

High prevalence of benzodiazepine dependence in out-patient users, based on the DSM-III-R and ICD-IO criteria

Kan CC, Breteler MHM, Zitman FG. High prevalence of benzodiazepine dependence in out-patient users, based on the DSM-III-R and ICD-IO criteria.

Acta Psychiatr Scand 1997; 96: 85-93. © Munksgaard 1997.

C. C. Kan', M. H. M. BretelerZ.

F. G. Zitman'

'Department of Psychiatry and Department of Clinical Psychology, University of Nijmegen Research Group on Addictive Behaviours (UNRAB), University of Nijmegen, University Hospital, Nijmegen, The Netherlands

Despite the fact that there have been many reports on benzodiazepine (BZD) dependence, consensus about its definition has not been reached. Reliable prevalence data to estimate the dependence liability of BZDs are therefore lacking. This study is the first to assess the prevalence of BZD dependence in out-patient BZD users (115 general practice (GP) patients, 124 psychiatric out-patients and 33 self-help patients) on the basis of the DSM-III-R and ICD-IO substance dependence criteria. Past year and lifetime diagnoses of BZD dependence were made by means of the Schedules for Clinical Assessments in Neuropsychiatry (SCAN). High prevalence figures were found, ranging from 40% in the GP patients (DSM-III-R past year) to 97% in the self-help patients (ICD-10 lifetime), indicating that BZD users run a high risk of developing BZD dependence. The clinical management of BZD use could benefit from further development of diagnostic instruments such as a self-report questionnaire which reflects the severity of BZD dependence.

Key words: epidemiology; benzodiazepines; substance dependence

EG. Zitman, Professor of Biological Psychiatry, University Hospital of Nijmegen, Department of Psychiatry, PO Box 9101, 6500 HB Nijmegen, The Netherlands

Accepted for publication November 23, 1996

Introduction

Since the benzodiazepines (BZDs) were introduced in the early 1960s, the number of reports on their liability to cause dependence has been increasing steadily. The earliest reports in which the term BZD dependence was used were concerned with withdrawal reactions after the abrupt cessation of high doses of BZDs (1, 2).

In 1964, the World Health Organization (WHO) expert committee on dependence-producing drugs (3) adopted "the term dependence in a broader sense by replacing the confusing former terms 'addiction' and 'habituation' with definitions of physical and psychological dependence. Nevertheless, in many reports the term 'BZD dependence' continued to be used for the physical phenomena of tolerance and withdrawal, while the term 'addiction' was still used to refer to psychological aspects of dependence, such as 'compulsion to use', 'loss of control', 'continued use despite adverse consequences' and 'drug-seeking behaviour' (4,5).

Since 1981, the WHO has been propagating a psycho-physiological-social model for dependence on psychoactive substances, including the BZDs,

called the 'drug dependence syndrome' (6). This syndrome acquired enough support in studies in which it was applied to alcohol and other substances (7, 8) for it to become the primary source of the general substance dependence criteria of the *Diagnostic and Statistical Manual of Mental Disorders-III-Revised* (DSM-III-R) (9) and the *International Classification of Diseases, 10th edition* (ICD-10) (10).

In a recent literature review on the definition of 'BZD dependence, Unsen et al. (11) found that DSM and ICD substance dependence criteria had been used in only a small number of the 250 papers reviewed. Definitions of BZD dependence which emphasized the physical aspects were still predominant. It was concluded that consensus about the definition of BZD dependence had not yet been reached, and that this limited the scope for assessing the prevalence of BZD dependence. We confirmed this view by a search in the medical literature for reports in which the prevalence of BZD dependence was assessed, which yielded the limited number of reports shown in Table 1 (12-20).

Studies published on the prevalence of BZD dependence. Study Sample

Author (Year)	Study Sample	Definition of BZD dependence	Method/instrument	Results
et al. 1982 (121)	58 long-term BZD users (phobics Society)	(a) two or more withdrawal symptoms (b) withdrawal symptoms emerging and subsiding spontaneously	Tranquillizer Usage Survey	(a) 26% (14/58) (b) 5% (3/58)
ig 1985 (131)	33 000 admissions in psychiatric registers	No definition given	Retrospective register study	0.5% (1150/33000)
ker et al. 1986 (141)	(i) 10861 psychiatric in- and out-patients (BZD and non-BZD users) (ii) estimated BZD-using in-patients: 70% psychiatric	li (a) WHO/ICD-9 criteria lb) WHO/ICD-9 and DSM-III criteria liii WHO/ICD-9 criteria	(ii) retrospective chart study liii estimation	(ii) in-patients/out-patients: (a) 1.3% (19/5304) 1.7% (94/5557) (b) 0.2% (19/5304) 0.4% (21/5557) (ii) in-patients, 1.8%
al. 1989 (15)	15296 psychiatric inpatients	DSM-III criteria	Drug surveillance system and case conferences	4.7% (726/15296) BZD dependence or abuse
l. 1989 (16)	134 BZD-positive (tested in urine) psychiatric in-patients out of a sample of 899 psychiatric in-patients	ICD-9 criteria	Thorough psychiatric examination	4% (6/134) BZD dependence
1989 (171)	Psychiatric in-patients	WHO criteria (equivalent to ICD-9)	Structured questionnaire, case conference	5.6% (633 patients) BZD dependence or abuse
Helzer 1991 (118)	Epidemiologic Catchment Area (ECA) Surveys of residents aged 18 years and older between 1980 and 1984	DSM-III criteria for lifetime dependence on and abuse of barbiturates, sedatives or hypnotics	Diagnostic Interview Schedule (DIS)	1.2% non-prescription use and abuse/dependence in total surveyed population
1191	443 patients with DSM-III alcohol dependence or abuse	DSM-III criteria for lifetime dependence on barbiturates, sedatives or hypnotics	DIS, 3rd version	18% dependence (of which 8% was also abuse)
al. 1994 (201)	National Comorbidity Survey (NCS) of US household residents 15 to 54 years of age between 1990 and 1992	DSM-III-R criteria for lifetime dependence on and abuse of barbiturates, sedatives or hypnotics	Composite International Diagnostic Interview (CIDI)	1.2% in total surveyed population; 9.2% dependence in non-medical users of barbiturates, sedatives or hypnotics

The prevalence data on BZD dependence would be of most value if they could be based on uniformly accepted general criteria. The DSM-III-R and ICD-10 classifications have gained worldwide recognition, and their substance dependence criteria have been employed with promising results in addiction research concerning a number of different substances (7, 8). From the premises of the WHO that the drug dependence syndrome is a uniform construct for all substances, including BZDs, it follows that the DSM-III-R and ICD-10 substance dependence criteria should be used to assess the prevalence of BZD dependence. In fact, we found that in most of the studies listed in Table 1 (14-19), the DSM-III (21) and/or the ICD-9 (22) versions were used, while the DSM-III-R had only been applied in the National Comorbidity Survey (NCS) to date (20). As the concept of the drug dependence syndrome was introduced in the DSM-III-R and the ICD-10, it was only taken into account in the NCS. Unfortunately, in the NCS as well as in the Epidemiologic Catchment Area (ECA) Survey (18) and the study of Ross et al. (19), no distinction was made between the BZDs and the other anxiolytics, sedatives and hypnotics. This unnecessary masking of the BZDs is probably due to the fact that this distinction is not standardized in the structured diagnostic interviews which were used. We recommend the use of such instru-

ments, because this improves diagnostic reliability, but if meaningful prevalence data on the BZDs are required, a distinction should be made between the BZDs and the other sedatives, anxiolytics and hypnotics. Another distinction, namely that between BZD dependence and abuse, was not made in the studies of Schmidt et al. and Wolf et al. (15, 17), which made it impossible to interpret their prevalence results in terms of dependence alone.

As BZD use is a *conditio sine qua non* for BZD dependence, the prevalence in patients who use BZDs most clearly reflects the risk of BZD dependence. In the ECA Survey (18) and the NCS (20), the prevalence of dependence was assessed in the subpopulations of non-medical BZD users only, which excluded the medical users. Only Fleischhacker et al. (14) recognized that all BZD users should be considered as a separate subgroup. They estimated a BZD dependence rate of 1.8% in their psychiatric in-patients who were using BZDs, on the basis of the ICD-9 criteria and a figure of 70% BZD use in their in-patients on one particular day.

To obtain more reliable data which would provide more insight into the liability of BZDs to cause dependence, we decided to assess the prevalence of BZD dependence in three groups of out-patient BZD users using a structured diagnostic instrument

based on the DSM-III-R and ICD-10 substance dependence criteria. In the light of the results obtained, the management of BZD use in clinical practice is discussed.

Material and methods

Settings and subjects

This study was conducted at four general practices, three psychiatric out-patient departments and two self-help groups concerned with the use of addictive medication. The general practices were located in Nijmegen or nearby, while the psychiatric outpatient departments were located in Nijmegen, Eindhoven and Apeldoorn. The self-help groups 'Stichting Vrouwen en Medicijngebruik' (Women and Medication Use Foundation) and 'Stichting Phoenix' (Phoenix Foundation) are active at various locations in The Netherlands.

To be eligible to participate in the investigation, the subjects had to fulfil the following inclusion criteria: (i) actual BZD use; (ii) average frequency of BZD use of at least once a week; (iii) age between 17 and 70 years; (iv) ability to speak and read Dutch.

The patients who visited the general practices, psychiatric out-patient departments or self-help group meetings during the study period, or who had an individual contact with a self-help team member, were screened according to these inclusion criteria. Eligible patients were asked to participate by a representative of the treatment or self-help team. Informed consent was obtained from the majority of the selected subjects, i.e. 67% (115 of 172) of the general practice (GP) patients, 70% (124 of 178) of the psychiatric out-patients and 70% (33 of 47) of the self-help patients. The total sample of participants consisted of 272 subjects. In addition, 16% (27 of 172) of the GP patients and 18% (32 of 178) of the eligible psychiatric out-patients who did not participate in the entire study were prepared to provide their sociodemographic data on request. No significant differences were found in the sociodemographic data (χ^2 and t -tests; $P > 0.05$) between the abovementioned non-participants and the participants, which argues in favour of the representativeness of the data for the participating GP patients and psychiatric out-patients.

Study design

This study forms part of a larger project being conducted by the University of Nijmegen Research Group on Addictive Behaviours (UNRAB) in The Netherlands on the diagnosis and detection

of BZD dependence. The study population participated in two interviews, separated by an interval of 3 weeks. During the first interview, sociodemographic data were collected, followed by the administration of the Benzodiazepine Dependence-Self Report Questionnaire (Bendep-SRQ), the L-scale of the Minnesota Multiphasic Personality Inventory (MMPI-2), the Benzodiazepine Dependence-Structured Diagnostic Interview (Bendep-SDI) and the Schedules for Clinical Assessments in Neuropsychiatry (SCAN) (23). The Bendep-SRQ and Bendep-SDI have been constructed by our own research group. The second interview, which was conducted by the same interviewer as the first, consisted of the repeated administration of the Bendep-SRQ, followed by the Symptom Checklist-90 (SCL-90) (24) and the Addiction Severity Index-Revised (ASI-R). This report focuses mainly on the results of the SCAN.

The Schedules for Clinical Assessments in Neuropsychiatry (SCAN)

The SCAN, in which both the DSM-III-R and ICD-10 criteria are operationalized in a semi-structured format, were developed in the WHO/US National Institutes of Health (NIH) Joint Project on Diagnosis and Classification of Mental Disorders and Alcohol- and Drug-Related Problems (25). In this study, we administered the sections 'Alcohol' and 'Use of psychoactive substances other than alcohol' from the SCAN in the official Dutch translation (23), while reserving the category 'sedatives' for BZDs only. The DSM-III-R and ICD-10 past year (PY) and lifetime (LT) diagnoses of BZD dependence were calculated using the algorithms that are also being used in the WHO/NIH Reliability and Validity Study on Alcohol and Drugs, an international multicentre trial which is currently in progress at the Amsterdam Institute for Addiction Research and other centres.

Statistical analysis

To determine whether the prevalence of BZD dependence differed significantly between the three out-patient groups, contrasts were tested pairwise by Chi-square analyses. Therefore, Bonferroni's correction was applied, lowering the threshold for significance from $P < 0.05$ to $P < 0.017$.

Results

Sociodemographic characteristics, pattern of BZD use and degree of psychopathology

The sociodemographic characteristics of our out-

of BZD use and the degree of psychopathology are shown in Table 2.

In all three groups female subjects outnumbered male subjects. However, it should be pointed out that the very high female: male ratio (85: 15) in the self-help sample is partly due to the fact that membership of one of the self-help groups was restricted to women. The mean age ranged from 44 years in the self-help patients to 50 years in the GP patients. All of the subjects were of Dutch nationality, and the majority (96-98%) also had a Dutch cultural background. In all three groups most out-patients were married or in a steady relationship. Our samples showed different profiles with regard to living arrangements, level of education and financial income. It appeared that most GP patients were living without a partner and supporting themselves financially, while most self-help patients were living with a partner and were supported by their partner's income. Most of the psychiatric out-patients were living with a partner and were supporting themselves.

To reflect the mean BZD dose used daily of all the different BZDs by one parameter, we calculated the 'mean daily BZD dose/defined daily BZD dose ratio (MDD/DDD)', where the 'DDD' is the defined daily dose recommended by the WHO. If more than one BZD was used, the mean of the separate MDD/DDD values was used. On average, the GP patients used the lowest BZD dose, even lower than the recommended therapeutic level, shown by a MDD/DDD ratio of 0.9. The present duration of use of BZDs was expressed as the number of months as recalled by the patient. Only short durations (less than 2 months) were expressed in weeks. If more than one BZD was used, the duration of the BZD first prescribed was used to obtain the mean duration of BZD use, which is shown in Table 2.

In all of the groups the mean duration of BZD use indicated long-term use. In the psychiatric out-patients the average value of 40 months of BZD use was much lower than in the other two groups, which might be due to the transfer of long-term BZD prescription from psychiatrists to general practitioners.

The highest degree of psychopathology, as reflected by the total score on the SCL-90, was observed not in the psychiatric out-patients but in the self-help patients. Of course, self-help for addictive medication use does not exclude the possibility that these self-help patients might have been receiving psychiatric help as well. On the other hand, it is also possible that a number of these self-help patients did not find the professional help they were seeking despite, or as a result of, their psychopathology.

Prevalence of benzodiazepine dependence

Table 2. Sociodemographic characteristics of BZO users, BZO dose, duration of BZO use and SCL-90 total score

	General practice patients (n=115)	Psychiatric out-patients (n=1241)	Self-help patients (n=33)
Sociodemographic variables			
Sex (%1)			
Male	30	42	15
Female	70	58	85
Mean age:t SO (years)	50:t13	47:t 12	44:t 11
Marital/social status (%1)	23	13	12
Single/never married Engaged/in steady relationship Married	4	10	12
~ivorced	48	55	58
Widowed	17	15	18
Living arrangement (%1)	10	,7	0
Alone	49	29	27
With partner	40	61	67
Other	11	10	6
Level of education (%1)			
Primary	46	50	33
Secondary Advanced	23	31	49
Financial income (%)	31	19	18
Profession			
Unemployment benefit	23	23	9
Disability benefit	15	10	18
Pension	26	36	27
Partner's income Other	13	12	6
MOO/ODDa	14	15	36
Quartiles	10	3	3
Mean duration of BZO use (months)	0.9	1.2	1.3
Quartiles	0.25-0.5-1.0	0.5-0.9-1.5	0.5-1.0-2.0
SCL-90 mean total score	88	40	
Psychoneuroticism:t SO	9-48-120	6-13-42	20-90-152
	169b :t 63	177C :t62	223:t 69

^a MOD/ODD, mean daily BZO dose/defined daily BZO

dose. ^b n = 112, due to drop-outs after the first interview.

^c n = 120, due to drop-outs after the first interview.

^d Data are expressed as rounded-up figures.

Diagnostic results

The group results after applying the DSM-III-R and ICD-IO criteria are shown in Tables 3 and 4. These values were derived from the same responses on the same SCAN items, with the exception of 'social harm or repeated risk-taking behaviour' (only a DSM-III-R criterion) and 'craving' (only an ICD-IO criterion). Furthermore, in contrast to the DSM-III-R criteria, a number of ICD-IO criteria are reflected by a combination of SCAN items, and the ICD-IO sets a lower cut-off point for 'tolerance' than the DSM-III-R. These systematic differences resulted in a higher prevalence of all ICD-IO diagnoses than DSM-III-R diagnoses.

The GP patients showed low prevalences of the criteria 'time involved in BZD-related activities', 'salience of BZD activities' and also 'tolerance' if the cut-off point of the DSM-III-R was used. By comparison, the prevalence data for almost all of the criteria in the psychiatric out-patients were higher, and the self-help patients showed the highest prevalence values for all of the dependence criteria.

All of the observed prevalence values for PY and LT BZD dependence reflected by the DSM-III-R and ICD-IO must be regarded as unexpectedly high. The lowest PY prevalence of BZD dependence was found in the GP patients, and it still amounted to 40% (for DSM-III-R) and 52% (for ICD-IO). All of the LT prevalences were higher than

Table 3. Past year (PY) and lifetime (LT) prevalence of positive DSM-III-R substance dependence criteria and the diagnosis benzodiazepine (BZD) dependence^a

Dependence criteria	General practice patients (n=1151)		Psychiatric out-patients (n=124)		Self-help patients (n=331)	
	PY	LT	PY	LT	PY	LT
Impaired ability to control BZD use once started	14	26	14	15	36	67
Impaired ability to abstain from or reduce BZD use	59	67	70	77	79	94
Time involved in BZD-related activities	5	11	12	16	61	67
Social harm or repeated risk-taking behaviour	24	34	37	47	39	61
Salience of BZD activities	14	24	35	36	49	67
Persistence in use despite harmful effects	12	17	27	27	42	58
Tolerance	9	17	13	17	27	58
Withdrawal symptoms	48	56	66	69	88	94
BZD use to relieve withdrawal symptoms	33	40	43	48	67	82
DSM-III-R diagnosis of BZD dependence (95% CI)	40 (131-501)	51 (41-601)	63 (154-71)	69 (60-77)	82 (164-931)	97 (184-1001)

^a Data are expressed as rounded-up percentages of respondents.

the respective PY prevalences, which indicates that there were some BZD users who had been dependent in their lifetime, but who had not been dependent during the past year, despite actual BZD use.

To determine whether the differences in the prevalence of BZD dependence between the three groups were significant, the differences between pairs were tested by Chi-square analyses. The difference between the GP patients and the selfhelp patients was significant for all of the diagnoses ($P < 0.017$). The difference between the GP patients and the psychiatric out-patients was significant ($P < 0.017$) for all of the diagnoses except for the ICD-10 LT diagnosis ($P = 0.05$). The difference between the psychiatric out-patients and the self-help patients was significant for the LT diagnoses, but not for the PY diagnoses. On the whole, the difference in the prevalence of BZD dependence between the GP patients and the self-help patients appears to be generalizable. However, differences in the prevalence of BZD dependence between the psychiatric out-patients and the other two groups should be interpreted with more caution.

Discussion

In many countries, BZDs are widely prescribed

psychotropic drugs. Recent research in The Netherlands has shown that the I-year prevalence of BZD use in the general population was 10.6% in 1992 (26). Combined with the high DSM-III-R and ICD-10 PY and LT prevalences of BZD dependence in the out-patient BZD users described in the present study, this suggests that BZD dependence is a major health problem. We do not expect that the substance dependence criteria of the recent DSM-IV will reflect a reduction in these prevalence figures, because the changes with regard to the former DSM-III-R have resulted in a closer resemblance to the ICD-10.

The three groups in this study were found to differ with respect to several sociodemographic characteristics, BZD dose, duration of BZD use and degree of psychopathology. The PY and LT prevalence of BZD dependence in the GP patients (according to DSM-III-R and ICD-10) differed significantly from the prevalence values in the self-help patients. The fact that the highest prevalence of BZD dependence was observed in the self-help patients was not surprising, as medication dependence was the major issue of concern in the participating self-help groups. In addition, the higher degree of psychopathology (as reflected by the SCL-90 total score) and the overrepresentation of female subjects, might be other related factors.

Prevalence of benzodiazepine dependence

Table 4. Past year (PY) and lifetime (LTI) prevalence of positive ICD-10 drug dependence criteria and the diagnosis benzodiazepine (BZD) dependence'

Dependence criteria	General practice patients (n=1151)		Psychiatric out-patients (n=1241)		Self-help patients (n=331)	
	PY	LT	PY	LT	PY	LT
Craving	84	85	88	89	91	94
Impaired ability to control BZD use once started, or to abstain from or reduce BZD use	64	71	74	80	79	97
Withdrawal symptoms or BZD use to relieve withdrawal symptoms	48	56	66	69	88	94
Tolerance	27	41	31	36	64	82
Saliency of BZD activities or time involved in BZD-related activities	15	26	37	39	73	85
Persistence in use despite harmful effects	12	17	27	27	42	58
ICD-10 diagnosis of BZD dependence (95% CII)	52 (42-61)	63 (53-71)	69 (60-77)	74 (65-81)	88 (72-97)	97 (84-100)

, Data are expressed as rounded-up percentages of respondents.

Evidently caution is required when generalizing the results of this study. Undoubtedly there has been some selection bias due to the fact that the selection of BZD users was carried out over a period long enough to include all long-term BZD users, while due to varying prescription habits in the participating settings there has probably been variation in the selected numbers of short-term BZD users. Furthermore, BZD users living in towns in particular were selected, due to the nonrural nature of most of the participating settings and, although this was not apparent in any way, the compliance of the participating settings might have been related to a special interest in BZD dependence. As we have already mentioned, more women were selected in the relatively small self-help group sample, due to the restricted target membership of one of the two self-help groups. Finally, even if the nature of BZD dependence does not differ between countries, the prevalence figures in this study relate to the management of BZD use in The Netherlands, which will indeed be different in many other countries. However, in view of the fairly good response rates of around 70% in all of the samples, the absence of significant sociodemographic differences between the participants and a substantial proportion of the non-participants, and the fact that this study was conducted in a number of different settings, we expect that the samples are at least reasonably

representative of these types of settings in The Netherlands.

Compared to the earlier studies shown in Table 1, in which the prevalence of BZD dependence ranged from 0.2 to 26% (12-20), our prevalence figures appear to be unexpectedly high. This could be due to several methodological differences. Unlike most of the earlier studies (13, 15-20), in which the prevalence of BZD dependence was assessed in patient samples consisting of BZD users and non-users, the present study was confined to BZD users, which obviously increased the prevalence figures. Furthermore, a lack of distinction between BZDs and other sedatives, anxiolytics and hypnotics (18-20), and between BZD dependence and abuse (15, 17), was avoided. However, we consider the conceptual changes that have been introduced in the DSM-III-R and ICD-10 in line with the substance dependence syndrome to be the most important methodological differences. Only one of the earlier studies (20) was also based on the DSM-III-R criteria. In most of the other studies the DSM-III and/or the ICD-9 criteria were used (14-19). In contrast to the DSM-III, in which tolerance and withdrawal were required for the diagnosis of dependence, the psycho-physiological-social approach of the DSM-III-R has made it possible to diagnose BZD dependence even in the absence of tolerance and withdrawal, which increases the prevalence figures.

A high prevalence implies that BZD users run a high risk of developing BZD dependence. This gives rise to the question of whether changes should be made in the management of BZDs in clinical practice. Warnings about the liability of BZDs to cause dependence have been expressed before (27), but they could not be substantiated by prevalence figures based on generally accepted diagnostic criteria. This enabled other authors to state that the therapeutic benefits and safety of BZDs outweigh the small risk of dependence (28, 29). In an official task-force report by the American Psychiatric Association, the liability of BZDs to cause dependence was still not considered to be a major problem (30), but the long-term use of BZDs was discouraged. The state of New York, by contrast, took the matter very seriously by deciding to add BZDs to its triplicate prescription programme, which obliges physicians to supply a copy of each BZD prescription to the dispensing pharmacist and the state Department of Health, and to adhere to some prescription-limiting rules (31). This continuing debate has raised sufficient concern for guidelines to be put forward for the prescription of BZDs in order to limit the occurrence of BZD dependence and abuse as much as possible. The English Committee on Safety of Medicines (1988) recommended that BZDs should not be used for more than 4 consecutive weeks, and that the lowest possible dosage should not be exceeded (32). Similar guidelines have been drawn up by the Department of Health (in 1992) and the British Medical Association (in 1993) (33). However, it is questionable whether such guidelines can be followed adequately in clinical practice. In a recent study (34) it was reported that it was not uncommon for Dutch general practitioners to prescribe BZDs without a well-recognized indication. In addition, they rarely re-evaluated a patient's continuing need for BZDs. Apparently the risk of BZD dependence is still being underestimated, or it might be too demanding in clinical practice to follow the present guidelines for the prescription of BZDs. In our opinion, more attention should be paid to factors which maintain a pattern of repeated BZD prescription over longer periods of time in order to determine which measures could be adopted to improve its clinical management. Recognition of patient risk factors, careful patient screening, use of fewer reinforcing compounds in high-risk patients and careful monitoring of prescription are valuable strategies that have been suggested by Sussman to minimize abuse and dependence (35). However, such indirect measures would demand continuous monitoring efforts, which can hardly be expected to occur in (general) practice. Moreover, the interpretation of such indirect measures

is complicated and highly subjective. A structured instrument to diagnose BZD dependence, such as the SCAN, would be a direct and more objective measure to facilitate the monitoring of BZD users, but it would still be too time-consuming for routine use in clinical practice, and it would require interview training. Instead of a structured diagnostic interview, a reliable self-report questionnaire could be developed for routine use in order to rate the severity of BZD dependence. Such an approach would be more suitable for clinical practice, and could become an important asset in the clinical management of BZD use that aims to reduce non-indicated chronic BZD use.

Acknowledgements

We thank M.A. van het Hof for statistical advice, and all the staff and team members of the general practices, psychiatric out-patient departments and self-help groups who contributed to this study.

References

1. SLATER I. Suspected dependence on chlordiazepoxide hydrochloride (Librium). *Can Med Assoc J* 1966; 95: 416.
2. SELIG JW. A possible oxazepam abstinence syndrome. *JAMA* 1966; 198: 951-952.
3. WHO Expert Committee on Addiction-Producing Drugs. Thirteenth report. World Health Organization Technical Report Series 1964; no. 273.
4. SENA y EC. Addictive behaviors and benzodiazepines. 1. Abuse liability and physical dependence. *Adv Alcohol Subst Abuse* 1989; 8: 107-124.
5. MILLER NS, MAHLER Jc. Addiction to and dependence on benzodiazepines. Diagnostic confusion in clinical practice and research studies. *J Subst Abuse Treat* 1991; 8: 61-67.
6. EDWARDS G, ARIF A, HODGSON R. Nomenclature and classification of drug- and alcohol-related problems: a WHO Memorandum. *Bull WHO* 1981; 59: 225-242.
7. EDWARDS G. The alcohol dependence syndrome: a concept as stimulus to enquiry. *Br J Addiction* 1986; 81: 171-183.
8. KOSTEN TR, ROUNSAVILLE BJ, BABOR TF, SPITZER RL, WILLIAMS JB. Substance-use disorders in DSM-III-R. Evidence for the dependence syndrome across different psychoactive substances. *Br J Psychiatry* 1987; 151: 834-843.
9. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, revised 3rd edn. Washington, DC: American Psychiatric Association, 1987.
10. World Health Organization. The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research. Geneva: World Health Organization, 1992.
11. LINSEN SM, BRETHER MHM, ZITMAN FG. Defining benzodiazepine dependence: the confusion persists. *Eur Psychiatry* 1995; 10: 306-311.
12. HALLSTROM C, LADER M. The incidence of benzodiazepine dependence in long-term users. *J Psychiatr Treatment Eval* 1982; 4: 293-296.
13. LAUX G, KONIG W. Benzodiazepine: long-term use or abuse? Results of an epidemiological study. *Dtsch Med Wochenschr* 1985; 110: 1285-1290.
14. FLEISCHHACKER WW, BARNAS C, HACKENBERG B. Epidemiology of benzodiazepine dependence. *Acta Psychiatr Scand* 1986; 74: 80-83.

Prevalence of benzodiazepine dependence

15. SCHMIDT LG, GROHMANN R, MULLER OERLINGHAUSEN B, OTTO M, RUTHER E, WOLF B. Prevalence of benzodiazepine abuse and dependence in psychiatric in-patients with different nosology. An assessment of hospital-based drug surveillance data. *Br J Psychiatry* 1989; 154: 839-843.
16. PRIEBE S, LIESENFELD O, MULLER OERLINGHAUSEN B. Does routine screening for benzodiazepines help to diagnose dependence in psychiatric inpatients? *Acta Psychiatr Scand* 1989; 80: 514-517.
17. WOLF B, GROHMANN R, BIBER D, BRENNER PM, RUTHER E. Benzodiazepine abuse and dependence in psychiatric inpatients. *Pharmacopsychiatry* 1989; 22: 54-60.
18. ANTHONY JC, HELZER JE, Robins LN, Regier DA, ed. Syndromes of drug abuse and dependence. In: *Psychiatric disorders in America*. New York: The Free Press, 1991: 116-154.
19. ROSS HE. Benzodiazepine use and anxiolytic abuse and dependence in treated alcoholics. *Addiction* 1993; 88: 209-218.
20. ANTHONY JC, WARNER LA, KESSLER RC. Comparative epidemiology of dependence on tobacco, alcohol, controlled substances, and inhalants: basic findings from the National Comorbidity Survey. *Exp Clin Psychopharmacology* 1994; 2: 1-24.
21. American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*, 3rd edn. Washington DC: American Psychiatric Association, 1980.
22. World Health Organization. *The ICD-9 classification of mental and behavioural disorders. Clinical descriptions and guidelines*. Geneva: World Health Organization, 1975.
23. GIEL R, NIENHUIS FJ. SCAN. Vragenschema's voor de klinische beoordeling in de neuropsychiatrie. (SCAN. Schedules for Clinical Assessment in Neuropsychiatry) Geneva: World Health Organization, Division for Mental Health, 1992.
- 24. ARRINDELL WA, ETTEMA H. Dimensionele structuur, betrouwbaarheid en validiteit van de Nederlandse bewerking van de Symptom Checklist (SCL-90): gegevens gebaseerd op een fobische en een 'normale' populatie (Dimensional structure, reliability and validity of the Dutch version of the Symptom Checklist (SCL-90); data based on a phobic and a 'normal' population). *Nederlands Tijdschrift voor de Psychologie en haar grensgebieden* 1981; 36: 77-108.
25. JANCA A, USTUN TB, SARTORIUS N. New versions of World Health Organization instruments for the assessment of mental disorders. *Acta Psychiatr Scand* 1994; 90: 73-83.
26. HE RINGS RMC. Geneesmiddelen als determinant van ongevallen (Medications as determinants of accidents). Utrecht: Faculty of Pharmacy, 1994.
27. CLINTHORNE JK, CISIN IH, BALTER MB, MELLINGER GD, UHLENHUTH EH. Changes in popular attitudes and beliefs about tranquilizers, 1970-1979. *Arch Gen Psychiatry* 1986; 43: 527-532.
28. UHLENHUTH EH, DEWIT H, BALTER MB, JOHANSON CE, MELLINGER GD. Risks and benefits of long-term benzodiazepine use. *J Clin Psychopharmacology* 1988; 8: 161-167.
29. MARKS I. *The benzodiazepines. Use, overuse, misuse, abuse*. Lancaster: MTP Press, 1985.
30. American Psychiatric Association. *Benzodiazepine dependence, toxicity and abuse. A task force report of the American Psychiatric Association*. Washington, DC American Psychiatric Association, 1990.
31. APPELBAUM PS. Controlling prescription of benzodiazepines. *Hosp Commun Psychiatry* 1992; 43: 12-13.
32. Committee on the Safety of Medicines (CSM). *Benzo diazepines, dependence and withdrawal symptoms*. *Current Problems* 1988; 21: 1-2.
33. GABE I. Promoting benzodiazepine withdrawal. *Addiction* 1994; 89: 1497-1504.
34. VAN DER WAALS FW, MOHRS J, FOETS M. Sex differences among recipients of benzodiazepines in Dutch general practice. *Br Med J* 1993; 307: 363-366.
35. SUSSMAN N. Treating anxiety while minimizing abuse and dependence. *J Clin Psychiatry* 1993; 54 (Suppl. 5): 44-51.

