criteria for dependence.[1,2] Craving has been proposed as a factor in maintaining continued use or relapse in substance-dependent subjects, although, study results have been ambiguous (e.g. [3-6]). In a cross-sectional study Bohn et al. found that the scores on the Alcohol Urge Questionnaire (AUQ) showed significant negative correlations with the duration of abstinence before completing the questionnaire, suggesting a decrease of craving over time in abstinent patients.[7] Nevertheless, subjects attempting to remain abstinent from drugs frequently complain about craving and describe it as having a disruptive effect on their daily functioning (e.g. [8] in cocaine abusers). Dependent subjects may continue to experience craving years after their last drug use (e.g. [8-10]) and regular substance users describe experiencing craving even when they are not attempting to abstain from drug use (e.g. [11,12]).

Also, other findings about the longitudinal course of craving are ambiguous. For example, Gawin and Kleber[8] and also Halikas et al.[13] found craving in cocaine users undergoing treatment as a phenomenon to be episodic, waxing and waning over time. Others have found relatively stable average craving scores over time. McMillan and Gilmore-Thomas, for example, asked opiate addicts on methadone maintenance not attempting to remain abstinent to rate their 24-h recall of peak craving scores, as measured with a visual analogue scale (VAS), on weekdays during a 4-week study period.[14] Although average craving scores over time were relatively stable, there were large individual differences in subjects' weekly scores and day-to-day variability within subjects was quite high for many subjects. Anton, Moak and Latham, on the other hand, found that all alcohol-dependent subgroups (abstinent, 'slip' drinking and relapse drinking) showed a reduction in scores on the Obsessive Compulsive Drinking Scale (OCDS), assessing the craving experience of the previous week during the course of a 12-week pharmacological and cognitive-behavioural treatment trial.[15] Although relapsed patients showed an increase in the OCDS scores after a period of improvement, scores did not return to baseline prestudy levels. Treatment may have allowed these patients to stabilise at a lower level of alcohol craving.[15] Weddington et al. also found statistically significant decreases in cocaine craving during short-term abstinence, as measured with VAS, in a 28-day study among male long-term cocaine-dependent subjects.[16] West, Hajek and Belcher have found similar results among abstinent smokers chewing nicotine gum.[17] The frequency of experiencing the urge to smoke was highest at 24 h and 1 week, and then declined over a 4-week period of abstinence. However, the average strength of urges did not decline until the fourth week.

Taking into account the various substances discussed, no clear picture emerges about the time course of craving, the association with various use patterns, or its relationship with different treatment modalities.

In benzodiazepine (BZ) research, studies on craving are scarce and have shown contradicting results about the occurrence of BZ craving. For example, Lucki, Volpicelli

and Schweizer found that treated chronic users of therapeutic doses of BZs after 3 months of abstinence expressed little craving for the drug.[18] Whereas, Linden, Bar and Geiselmann argued that the refusal of about two-thirds of their general practice patients with long-term low-dose BZ dependence to accept a short drug-free intermission, provided evidence for drug-seeking or craving behaviour, regarding craving to be the equivalent of drug insistence.[19]

Recent research has shown that in a sample of Dutch general practice patients about 33% of the long-term BZ users or former users experienced craving. However, the average craving severity was limited.[20] Patients still using BZs had significantly higher craving scores than patients who had recently quit their BZ use.[21]

Craving has been defined in physiological and behavioural terms, but the assessments most widely used in substance abuse research have been subjective.[15] In most studies on craving simple visual analogue scales to quantify craving or single-item ratings of craving of unknown reliability and validity are used. In recent years, however, several multi-item craving questionnaires have been developed (e.g. [7,11,12]). One of them is the Benzodiazepine Craving Questionnaire (BCQ), a self-report instrument to assess BZ craving.[21]

The present study is the first study to assess BZ craving longitudinally. Repeated measures of the BCQ were taken over a 21-month study period in a group of long-term BZ users participating in a two-part treatment intervention aimed to reduce long-term BZ use. Research questions were: (1) Does the reported craving severity differ among the several assessments in time? (2) Does the overall experienced craving severity differ between patients who have quit their BZ use, patients who continue using BZs and those with intermittent use patterns, over the study period? (3) Is the way in which patients have attempted to quit their use (of own accord vs. with help from their general practitioner) related to the severity of craving they experience over time?

METHODS

Setting and design

This study was conducted as part of a large study on the efficacy of a two-part treatment intervention that aimed to reduce long-term BZ use in general practice in the Netherlands. Participants were known to their general practitioner (GP) to be long-term BZ users. They received a letter from their GP (first intervention) with the advice to gradually cut down the use of BZs by themselves and if possible to stop using them altogether. The letter also informed patients about the drawbacks of long-term BZ use and provided information on (how to deal with) withdrawal symptoms.[22] The letter from the GP was used as a pre-selection for the second part of the study: a randomised controlled discontinuation trial (second intervention), comparing tapering off alone (TO) with tapering off with additional group cognitive-behavioural therapy (CBT), and with a control group receiving usual care (UC).[23]

The study received ethical approval from the University Medical Centre Nijmegen, and took place from 1998-2001. Patients' responses to the Benzodiazepine Craving Questionnaire[21] at four assessments in a 21-month time span formed the basis of present study.

Subjects and procedure

We identified long-term BZ users by means of a computerised search for BZ prescriptions at 30 general practices. Long-term use was defined as BZ use for at least 3 months with a prescribed amount sufficient for at least 60 days of consumption in accordance with the recommended dosage. Exclusion criteria were: current psychiatric treatment, current treatment for drug or alcohol dependence, psychosis in medical history, epilepsy, insufficient mastery of the Dutch language, or terminal illness. Patients could also be excluded specifically on the GPs request, because of severe co-morbidity or for psychosocial reasons. Two thousand and four patients met the definition of long-term use and were sent a letter by their GP (first intervention). Three months after receipt of the letter with the advice to gradually discontinue their BZ use, patients were invited to consult their GP to evaluate their current BZ use status and the preceding period. Patients who did not succeed in discontinuing on their own accord were asked to participate in the second part of the study (discontinuation trial). The tapering off procedure was based on Schweizer et al., transferring participants to an equivalent dose of diazepam and reducing dosages by 25% a week during four weekly visits to the GP.[24] The last visit took place 2 weeks after the last reduction step. GPs were allowed to extend the tapering period if necessary. Group cognitive-behavioural therapy consisted of five weekly 2-h sessions, starting halfway through the tapering off period and ending 2 weeks thereafter. It aimed to support the participants during tapering off and to prevent relapse afterwards. The usual care control group did not receive any help with BZ reduction and GPs were instructed to give care as usual. Patients who did not quit BZ use after the first intervention were randomised for the second part of the study in a ratio of 2:2:1 (TO:CBT:UC) to achieve maximum discriminative power between the two experimental groups (TO and CBT).[23]

Measurements

In this study the course of craving is described by means of four assessments during a 21-month study period. The baseline assessment (T1) was carried out after receiving informed consent. It took place approximately 3 months after the start of the first intervention (letter from the GP). Three months after the start of the second intervention (discontinuation trial) patients received a short-term outcome assessment (T2), followed by two follow-up assessments (T3 and T4), 6 and 18 months, respectively, after the start of the discontinuation trial. All four assessments consisted of structured interviews and were carried out at the patients' homes by trained interviewers.

Measures

BCQ

The Benzodiazepine Craving Questionnaire (BCQ) was developed by our research group.[21] It is a reliable and psychometrically sound Rasch homogeneous self-report questionnaire to assess BZ craving in a general practice sample of long-term BZ users. Patients completed the original version of the BCQ according to their current experience, by indicating the

extent to which they agreed or disagreed with each item on a seven-point Likert-type scale. The endpoints of the scale were labelled 'strongly disagree' (1) and 'strongly agree' (7). For analysis, items of the BCQ were dichotomised between response options four and five of the Likert-type scale. Sum scores could range from 0 to 20.

Other measures

In addition to BZ craving, data were gathered concerning, among others, lifestyle characteristics (T1 only), BZ use, BZ withdrawal symptoms and BZ dependence. Number and severity of BZ withdrawal symptoms during discontinuation were assessed with the Benzodiazepine Withdrawal Symptom Questionnaire (BWSQ), a 20-item self-report questionnaire.[25,26] Severity of BZ dependence was assessed with the Benzodiazepine Dependence Self-Report Questionnaire (Bendep-SRQ), a 20-item self-report questionnaire consisting of four Rasch homogeneous scales, namely, problematic use, preoccupation, lack of compliance and withdrawal.[27] All questionnaires show good reliability and validity for the Dutch population. Results from the Bendep-SRQ, BWSQ and other variables at first assessment are used to describe the study sample.

Sample size

Of 1321 patients consulting their GP 3 months after the first intervention, 317 patients gave their informed consent to participate in the discontinuation trial. Patients who had quit their use of their own accord are also included in this number. They gave informed consent for follow-up assessments (as described above). For a graphic representation of the patient flow and dropout we refer to Oude Voshaar et al..[22,23] Of the 317 patients providing informed consent, 28 patients dropped-out before the first assessment, leaving 289 patients for the baseline interview. The BCQ was developed shortly after the study had started. Due to this delay in the development of the BCQ, 193 patients (of 317) filled in the BCQ at baseline. There were no significant differences in background and BZ use characteristics between patients who had received the BCQ at baseline and patients who had not or had missing BCQ values.[21] Of 193 patients who filled in the BCQ at baseline, 117 completed the BCQ at four assessments. The remaining 76 patients had missing BCQ values at one or more of these assessments and were left out of the analyses. There were no significant differences in background and BZ use characteristics between patients who had completed the BCQ at four assessments and patients who had not or had missing values. Oude Voshaar et al. have mentioned that some patients allocated to the treatment groups had already quit their BZ use before the treatment had started.[23] Since we were particularly interested in patients' actual BZ use behaviour, we did not commit to Intention to Treat analyses based on randomisation outcome. We distinguished three main subgroups in our data, based on patients' self-reported BZ use behaviour or 'pattern', namely, (1) BZ users, (2) former users, who had discontinued their BZ use, and (3) intermittent users, who were using and abstinent, respectively, at one assessment, and abstinent and using, respectively, at another assessment. These three groups could then be subdivided according to the

intervention the patients had received: (A) the letter from the GP only (first intervention) and (B) a discontinuation trial additional to the first intervention (second intervention, only for patients who had not quit their use after the first intervention). Interim analyses showed that BCQ scores did not differ significantly between patients receiving tapering off alone and patients receiving tapering off with additional group CBT, irrespective of their BZ use status (quit or using). Consequently, these two patient groups (tapering off alone and additional group CBT) were combined for the purpose of analysis. For an overview of the patient subgroups and numbers, we refer to Table 2.

Statistical analysis

To check for baseline differences between the patients who had quit and had not quit their use after the letter from the GP, SPSS 10.0.5 (SPSS Inc, Chicago, IL) was used to perform a series of univariate *t*-tests or non-parametric equivalents on socio-demographic and BZ use variables. For purpose of analysis, as described above, all 117 subjects were classified into six categories based on their actual self-reported BZ use 'pattern' (1 = quit, 2 = using, 3 = using intermittently) and the treatment they had received (A = first intervention (letter) only, B = additional second intervention (discontinuation trial)). The six categories were: (A1) patients who only received the first intervention (letter), had quit BZ use thereafter and remained abstinent for the duration of the study (n = 36); (A2) patients who only received the first intervention, but continued using BZs thereafter (n = 8); (A3) patients who only received the first intervention, had quit BZ use at a certain assessment but relapsed at another assessment (n = 19); (B1) patients who received the additional second intervention (discontinuation trial), had quit their BZ use thereafter and remained abstinent for the duration of the study (n = 20); (B2) patients who received the additional second intervention and continued using BZs (n = 23); (B3) patients who received the additional second intervention, had quit BZ use at a certain assessment but relapsed at another (n = 11).

We performed analysis of variance with three factors and first-order interactions. Square root transformation was performed to normalise the skewed data. Untransformed data are reported in the text. Scheffe's ratio, a method of post hoc comparison, was calculated on the transformed means to identify where the significant differences occurred.

RESULTS

Baseline characteristics of the patients who completed all four assessments (n = 117) are presented in Table 1. The majority of patients was female, elderly, married, had a secondary education level and was living on a pension. About 40% of the patients were smokers, about half used alcohol, and the majority used caffeine. The average BCQ score indicated a relatively low craving severity. On average, BZ dosage did not exceed the therapeutic dosage recommended by the WHO. Mean duration of BZ use exceeded 10 years. The overall

average severity of BZ dependence in our patient group was low.

Patients who had not quit their BZ use after the letter from their GP (first intervention) had used BZs for a significantly longer period of time (11.7 vs. 8.1 years; Mann–Whitney $U = 117.5$, $z = -2.4$, $p = .016$), had used BZs in significantly higher daily dosages prior to the intervention (7.8 vs. 2.2 mg of diazepam equivalents; Mann–Whitney $U = 1145.5$, $z = -2.6$, $p = .009$), scored significantly higher on three of four BZ dependence severity subscales, namely, problematic use (mean total score 1.7 vs. 0.6; Mann– Whitney $U = 746.5$, $z = -4.8$, $p < .0001$), preoccupation (2.2 vs. 0.5; Mann–Whitney $U = 670.0$, $z = -5.4$, $p < .0001$), and withdrawal (1.6 vs. 0.8; Mann–Whitney $U = 933.5$, $z = -3.2$, $p = .002$), and had significantly higher mean BCQ sum scores (1.9 vs. 0.3; Mann–Whitney $U = 1231.5$, $z = -2.5$, $p = .013$) compared to patients who had quit their BZ use after the discontinuation letter.

Data analysis for the course of BZ craving was based on 117 patients categorised as described above. Mean BCQ sum scores for the six subgroups at four assessments are shown in Table 2. There was no significant correlation between reported craving severity and BZ dosage. Percentages of patients experiencing BZ craving (BCQ sum score > 0) are presented in Table 3.

To answer our research questions we performed analysis of variance with three factors and first-order interactions. We found a main effect of time on the BCQ sum scores ($F_{3,450} = 9.9$, $p < .0001$). There was an overall decrease in BCQ sum scores during the course of the study (first research question). Scheffe's Test revealed a significantly lower mean BCQ sum score at the long-term follow-up assessment (T4) 18 months after the start of the second intervention, compared to all other assessments. In addition, there was a main effect of BZ use ´pattern´ (quit, use, intermittent) on the BCQ sum scores ($F_{2,450} = 3.7$, $p = .025$). On average (independent of time and intervention), there was a significant difference in self-reported craving severity between patients who had quit their BZ use, were still using and patients who were using intermittently (second research question). This ´effect of self-reported behaviour´ could be explained with Scheffe's Test by a significant difference in mean BCQ sum scores between patients who had quit their BZ use and patients who were still using BZs, users reporting more severe craving overall. The answer to our third research question was negative. There was no interaction between time and intervention, i.e., the way in which patients attempted to quit their BZ use (letter only or additional discontinuation trial guided by the GP) did not influence the BZ craving they experienced during the course of the study. However, on average (independent of time and BZ use pattern) there was a significant difference in experienced craving severity between patients who only received the letter as an incentive to quit their BZ use and patients who also completed the discontinuation trial (main effect of intervention: $F_{1,450} = 15.3$, $p = .0001$), suggesting that craving does play a role in discontinuing BZ use. Patients who had received the additional intervention reported significantly more severe craving (overall mean BCQ sum scores .55 vs. .25). Although marginally significant, the effect of BZ use pattern on the reported craving differed for each intervention (BZ use pattern * intervention effect: $F_{2,450} = 3.1$, $p = .045$), in other words, craving reported by the three groups (quit, use,

intermittent) had a different course for the patients who received only the letter (first intervention) compared to patients who received additional tapering off (second intervention). Scheffe's Test could not be performed on a compound variable. Additional analyses showed that the patients still using after the additional second intervention had significantly higher BCQ sum scores than patients who had quit after the additional second intervention and patients who had already quit or were using intermittently after the first intervention. There was no interaction effect between time and BZ use pattern.

Table 1 Baseline characteristics of the study sample

	Total group	(n = 117)
	n/mean	%/SD
Demographic variables		
Gender (female)	75	64.1%
Age (years)	62.4	12.0
Marital status		
Steady relationship (incl. married)	72	61.5%
Living alone	40	34.2%
Highest level of education		
Secondary level	81	69.2%
Financial income		
Pension	57	48.7%
Benzodiazepine usage		
Duration of benzodiazepine use (months)[a]	124.1	100.4
Quartiles	48.0 – 96.0 – 180.0	
Daily dose at first assessment (mg diazepam equivalents)[b]	7.4	9.5
Quartiles	2.9 – 5.0 – 8.3	
Daily dose 3 months previous to first intervention (mg diazepam equivalents)[c]	7.0	6.9
Quartiles	3.0 – 6.0 – 9.0	
Craving		
Craving severity (BCQ sum score)	1.3	3.5
Quartiles	0.0 - 0.0 – 1.0	
Benzodiazepine dependence characteristics		
Dependence severity (Bendep-SRQ sum score)		
Problematic use (*n* = 115)	1.3	1.2
Preoccupation (*n* = 116)	1.6	1.6
Lack of compliance (*n* = 117)	0.2	0.7
Withdrawal (*n* = 109)	1.3	1.7
Withdrawal symptoms (BWSQ sum score)	6.4	6.7
Substance/drug use		
Nicotine use		
Nicotine users	49	41.9%
Number of cigarettes/day among cigarette smokers (*n* = 48)	14.2	7.9
Alcohol use		
Drinking alcohol	58	49.6%
Units of alcohol/week	10.0	8.5
Caffeine use		
Caffeine users	75	64.1%
Units of caffeine/day	4.4	2.9

[a] Based on patients who discontinued and did not discontinue their BZ use in the previous 3 months.

[b] BZ users only.

[c] Based on recorded consumption extracted from the GP's clinical database.

Table 2 Mean BCQ sum score and standard deviation (SD) per patient subgroup, overall and at four assessments separately

		First intervention only (letter from GP)			Second intervention (additional) (discontinuation trial)*		
Self-reported BZ use pattern:		**Quit**	**Use**	**Intermittent**	**Quit**	**Use**	**Intermittent**
N (total = 117):		36	8	19	20	23	11
BCQ sum scores							
Assessment 1**	**Mean (SD)**	.33 (.83)	1.13 (2.03)	1.26 (3.89)	1.30 (2.94)#	2.48 (5.37)	2.64 (4.61)
Assessment 2	**Mean (SD)**	.33 (.72)	.25 (.71)	.26 (.56)	.60 (1.19)	1.78 (3.15)	1.27 (1.79)
Assessment 3	**Mean (SD)**	.67 (1.93)	.13 (.35)	.42 (.77)	.15 (.37)	1.48 (2.89)	2.55 (5.52)
Assessment 4	**Mean (SD)**	.28 (1.19)	.00 (.00)	.00 (.00)	.00 (.00)	.65 (2.35)	.09 (.30)
Overall BCQ sum scores	**Mean (SD)**	.24 (.59)	.25 (.57)	.27 (.65)	.30 (.65)	.71 (1.05)	.68 (1.10)

* This intervention includes only patients who did not quit their BZ use after the first intervention (letter). Before the start of the second intervention these patients were randomised either for tapering off alone or for group CBT. In this study the usual care control patients were considered as only receiving the first intervention and were placed in the use-group of the first intervention.

** Assessment 1: 3 months after the sending of the letter from the GP (first intervention); assessment 2: 3 months after the start of the discontinuation trial; assessment 3: 6 months after the start of the discontinuation trial; assessment 4: 18 months after the start of the discontinuation trial.

Since assessment 1 took place before the second intervention these patients were still using BZs at assessment 1.

Table 3 Percentage of patients experiencing craving in each patient subgroup*

		First intervention only (letter from GP)			Second intervention (additional) (discontinuation trial)#		
Self-reported BZ use pattern:		**Quit**	**Use**	**Intermittent**	**Quit**	**Use**	**Intermittent**
Assessment 1	%	19.4	50.0	31.6	45.0#	47.8	36.4
Assessment 2	%	22.2	12.5	21.1	25.0	52.2	54.5
Assessment 3	%	19.4	12.5	26.3	15.0	52.2	45.5
Assessment 4	%	5.6	0.0	0.0	0.0	13.0	9.1

* BCQ sum score > 0.

Since assessment 1 took place before the second intervention these patients were still using BZs at assessment 1.

DISCUSSION

This is the first study in which the long-term course of BZ craving has been described. The main findings of our study were:

1 Over the 21-month study period the reported craving severity decreased for all patient subgroups, regardless of their use status and the intervention they had received (main effect of time). At the long-term follow-up assessment 18 months after the start of the second intervention, the overall reported craving severity was significantly lower than the craving severity reported at earlier assessments for all subgroups, and negligible from a clinical point of view. Since patients who had only received the first intervention (letter) showed a decrease as well, the decrease in craving severity could not be due to the intensive GP guided tapering off (second intervention). Cue-reactivity studies might offer an explanation for this finding. Some of these studies have demonstrated that

craving can be highly stimulus specific (e.g. [28,29]). The two treatment phases of our study and the process of abstaining from BZs, focus patients on different kinds of discontinuation and withdrawal cues that may lead them to experience craving. At the fourth assessment, 18 months after the start of the second intervention, involvement from the GP has worn off as might have the patient's focus on BZ-related (withdrawal) cues, everything returning back to normal. Hence, less severe craving is being reported. Gritz et al. have found similar decreases over time, although, methods are not completely comparable since they asked their subjects to rate how frequently they experienced a craving.[30] After unaided smoking cessation on a self-determined target quit date, frequency of craving (varying from ´never´ through ´constantly´) gradually declined from months 1 to 12 among subjects who were abstinent at all follow-ups.[30]

2 Overall, patients still using BZs reported significantly more severe craving than patients who had quit their BZ use during the study (main effect of BZ use pattern). Possibly, continued use fosters BZ craving, or vice versa. Bordnick and Schmitz have found similar results in cocaine users.[3] Craving intensity during the past week of their outpatient treatment and 24-week follow-up was lowest among abstinent subjects and highest among subjects with moderate and heavy levels of cocaine use, as measured with the visual analogue scale of the Cocaine Craving Scale (CCS). In our study, however, there was no significant association between changes in experienced craving and changes in BZ dosage. Possibly, the fact that our subjects were all low-dose therapeutic BZ users may have accounted for this latter result.

3 The way in which patients had attempted to quit BZ use (of their own accord only or with additional GP guided tapering off with or without additional group CBT) did not influence the experienced craving severity over time (there was no interaction effect between time and intervention). However, patients who had received the additional tapering off intervention, on average, reported significantly more severe craving than patients who had only received the letter from the GP (main effect of intervention). In addition, patients who had received the additional second intervention but kept on using BZs experienced the most severe craving overall. Patients who had quit BZ use after the letter (first intervention) experienced the least severe craving. These findings suggest that for patients trying to discontinue their BZ use who are reporting more severe craving a ´minimal intervention´ alone may not be sufficient and a more intensive intervention, such as GP guided tapering off, may be appropriate. We have also found that patients who did not quit after the first intervention were more severely dependent on their BZs.

From a methodological point of view our study is in line with Linden et al.[19] They found that two-thirds of their GP patients with low-dose BZ dependence refused to accept a short drug-free intermission, referring to this drug insistence as craving. Kan et al. found that 40% of all those prescribed BZs in GP were dependent according to DSM-III-R criteria.[31] Craving and/or dependence might be an explanation for the relatively low participation rate in our study. However, Oude Voshaar et al. have mentioned that success rates for the

first intervention were fairly comparable to success rates reported by others.[22] This suggests that the patients who responded to the evaluation with the GP 3 months after sending the letter were representative of all patients who received the discontinuation letter with respect to BZ use.

One apparent finding in our study was that, although we found a considerable percentage of patients that experienced craving, the severity of the reported craving over time was relatively low for all subgroups. The majority of (former) BZ using GP patients hardly experienced any craving at all, either during or after their discontinuation process. Mol et al. have offered a tentative explanation in their earlier report, referring to the long half-lives and slow onset of action of most BZs compared to other substances of abuse in which craving is reported to a much higher extent.[21] Since our study sample consisted primarily of long-term, low-dose BZ users with the intention to quit, as they expressed this intention by giving informed consent to participate in a BZ discontinuation trial, future research needs to be conducted to evaluate the nature of BZ craving in untreated BZ users and in heavy users. Another possible explanation for the low BCQ scores over time might be a potential retest effect of the BCQ. Further longitudinal research, however, needs to provide more insight in these matters.

There is one major strong point compared to most other studies assessing self-reported craving. While in most other studies craving is assessed with VAS or single-item rating scales of unknown psychometric quality, we have assessed craving using a psychometrically sound multi-item questionnaire.

Since this is only the first study to describe the course of BZ craving longitudinally, one should be cautious in generalising and interpreting the results. However, this study further supports the notion that BZ craving is prevalent among (former) long-term BZ using GP patients, although it seems that severe or intense craving is almost absent.

The BCQ proved to be an instrument sensitive in discriminating the course of craving between different subgroups. Although data of other populations, e.g., BZ using psychiatric patients and (multi-)drug users, can further substantiate the validity of the BCQ, current data have shown that the BCQ is an instrument capable of quantifying craving for BZs longitudinally in (former) long-term general practice BZ users. The BCQ sum scores may give direction to the advisable treatment intensity, in terms of interference by the GP, when a patient is trying to abstain from BZs.

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