

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/20252> holds various files of this Leiden University dissertation.

Author: Manthey, Leonie

Title: Determinants and consequences of long-term benzodiazepine use

Date: 2012-12-06

Are General Practitioner Attitudes and Characteristics associated with Patient Benzodiazepine Use?

Leonie Manthey
Erik J. Giltay
Tineke van Veen
Miranda G.H. Laurant
Stasja Draisma
Arie Knuistingh Neven
Ron Wolterbeek
Brenda W.J.H. Penninx
Frans G. Zitman

Submitted for publication



ABSTRACT

Background: The patient correlates of benzodiazepine (BZD) use have received much attention in the past. Less attention has been paid to the contribution of general practitioners' (GP) attitudes and characteristics to patient BZD use.

Aim: We aimed to investigate GP attitudes and characteristics as possible correlates of patient BZD use and inappropriate use.

Design: Cross-sectional cohort study.

Setting: The Netherlands.

Method: A total of 1433 GP patients of the Netherlands Study of Depression and Anxiety (NESDA) and 62 general practitioners (GPs) participated. Physician- and patient characteristics were measured through questionnaires and interviews. Logistic multilevel regression analyses were used to identify GP characteristics as possible correlates of patient BZD use and inappropriate use.

Results: Patient BZD use and inappropriate use did not vary significantly between GPs and were only associated with few attitudes and characteristics of GPs (after correction for patient correlates of BZD use). Only the GP's perceived 'disability to differentiate unhappiness from depression' was weakly associated with less patient BZD use (OR = 0.98, P = 0.048) and higher 'professional comfort and competence with mental health care' of the GPs correlated with less inappropriate patient BZD use (OR=0.29, P = 0.03).

Conclusions: Our results indicate that the attitudes and characteristics of GPs barely affect patient BZD use. Instead, patient characteristics seem to be decisive in whether BZDs are used (inappropriately) or not. Interventions should target patients at risk of inappropriate use to educate them about the downsides of BZD use, and the prescribing physicians to teach them alternative treatments for their patients.

INTRODUCTION

Benzodiazepines (BZDs) are an effective short-term treatment of anxiety and insomnia,^{1,2} but guidelines advise against longer-term use,^{3,4} as the risk of side effects⁵ and dependence development is high.^{1,6} Regardless, (inappropriate) BZD use is common.^{7,8} In the past, many studies focused on user characteristics⁹⁻¹² and identified old age, severe psychopathology and chronic illnesses as important correlates of (inappropriate) BZD use.⁹⁻¹³ Less attention has been paid to the contribution of physician characteristics to patient BZD use.¹⁴

Qualitative research on physician characteristics showed that the majority of physicians were aware of the treatment guidelines.¹⁵⁻¹⁷ Yet, BZDs were inappropriately prescribed due to 1) a presumed lack of time,¹⁸⁻²² alternatives^{16,19,20,23} and skills,¹⁹⁻²² 2) the idea that BZDs are appropriate for vulnerable patients,^{17,19,23} and 3) the wish to maintain a good-doctor patient relationship.^{15,20-22}

Quantitative studies identified male gender,^{24,25} personal usage of BZDs,²⁶ being a general practitioner (GP) versus a psychiatrist,^{24,26} allowing patients to influence prescription decisions,²⁵ prolongation of prescriptions without direct doctor-patient contact,²⁵ and multiple drug prescribing²⁷ as important correlates of patient BZD use. A substantial number of studies did not identify any significant physician related factors in the fully adjusted model^{28,29} or found inconsistent results.^{24-27,30} Most of these studies did not correct for patient characteristics²⁴⁻²⁶ so that it is unclear if the found differences were due to variation between physicians or due to differences between the treated patients. The attitudes of physicians towards depression and anxiety, guideline implementation, and collaboration with health care specialists have received little attention in previous research.^{24,28,30,31}

This study aims to investigate the GP attitudes and characteristics as possible correlates of (aim 1) patient BZD use and (aim 2) inappropriate patient BZD use.

MATERIALS AND METHODS

Subjects

Subjects participated in the baseline assessment of the Netherlands Study of Depression and Anxiety (NESDA), a longitudinal cohort study of 2981 respondents at different stages of depressive or anxiety disorder.³² Details on objectives, recruitment, and methods of NESDA have been described elsewhere.³² The study protocol was approved by the Ethical Review Board of each participating center and all subjects signed an informed consent at the baseline assessment.³²

Of the 2981 respondents, 1610 were recruited via their 67 general practitioners (GPs).^{32,33} GPs who did not return the NESDA self-report questionnaires (n=5), the patients registered with those GPs (n=164) as well as patients with epilepsy (n=13)³⁴ were excluded. Accordingly, 1433 patients and 62 GPs remained for analyses.

To identify the GP correlates of patient BZD use, (aim [1]), two groups were defined: GP patients who reported BZD use in the month prior to the baseline interview ('BZD users', n=173) and those who reported no use of BZDs during the month before the baseline interview ('non-users', n=1260). For the investigation of GP correlates of inappropriate patient BZD use (aim [2]), non-users were excluded and the BZD user group was defined into appropriate BZD users (n=18) and inappropriate BZD users (n=155).

Patient BZD Use

Two indicators of patient BZD use were investigated:³⁵ patient BZD use and inappropriate patient BZD use. *Patient BZD use* was registered by self-report or observation of drug containers. It was defined as daily or infrequent BZD use in the month prior to the baseline interview. BZD using patients reported the type and dosage of BZD taken on an average day of use. The daily BZD dose was computed according to the coding system of the Anatomical Therapeutic Code (ATC) and Defined Daily

Dose (DDD) system.³⁶ The Mean Daily Dose was calculated by division of the individual daily doses (in milligrams) of BZDs by the DDD for the particular BZD.³⁵ BZDs were classified as ATC-coded groups N05BA, N05CD, and N03AE01. The non-BZD hypnotics zopiclone and zolpidem (ATC code N05CF), were also included.³⁵ For GP patients who used BZDs other than diazepam, conversion tables were used to calculate equivalent daily doses.^{37,35} If more than one BZD was used, dosages were summed. The duration of BZD use was reported in months. The number of different types of BZDs used concomitantly was recorded. *Inappropriate patient BZD use* criteria were derived from Dutch and British treatment guidelines.^{4,38,39} The following criteria for appropriate use were derived: 1) mean daily dosage \leq DDD, 2) duration of benzodiazepine use \leq 3 months in case of no concomitant antidepressant (AD) use and \leq 2 months in case of concomitant AD use, and 3) only one type of BZDs is used at a time. Patients who met all 3 appropriateness criteria were categorized as appropriate users and patients who did not meet one or more criteria were categorized as inappropriate users.

Physician Characteristics

Physician characteristics were measured by questionnaires. The first part of the questionnaire contained demographic data including age, gender, clinical experience (in years), employment status of the GP (in full-time equivalents [fte]), the trainer status of the GP (i.e., approved clinical supervisor and mentor of GP registrars yes/no),³³ the type of practice the GP belonged to (i.e., solo vs. group practice), access to health care personnel, and the number of patients per GP. These characteristics were measured by the 'Visit instrument to assess practice management',⁴⁰ which was filled in by the practice assistants or practice nurses of the GPs. In part two, the GP's interest and attitudes towards depressive and anxiety disorders were assessed with the Depression Attitude Questionnaire (DAQ)⁴¹ and a questionnaire to measure GPs' attitudes to their role in the management of patients with depression and anxiety.^{33,42} In part three,

the collaboration of GPs with professionals and institutions specialized in mental health care was investigated.³³ In part four, the GPs' perceived workload and level of burnout were measured.³³ The Utrecht Burn-Out Scale (UBOS-C) investigated the GPs' perceived level of burn-out.⁴³ An additional item measured to what extent time limitations were perceived as barriers to the provision of mental health care on a 6 point Likert scale (from 'not at all' to 'very much').³³ The self-report questionnaires of parts two, three and four were filled in by the GPs personally.

Covariates: Patient Characteristics

The patient characteristics older age, singleness, unemployment, severity of anxiety, depression, comorbidity, and insomnia were associated with BZD use in previous research of this study group.¹³ Inappropriate patient BZD use was associated with higher age and chronic illnesses.¹³ These characteristics were corrected for in the regression analyses in order to identify the GP attitudes and characteristics, which were associated with patient BZD use independent of the characteristics of the patients themselves.

Patients reported gender, age, work status, and partner status in the baseline interview. Depressive and anxiety disorders were measured by the Composite International Diagnostic Interview (CIDI, life time version 2.1).⁴⁴ For the present analysis, 1 year CIDI diagnoses of anxiety only, depression only or comorbidity at baseline were established. The severity of generalized anxiety and panic symptoms at baseline was assessed with the Beck Anxiety Inventory (BAI).⁴⁵ The severity of insomnia at baseline was determined using the Insomnia Rating Scale (IRS).⁴⁶ The presence of chronic illnesses such as chronic lung disease, heart condition, and diabetes mellitus was recorded during the interview and the number of chronic illnesses a person suffered from were counted.

Statistical Analysis

Sample characteristics were expressed by frequencies, means or medians. Because of the hierarchical structure of the study (patients nested within GPs) and the dichotomous outcome variables (BZD use and inappropriate use) univariable and multivariable multilevel logistic models (Proc Glimmix; SAS 9.2; SAS Institute Inc., Cary, NC, USA) were conducted. We started with two separate models that did not contain any GP characteristics yet, but only one of the dependent variables 'BZD use' or 'inappropriate BZD use' and the above mentioned patient characteristics as covariates. As a next step, all above described GP characteristics were considered as potential correlates of BZD use and inappropriate use in separate univariable analyses. Univariable analyses were corrected for the patient characteristics age, sex and employment status. Further, the analyses of BZD use were corrected for the patient characteristics partner status, 1 year diagnosis of depression and/or anxiety, Beck Anxiety Inventory, and Insomnia Rating Scale.¹³ The analyses of inappropriate use were additionally corrected for the patient characteristic number of chronic illnesses.¹³ GP characteristics with $P < 0.10$ in univariable analyses and above mentioned covariates were entered in the multivariable model. All independent variables were entered as fixed factors. We added a random intercept at the GP level. Two-sided P-values equal or smaller than 0.05 were considered as significant in the multivariable model.

RESULTS

Table 1 shows the characteristics of the 62 GPs. GPs were more often male (54.8%), had an average age of 49.2 years and an average clinical experience of 17.8 years. At least half of the GPs reported good collaboration with social workers, psychologists and social psychiatric nurses, but not with mental health care institutions. Most GPs worked in group practices (93.5%). All GPs had a practice assistant and most GPs had access to mental and non-mental health care professionals. The

GPs were responsible for a median number of 1500 patients, of whom a median of 20 patients were NESDA participants in the current analysis.

GP Correlates of BZD Use

The patient group consisted of 1260 non-users (87.9%) and 173 BZD users. BZD use of patients did not differ between GPs (data not shown, $P>0.05$). In the multivariable analysis, only the perceived 'disability to differentiate depression from unhappiness' remained a significant correlate of less patient BZD use (Odds ratio [OR]=0.98, $P=0.048$, Table 2), independent of the included patient characteristics.

GP Correlates of inappropriate BZD Use

Inappropriate BZD use of patients did not differ between GPs ($P>0.05$, data not shown). In the multivariable analysis, higher 'professional comfort and competence with mental health care' (OR = 0.29, $P=0.03$) remained the only GP characteristic that was associated with less inappropriate BZD use, independent of the included patient characteristics.

TABLE 1. Characteristics and Attitudes of GPs (n=62)

| Sociodemographic characteristics | |
|---|--------------------|
| Gender (female, %) | 45.2 |
| Age (years), mean (sd) | 49.2 (8.5) |
| Clinical experience (in years), mean (sd) | 17.8 (10.1) |
| Employment status (in fte), median (IQR) | 0.7 (0.6-0.8) |
| Approved clinical supervisor of GP registrars (%) | 54.8 |
| Employed in a group practice (vs. solo, %) | 93.5 |
| Access to health care professionals (%) | |
| (Non-mental) health care professionals (except practice assistant) | 83.9 |
| Mental health care professionals | 87.1 |
| Number of patients per GP (per 100), median (IQR) | 15.0 (14.6 – 16.3) |
| GPs interests & attitudes towards depression and anxiety | |
| Depression Attitude Questionnaire (mean score), mean (sd) | |
| Preference for drug therapy | 44.1 (9.1) |
| Uncomfortable feeling dealing with depressed patients | 44.2 (11.1) |
| Belief in the inevitability of depression | 35.1 (13.2) |
| Perceived disability to identify depression | 39.0 (12.8) |
| GPs' attitudes on depressive and anxiety disorder management | |
| Professional comfort and competence with mental health care, mean (sd) | 4.5 (1.0) |
| GPs concerns about difficulties with the health care system, median (IQR) | 3.0 (2.6-3.5) |
| Collaboration with mental health care professionals / institutions | |
| Good collaboration with social workers (%) | 53.2 |
| Good collaboration with primary care psychologists (%) | 50.0 |
| Good collaboration with social psychiatrist nurses (%) | 67.7 |
| Good collaboration with mental health care institutions (%) | 6.5 |
| Perceived workload and level of burn-out | |
| Perceived time limitations, mean (sd) | |
| | 3.5 (1.3) |
| Utrecht Burnout Scale | |
| Emotional Exhaustion, mean (sd) | 1.4 (0.8) |
| Depersonalisation, mean (sd) | 0.9 (0.6) |
| Personal Accomplishment, median (IQR) | 4.5 (4.0 -4.9) |

sd indicates standard deviation; IQR indicates interquartile range, BZD indicates benzodiazepine, GP indicates general practitioner, fte indicates full-time equivalent. Mean (sd) is provided for normally distributed variables. Median (IQR) is provided for skewed variables.

TABLE 2. GP Characteristics and Attitudes as Correlates of Patient BZD Use

| | Univariable OR (95% CI) | P | Multivariable OR OR (95% CI) | P |
|---|----------------------------|------|---------------------------------|--------------|
| Sociodemographic characteristics | | | | |
| Gender (female) | 0.91 (0.62 – 1.33) | 0.62 | | |
| Age (years) | 1.00 (1.00 – 1.02) | 0.78 | | |
| Clinical experience (in years) | 1.00 (0.98 – 1.02) | 0.94 | | |
| Employment status (in fte), median (IQR) | 0.88 (0.31 – 2.53) | 0.82 | | |
| Approved clinical supervisor of GP registrars | 0.98 (0.68 – 1.41) | 0.90 | | |
| Employed in a group practice (vs. solo) | 1.06 (0.53 – 2.09) | 0.88 | | |
| Access to professionals | | | | |
| (Non-mental) Health care professionals (except practice assistant) | 1.45 (0.86 – 2.45) | 0.16 | | |
| Mental health care professionals | 1.28 (0.78 – 2.11) | 0.32 | | |
| Number of patients per GP (per 100) | 1.03 (0.98 – 1.08) | 0.23 | | |
| GPs interests & attitudes towards depression and anxiety | | | | |
| Depression Attitude Questionnaire | | | | |
| Preference for drug therapy | 0.99 (0.97 – 1.01) | 0.37 | | |
| Uncomfortable feeling dealing with depressed patients | 1.00 (0.98 – 1.02) | 0.81 | | |
| Belief in the inevitability of depression | 1.00 (0.99 – 1.02) | 0.66 | | |
| Perceived disability to identify depression | 0.99 (0.97 – 1.00) | 0.07 | 0.98 (0.97 – 1.00) | 0.048 |
| GPs' attitudes on depressive and anxiety disorder management | | | | |
| Professional comfort and competence with mental health care | 1.21 (0.95 – 1.55) | 0.13 | | |
| GPs concerns about difficulties with the health care system | 0.90 (0.74 – 1.08) | 0.26 | | |
| Collaboration with mental health care professionals | | | | |
| Good collaboration with social workers | 1.30 (0.90 – 1.88) | 0.16 | | |
| Good collaboration with primary care psychologists | 1.37 (0.96 – 1.95) | 0.08 | 0.92 (0.63 – 1.35) | 0.67 |
| Good collaboration with social psychiatrist nurses | 1.37 (0.92 – 2.05) | 0.12 | | |
| Good collaboration with mental health care institutions | 0.91 (0.46 – 1.78) | 0.78 | | |
| Perceived workload and level of burn-out | | | | |
| Perceived time limitations | 1.09 (0.95 – 1.26) | 0.21 | | |
| Utrecht Burnout Scale | | | | |
| Emotional Exhaustion | 1.20 (0.95 – 1.52) | 0.12 | | |
| Depersonalisation | 1.26 (0.97 – 1.64) | 0.08 | 1.25 (0.95 – 1.64) | 0.11 |
| Personal Accomplishment | 0.80 (0.61 – 1.06) | 0.12 | | |

BZD indicates benzodiazepine; GP indicates general practitioner; CI indicates confidence interval. ORs are calculated by univariable and multivariable logistic multilevel regression analyses (SAS glimmix). P Multilevel is derived by univariable and multivariable logistic multilevel analysis with two levels (doctors, patients). Univariable and multivariable analyses were corrected for patient's age, sex and employment status, partner status, 1 year diagnosis of anxiety and / or depression, Beck Anxiety Inventory, Insomnia rating scale. All GP characteristics with $P < 0.1$ in univariable analyses were included into the multivariable model

TABLE 3. GP Characteristics and Attitudes as Correlates of inappropriate Patient BZD Use

| | Univariable OR (95% CI) | P | Multivariable OR (95% CI) | P |
|---|-------------------------|--------------|---------------------------|-------------|
| Sociodemographic characteristics | | | | |
| Gender (female) | 1.81 (0.48-6.75) | 0.38 | | |
| Age (years) | 0.98 (0.91-1.05) | 0.50 | | |
| Clinical experience (in years) | 0.99 (0.93-1.05) | 0.67 | | |
| Employment status (in fte) | 0.32 (0.01-9.26) | 0.51 | | |
| Approved clinical supervisor of GP registrars | 0.84 (0.26-2.72) | 0.77 | | |
| Employed in a group practice (vs. solo) | 0.66 (0.06-7.06) | 0.73 | | |
| Access to health care professionals | | | | |
| (Non-mental) Health care professionals (except practice assistant) | 0.32 (0.10-1.02) | 0.43 | | |
| Mental health care professionals | 0.87 (0.17-4.45) | 0.87 | | |
| Number of patients per GP | 0.87 (0.17-4.45) | 0.49 | | |
| GPs interests & attitudes towards depression and anxiety | | | | |
| Depression Attitude Questionnaire | | | | |
| Preference for drug therapy | 1.03 (0.98-1.09) | 0.22 | | |
| Uncomfortable feeling dealing with depressed patients | 0.93 (0.88-0.97) | 0.003 | 0.97 (0.91-1.03) | 0.31 |
| Belief in the inevitability of depression | 0.97 (0.92-1.02) | 0.25 | | |
| Perceived disability to identify depression | 0.95 (0.90-1.00) | 0.07 | 0.94 (0.88-1.00) | 0.07 |
| GPs' attitudes on depressive and anxiety disorder management | | | | |
| Professional comfort and competence with mental health care | 0.41 (0.23-0.76) | 0.005 | 0.29 (0.10-0.88) | 0.03 |
| GPs concerns about difficulties with the health care system | 1.73 (1.03-2.90) | 0.04 | 0.89 (0.37-2.17) | 0.81 |
| Collaboration with mental health care professionals / institutions | | | | |
| Good collaboration with social workers | 0.67 (0.19-2.38) | 0.67 | | |
| Good collaboration with primary care psychologists | 1.17 (0.36-3.76) | 0.80 | | |
| Good collaboration with social psychiatrist nurses | 1.65 (0.45-6.05) | 0.45 | | |
| Good collaboration with mental health care institutions | 0.56 (0.09-3.66) | 0.54 | | |
| Perceived workload and level of burn-out | | | | |
| Perceived time limitations | 0.76 (0.50-1.17) | 0.21 | | |
| Utrecht Burnout Scale | | | | |
| Emotional Exhaustion | 0.77 (0.35-1.69) | 0.51 | | |
| Depersonalisation | 0.72 (0.31-1.69) | 0.46 | | |
| Personal Accomplishment | 1.41 (0.53-3.76) | 0.50 | | |

BZD indicates benzodiazepine; GP indicates general practitioner; OR indicates odds ratio. Appropriate use was defined as mean daily dosage \leq DDD, duration of benzodiazepine use \leq 3 months in case of no concomitant antidepressant (AD) use and \leq 2 months in case of concomitant AD use and use of only one type of BZDs at a time. Use was defined as inappropriate when at least one of these criteria was not met. ORs were calculated by univariable and multivariable logistic multilevel regression analyses (SAS glimmix). P Multilevel was derived by univariable and multivariable logistic multilevel analysis with two levels (doctors, patients). Univariable and multivariable analyses were corrected for patient's age, sex and employment status, and number of chronic illnesses. All GP characteristics with $p < 0.1$ in univariable analyses were included into the multivariable model.

DISCUSSION

Summary

In this cross-sectional multilevel study amongst 1433 GP patients of 62 GPs, we investigated possible GP correlates of (inappropriate) patient BZD use and corrected for previously identified patient characteristics. Patient BZD use and inappropriate use did not vary significantly among GPs. Most GP characteristics were not associated with patient BZD use and inappropriate BZD use in the multivariable model. Only the GP's perceived 'disability to differentiate unhappiness from depression' was associated with less patient BZD use and the GP's 'professional comfort and competence with the mental health care system' was a correlate of lower inappropriate patient BZD use. This indicates that patient characteristics rather than GP characteristics determine patient BZD use and inappropriate use.

Strengths and Limitations of the Study

Our study had several limitations. In the light of the number of tests conducted, multiple testing may have caused a type I error, indicating that the two significant associations we found might be a chance finding. Further, patient BZD use was established via self-report of the GP patients and might not perfectly reflect GP prescriptions or the actual BZD use. The GP characteristics used in NESDA mainly included attitudes on anxiety and depression and not on the prescription of BZDs. Possibly, more specific GP attitudes towards BZD use need to be investigated in order to be able to detect differences in GPs' BZD prescription behaviour. However, this is unlikely, as there was little variance of BZD use and inappropriate use between GPs. Despite these limitations, we feel that our study is a valuable addition to the existing literature as it is the first study to investigate a large number of potentially important physician characteristics and attitudes in concert as possible correlates of BZD use and inappropriate use. Additionally, we corrected for previously identified

patient characteristics to find out whether GP characteristics could add information on top of already known predicting patient characteristics.

Comparison with existing Literature

The GP's perceived 'disability to differentiate unhappiness from depression' was the only weak correlate of less patient BZD use in the fully corrected model. This was a rather unexpected finding. These GPs had expressed the assumption that depression develops as a consequence of personal misfortune and felt that they could do little to help. Possibly, these GPs were less likely to prescribe BZDs as they felt they could do nothing to improve the mental health of their patients. However, in general, GP characteristics provided little additional information in the prediction of patient BZD use on top of the patient characteristics identified as predictors in previous research. The small number of significant GP characteristics is largely in line with some earlier studies that did not identify any significant GP correlates.^{28,29} Other research identified GP correlates of BZD use (e.g. male GP gender^{24,25}) which were not significant in our research. These studies differed from our own as they did not correct for patient characteristics.^{24,25} Thus, the found differences between GPs in those studies might actually be explained by the variability in patient characteristics (instead of by differences between GPs).

Inappropriate patient BZD use was also hardly associated with the GP characteristics. Only the GPs' comfort with mental health care correlated with less inappropriate patient BZD use. This indicates that GPs who issued less inappropriate BZD prescriptions felt more comfortable in dealing with anxious and depressed patients. This may be in line with earlier qualitative research which reported that BZDs are often prescribed due to a presumed lack of (psychotherapeutic) skills.^{19,20} Our findings are also in accord with the earlier finding that subject characteristics are more important for the prediction of long-term BZD use than GP characteristics.³¹

Implications for future Research and clinical Practice

In general, it is striking that GP characteristics added little information on top of the patient characteristics which were shown to be significant correlates of BZD use and inappropriate BZD use in previous research.¹³ This refutes the previous notion that some physicians are particularly responsible for the (inappropriate) BZD use of their patients.¹⁶ Interventions to reduce chronic BZD use should target patients at risk and the prescribing physicians alike, with a focus on patient characteristics rather than physician characteristics. Physicians should receive training to improve their knowledge on alternative treatment strategies and interaction skills with subjects at high risk of inappropriate use. Future research will have to show which kind of trainings are most helpful for the GPs to do so. Patients at risk should receive information about the unfavourable consequences of (inappropriate) BZD use, as already minimal intervention was shown to reduce chronic BZD use.^{17,47,48}

Conclusion

In conclusion, this study revealed that GP characteristics had little value in the prediction of patient BZD use and inappropriate BZD use on top of the patient characteristics. Apparently, it is primarily dependent on patient characteristics whether BZDs are used (inappropriately) or not.

REFERENCES

1. Lader MH. Limitations on the use of benzodiazepines in anxiety and insomnia: are they justified? *European Neuropsychopharmacology*. 1999;9:399-405.
2. Hale AS. ABC of mental health: Anxiety. *BMJ*. 1997;314:1886.
3. Baldwin DS, Anderson IM, Nutt DJ, et al. Evidence-based guidelines for the pharmacological treatment of anxiety disorders: recommendations from the British Association for Psychopharmacology. *Journal of Psychopharmacology*. 2005;19:567-596.
4. Knuistingh Neven A, Lucassen P, Bonsema K, et al. Practice guideline for insomnia and hypnotics (Dutch College of General Practitioners). [In Dutch: NHG-Standaard Slapeloosheid en slaapmiddelen]. *Huisarts & Wetenschap*. 2005;48:402-415.
5. Glass J, Lanctot KL, Herrmann N, et al. Sedative hypnotics in older people with insomnia: meta-analysis of risks and benefits. *British Medical Journal*. 2005;331:1169-1173.
6. Kales A, Kales JD. Sleep Laboratory Studies of Hypnotic Drugs - Efficacy and Withdrawal Effects. *Journal of Clinical Psychopharmacology*. 1983;3:140-150.
7. Donoghue J, Lader M. Usage of benzodiazepines: A review. *International Journal of Psychiatry in Clinical Practice*. 2010;14:78-87.
8. Neutel CI. The epidemiology of long-term benzodiazepine use. *International Review of Psychiatry*. 2005;17:189-197.
9. Isacson D, Carsjo K, Bergman U, et al. Long-Term Use of Benzodiazepines in A Swedish Community - An 8-Year Follow-Up. *Journal of Clinical Epidemiology*. 1992;45:429-436.
10. Isacson D. Long-term benzodiazepine use: factors of importance and the development of individual use patterns over time--a 13-year follow-up in a Swedish community. *Soc Sci Med*. 1997;44:1871-1880.
11. Luijendijk HJ, Tiemeier H, Hofman A, et al. Determinants of chronic benzodiazepine use in the elderly: A longitudinal study. *British Journal of Clinical Pharmacology*. 2008;65:593-599.
12. Simon GE, VonKorff M, Barlow W, et al. Predictors of chronic benzodiazepine use in a health maintenance organization sample. *Journal of Clinical Epidemiology*. 1996;49:1067-1073.

13. Manthey L, van Veen T, Giltay EJ, et al. Correlates of (inappropriate) benzodiazepine use: the Netherlands Study of Depression and Anxiety (NESDA). *British Journal of Clinical Pharmacology*. 2011;71:263-272.
14. de Lusignan S, Buxton N, Kent A. 10-MINUTE CONSULTATION New patient asking for a benzodiazepine prescription. *British Medical Journal*. 2008;337.
15. Bendtsen P, Hensing G, McKenzie L, et al. Prescribing benzodiazepines - a critical incident study of a physician dilemma. *Social Science & Medicine*. 1999;49:459-467.
16. Cook JM, Marshall R, Masci C, et al. Physicians' perspectives on prescribing benzodiazepines for older adults: A qualitative study. *Journal of General Internal Medicine*. 2007;22:303-307.
17. Parr JM, Kavanagh DJ, Young RM, et al. Views of general practitioners and benzodiazepine users on benzodiazepines: A qualitative analysis. *Social Science & Medicine*. 2006;62:1237-1249.
18. Cormack MA, Howells E. Factors Linked to the Prescribing of Benzodiazepines by General-Practice Principals and Trainees. *Family Practice*. 1992;9:466-471.
19. Anthierens S, Habraken H, Petrovic M, et al. The lesser evil? Initiating a benzodiazepine prescription in general practice: a qualitative study on GPs' perspectives. *Scand J Prim Health Care*. 2007;25:214-219.
20. Srisurapanont M, Garner P, Critchley J, et al. Benzodiazepine prescribing behaviour and attitudes: a survey among general practitioners practicing in northern Thailand. *BMC Fam Pract*. 2005;6:27.
21. Subelj M, Vidmar G, Svab V. Prescribing of Benzodiazepines Among Slovenian Family Physicians. *Zdravstveno Varstvo*. 2009;48:162-169.
22. Anthierens S, Tansens A, Petrovic M, et al. Qualitative insights into general practitioners views on polypharmacy. *BMC Fam Pract*. 2010;11:65.
23. Damestoy N, Collin J, Lalande R. Prescribing psychotropic medication for elderly patients: some physicians' perspectives. *CMAJ*. 1999;161:143-145.
24. Jarbrink K, Carlsten A, Frederiksen SO. Swedish physicians' inclination to prescribe benzodiazepines: differences between regions and characteristics of the prescriber. *Scandinavian Journal of Public Health*. 1999;27:22-29.
25. Bjorner T, Laerum E. Factors associated with high prescribing of benzodiazepines and minor opiates - A survey among general practitioners

- in Norway. *Scandinavian Journal of Primary Health Care*. 2003;21:115-120.
26. Linden M, Gothe H. Specialty training and the personal use of benzodiazepines by physicians affect their proneness to prescribe tranquilizers. *Pharmacopsychiatry*. 1998;31:42-47.
 27. Hadsall RS, Freeman RA, Norwood GJ. Factors Related to the Prescribing of Selected Psychotropic-Drugs by Primary Care Physicians. *Social Science & Medicine*. 1982;16:1747-1756.
 28. Bjorndal A, Fugelli P. Can regional differences in consumption of tranquilizers and hypnotics be explained by variations in general practitioners' threshold of prescribing? A methodological study. *Scand J Prim Health Care*. 1989;7:67-71.
 29. Mant A, Mattick RP, de BS, et al. Benzodiazepine prescribing in general practice: dispelling some myths. *Fam Pract*. 1995;12:37-43.
 30. Balkrishnan R, Rasu RS, Rajagopalan R. Physician and patient determinants of pharmacologic treatment of sleep difficulties in outpatient settings in the United States. *Sleep*. 2005;28:715-719.
 31. Zandstra SM, Furer JW, van de Lisdonk EH, et al. What caused the ten-fold difference in the number of long-term prescriptions for benzodiazepines between the general practices? 2008;67-84.
 32. Penninx BW, Beekman AT, Smit JH, et al. The Netherlands Study of Depression and Anxiety (NESDA): rationale, objectives and methods. *Int J Methods Psychiatr Res*. 2008;17:121-140.
 33. Smolders M, Laurant M, Verhaak P, et al. Which Physician and Practice Characteristics are Associated With Adherence to Evidence-Based Guidelines for Depressive and Anxiety Disorders? *Medical Care*. 2010;48:240-248.
 34. Riss J, Cloyd J, Gates J, et al. Benzodiazepines in epilepsy: pharmacology and pharmacokinetics. *Acta Neurologica Scandinavica*. 2008;118:69-86.
 35. Manthey L, Giltay EJ, van Veen T, et al. Long-Term Benzodiazepine Use and Salivary Cortisol The Netherlands Study of Depression and Anxiety (NESDA). *Journal of Clinical Psychopharmacology*. 2010;30:160-168.
 36. WHO Collaborating Centre for Drug Statistics Methodology (2010).ATC/DDD System.WHO Collaborating Centre for Drug Statistics Methodology. Available via http://www.whocc.no/atc_ddd_index. Accessed 22 maart 2010. 2010.

37. Zitman FGr. Discontinueringsstrategieën. In: Kahn RS, Zitman FG, redacteurs Farmacotherapie in de psychiatrie. 1999;165-177.
38. Terluin B, van Heest F, van der Meer K, et al. NHG-Standaard Angststoornissen (eerste herziening). *Huisarts Wet.* 2004;47:26-37.
39. National Collaborating Center for Primary Care. Management of anxiety (panic disorder, with or without agoraphobia, and generalized anxiety disorder) in adults in primary, secondary, and community care. *NICE clinical guideline 22.* 2007;
40. van den Hombergh P, Grol R, van den Hoogen HJ, et al. Assessment of management in general practice: validation of a practice visit method. *Br J Gen Pract.* 1998;48:1743-1750.
41. Botega N, Blizard R, Wilkinson G. General practitioners and depression - first use of the depression attitude questionnaire. *Int J Methods Psychiatr Res.* 1992;4:169-180.
42. McCall L, Clark DM, Rowley G. A questionnaire to measure general practitioners' attitudes to their role in the management of patients with depression and anxiety. *Aust Fam Physician.* 2002;31:299-303.
43. Schaufeli WB, van Dierendonck D. UBOS (Utrechtse Burnout Schaal): handleiding. Lisse, *The Netherlands: Swets and Zeitlinger.* 2000.
44. Robins LN, Wing J, Wittchen HU, et al. The Composite International Diagnostic Interview - An Epidemiologic Instrument Suitable for Use in Conjunction with Different Diagnostic Systems and in Different Cultures. *Archives of General Psychiatry.* 1988;45:1069-1077.
45. Beck AT, Brown G, Epstein N, et al. An Inventory for Measuring Clinical Anxiety - Psychometric Properties. *Journal of Consulting and Clinical Psychology.* 1988;56:893-897.
46. Levine DW, Kripke DF, Kaplan RA, et al. Reliability and validity of the Women's Health Initiative Insomnia Rating Scale. *Psychological Assessment.* 2003;15:137-148.
47. Gorgels WJMJ, Voshaar RCO, Mol AJJ, et al. Discontinuation of long-term benzodiazepine use by sending a letter to users in family practice: a prospective controlled intervention study. *Drug and Alcohol Dependence.* 2005;78:49-56.
48. Mugunthan K, McGuire T, Glasziou P. Minimal interventions to decrease long-term use of benzodiazepines in primary care: a systematic review and meta-analysis. *British Journal of General Practice.* 2011;61:558-559.

