Journal of Affective Disorders 110 (2008) 84–93

Journal of Affective Disorders

www.elsevier.com/locate/jad

Research report

Clinical factors influencing the prescription of antidepressants and benzodiazepines: Results from the European study of the epidemiology of mental disorders (ESEMeD)

Koen Demyttenaere [a,*], Anke Bonnewyn [a], Ronny Bruffaerts [a], Giovanni De Girolamo [b], Isabelle Gasquet [c], Viviane Kovess [e], Josep Maria Haro [d], Jordi Alonso [f]

[a] *Department of Psychiatry, University Hospital Gasthuisberg, Leuven, Belgium*
[b] *Department of Mental Health, 2nd University Psychiatric Clinic, Bologna, Italy*
[c] *National Unit of Health and Medical Research (INSERM-U669), Hôpital Cochin, Paris, France*
[d] *Fundacao Sant Joan de Deu, Barcelona, Spain*
[e] *MGEN, Mental Health Foundation, Paris, France*
[f] *Health Services Research Unit, Institut Municipal d'Investigacio Medica (IMIM-IMAS), Barcelona, Spain*

Received 7 August 2007; received in revised form 9 January 2008; accepted 9 January 2008
Available online 10 March 2008

Abstract

Objective: To examine factors associated with the use of antidepressants (AD) and benzodiazepines (BZD) in 6 European countries.
Methods: A cross-sectional, population-based study was conducted in: Belgium, France, Germany, Italy, the Netherlands and Spain. 21,425 non-institutionalized individuals aged 18 years and over were interviewed using the third version of the Composite International Interview (CIDI-3.0). Respondents were asked about AD and BZD use, and whether they consulted formal health services for emotional problems in the previous year. Sociodemographic variables, presence of mood/anxiety disorders and of painful physical symptoms were collected.
Results: 34.38% and 9.17% of the sample reported the use of AD and BZD respectively in the previous 12 months. Only 29.95% of subjects with a 12-month prevalence of major depressive episode (MDE) had been taking antidepressants. After controlling for several clinical and non-clinical factors, help seeking for emotional problems was the most important independent predictor for the use of AD or BZD (OR: 13.58 and 5.17, respectively). Higher age was the second important predictor (OR: 6.52 and 4.86, respectively). A 12-month or lifetime prevalence of MDE or an anxiety disorder were also predictors for AD or BZD use (OR for MDE: 5.00 and 2.82, OR for anxiety disorders: 2.13 and 1.85). Finally, the presence of painful physical symptoms also predicted the use of AD and BZD, while female gender, lower education and higher age predicted only the use of BZD.
Conclusion: Less than one third of subjects with a 12-month prevalence of MDE had been taking antidepressants. But seeking help for emotional problems was a more important predictor of the use of ADs or BZDs than a formal (DSM-IV) psychiatric diagnosis, suggesting that usage of ADs is not always according to the licensed DSM-IV indication.

Keywords: Antidepressants; Benzodiazepines; Major depressive disorder; Anxiety disorders

* Corresponding author. University Psychiatric Center Kuleuven, campus Leuven, Herestraat 49, B-3000 Leuven, Belgium. Tel.: +32 1634 8701; fax: +32 1634 8700.
E-mail address: koen.demyttenaere@med.kuleuven.be (K. Demyttenaere).

0165-0327/$ - see front matter © 2008 Elsevier B.V. All rights reserved.
doi:10.1016/j.jad.2008.01.011

1. Introduction

Epidemiological studies have shown that antidepressants and benzodiazepines are the most common used psychotropic medications in the general population (Allgulander and Nasman, 1991). In a pan-European study (N=18,679), Ohayon et al. found that at the time of interview 6.4% took a psychotropic medication (Ohayon and Lader, 2002). Anxiolytics were reported by 4.3% of the sample, hypnotics by 1.5% and antidepressants by 1.0%.

For many years, the antidepressant market has been experiencing a double digit percentage sales growth, although sales seem to stabilize more recently (IMS Health). However, the appropriateness of the prescription of antidepressants or benzodiazepines has repeatedly been questioned (Linden et al., 1999). A rather poor relation between diagnosis and prescription has indeed been suggested. On one hand, recent investigations have highlighted that most of those who have a mental disorder are not treated adequately because they do not seek help for emotional problems or because they not always get adequate treatment when they do so. Indeed, results from the National Comorbidity Survey Replication (NCS-R) Study have shown that nearly 58.1% of the persons with a depressive disorder have not used any health service for the treatment of these disorders (Wang et al., 2005). Results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) have shown that 63.5% of those with a 12-month diagnosis of any mood disorder did not consult any type of formal health services and that among those seeking help medication was prescribed in only 71% of the cases (Alonso et al., 2004). Similarly, 73.9% of those with a 12-month anxiety disorder did not consult and among those seeking help medication was prescribed in only 57.3% of the cases. On the other hand, psychotropic medication is also prescribed 'for a wider range of emotional problems', i.e. in patients without a formal DSM diagnosis. For example, only 31% of subjects in a UK general population study using one psychotropic had a determined current mental disorder, compared with 58% of those using two psychotropics and 85% of those three or more. In a Finnish primary care study, psychotropic medication was prescribed to 70% of the patients with mental symptoms (which was defined much larger than only a formal DSM diagnosis) and to 13% of the patients without any mental symptoms (Joukamaa et al., 1995).

Several studies investigated variables that might influence the (adequacy of) prescription of psychotropic medication. Health care system, physician and patient characteristics have been investigated as well in general population, primary care and psychiatric care samples.

Health care system and physician characteristics have been found to be predictive for prescription patterns. Data from the Psychological Problems in General Health Care (PPGHC) study, an international primary care survey directed by the World Health Organization (WHO), a physician diagnosed depressive disorder (multiple choice list for physicians to report a diagnosis) resulted in the prescription of antidepressants and anxiolytics in respectively 32% and 25% of cases while a Composite International Diagnostic Interview (CIDI) diagnosis of a depressive disorder (depressive disorder current or dysthymia) resulted in even lower prescription rates, i.e. 24% and 25% respectively, suggesting that physicians use other than ICD-10 criteria to make prescription decisions (Linden et al., 1999). For example, physicians working in a 'client centered' practice (each patient has an identified personal physician, continuity of care, scheduled visits) prescribed significantly more antidepressants and anxiolytics but significantly less hypnotics than in a 'clinic centered' practice (no identified personal physician, walk-in appointments) suggesting that the doctor–patient relationship significantly interferes with the 'from diagnosis to treatment' decision making process (Kisely et al., 2000). Female physicians also prescribed psychotropic medication more commonly. Physicians who had had further postgraduate training in psychiatry prescribed significantly more antidepressants but significantly less anxiolytics and hypnotics. The National Comorbidity Survey showed that patients seeking help for depressive or anxiety disorders within the past 12 months received more commonly antidepressants, but only when seeing psychiatrists and not when seeing primary care physicians (Mojtabai, 1999). Moreover, patients with a disorder received more commonly psychotropic medication when they were seen by a psychiatrist while patients without a disorder received more commonly psychotropic medication when they were seen by a primary care physician.

Patient characteristics were also found to be predictive for prescription patterns. Age is probably the most consistent predictor of taking psychotropic medication: the consumption of antidepressants and especially of benzodiazepines increases with age (Joukamaa et al., 1995; Kisely et al., 2000; Nielsen et al., 2004; Ohayon et al., 1998; Olfson et al., 1998; Paulose-Ram et al., 2004). Gender is another predictor of taking psychotropic medication: most studies found that consumption of psychotropic medication is higher in women than in men although some studies no longer found a gender difference after controlling for mental

problems (Joukamaa et al., 1995; Kisely et al., 2000; Ohayon et al., 1998; Olfson et al., 1998; Paulose-Ram et al., 2004). Lower educational level, living below the poverty level and being unemployed are other predictors of taking antidepressants and especially of benzodiazepines, although not all studies controlled for different prevalence rates of depressive or anxiety disorders (Joukamaa et al., 1995; Kisely et al., 2000; Paulose-Ram et al., 2004).

A concomitant physical disorder was found to increase the likelihood of using a psychotropic agents. In a large European study (N=18.679), 2.3% of respondents without mental/sleep disorders or physical disorder, 6.0% of respondents with a physical disorder only, 10.8% of respondents with a mental/sleep disorder only and 24.4% of respondents with a mental/sleep disorder and a physical disorder had a current use of psychotropic medication (Ohayon and Lader, 2002). In a UK study, subjects currently treated for a physical disorder (especially arthritis, backaches, other musculo-skeletal pains and cancer) were more likely to use a psychotropic agent, compared to subjects with no physical disorder (Ohayon et al., 1998). In the same study, subjects were also asked whether they had been consulting a physician for mental health reasons and interestingly this was found to be a highly significant predictor of psychotropic use with about the same relative risk (RR: 3.4, C.I. 2.8–3.9) as a diagnosis of a depressive or anxiety disorder (RR: 2.4, C.I. 1.9–2.9 and 4.9, C.I. 4.4–5.4 respectively). It has also been documented that the proportion of subjects using a psychotropic medication increases significantly with the number of consultations in the previous year (4.8% in those who consulted once or twice; 10.2% in those who consulted a physician 3 to 5 times; and 13.9% in those who consulted 6 times or more) (Ohayon and Lader, 2002).

1.1. Aim of the study

The aim of this paper was to investigate patient characteristics associated with the use of antidepressants and benzodiazepines. Based on the data collected in the ESEMeD/MHEDEA project that involved an adult population of 21,425 in six European countries (Belgium, France, Germany, Italy, the Netherlands, Spain), we examined the influence of (1) sociodemographic factors, (2) help seeking, (3) diagnosis of mood (major depression episode (MDE) and dysthymia) and anxiety disorders, (4) painful physical symptoms (PPS) and presence of chronic somatic disorders on the use of antidepressants and benzodiazepines.

2. Methods

2.1. Sample

The study was cross-sectional in nature and individuals were assessed in person at their homes using computer-assisted interview (CAPI) techniques. The target population was the non-institutionalized adult population of Belgium, France, Germany, Italy, the Netherlands and Spain, a total of 212,000,000 Europeans. In total, 21,425 respondents were interviewed between January 2001 and July 2003. Prevalence estimates were weighted to account for the known probability of selection as well as to restore the distribution of the population within each country. The overall response rate in the six countries investigated was 61.2%. A stratified, multistage, clustered area, probability sample design was used. Further description of the sampling frame and selection is provided elsewhere (Alonso et al., 2004, 2002).

2.2. Measures

2.2.1. Assessment of 12-month/lifetime(but no 12-month) mood and anxiety disorders

The questionnaire was based on the third version of the World Mental Health Composite International Diagnostic Interview (CIDI-3.0) (Kessler and Ustun, 2004), which is a comprehensive, fully-structured interview designed to be used by trained lay interviewers for the assessment of mental disorders. Prevalence estimates of mood (major depressive episode [MDE] and dysthymia, respectively) and anxiety disorders (generalized anxiety disorder, social phobia, specific phobia, post traumatic stress disorder, agoraphobia, panic disorder) were determined by whether respondents' past or current symptomatology met the DSM-IV diagnostic criteria in the previous 12 months preceding the interview or any lifetime period before the specified 12-month window.

2.2.2. Help seeking

Help seekers were, in our study, defined as those who had consulted with any of formal healthcare providers (i.e. psychiatrist, psychologist, general practitioner or any other medical doctor) for their 'emotional or mental health problems' in the 12 months preceding the interview.

2.2.3. PPS and chronic somatic disorders

Painful physical symptoms (PPS) were assessed through questions about the lifetime presence of or treatment for any frequent or severe headache, neck,

or back pain. In the present report, subjects were considered to have PPS when they gave an affirmative answer on at least one of these three questions presented in Box 1, indicating whether they still had these pain symptoms in the past 12 months.

The PPS section was administered to 8780 respondents. Internal sub-sampling was used to reduce respondent burden by dividing the interview into two parts. Part 1 included the core diagnostic assessment of mental disorders. Part 2 included additional information relevant to a wide range of survey aims, including assessment of chronic somatic conditions. Details of the sub-sampling are described elsewhere (Kessler and Ustun, 2004). All respondents completed part 1. All part-1 respondents (N=21,425) who met criteria for any mental disorder and a probability sample of other respondents were administered part-2. Part-2 (N=8780) respondents were weighted by the inverse of their probability of selection for part-2 of the interview to adjust for differential sampling. Additional weights were used to adjust for differential probabilities of selection within households and for post-stratification (i.e. to match the samples to population socio-demographic distributions).

Participants were asked if they had ever had any of the following chronic somatic disorders in the past 12 months: arthritis or rheumatism, seasonal allergies, a stroke, a heart attack, heart disease, high blood pressure, asthma, tuberculosis, other chronic lung diseases, malaria or another parasitic disease, diabetes or high blood sugar, an ulcer in their stomach or intestine, a thyroid disease, a neurological problem, HIV, AIDS, or cancer. When a participant did report at least one of the latter somatic disorders, he/she was considered 'with somatic disorder', otherwise he/she was considered 'without somatic disorder'.

2.2.4. Assessment of antidepressants and benzodiazepines use

All respondents were asked about the use of antidepressants and benzodiazepines in the last 12 months. Box 2 contains drugs categorised to antidepressants (including tricyclic antidepressants and new generation antidepressants) and/or benzodiazepines in our study. In order to overcome possible recall bias, a standard booklet with high-quality pictures was provided to help respondents recall their drug usage.

2.3. Statistical analysis

Prevalence estimates were provided and expressed in weighted percentages with standard error (SE/100). The binary variable of being prescribed or not being used psychotropic medication (antidepressants and/or benzo-

Box 1

Selected questions about painful physical symptoms

Painful physical symptoms
Did you still have back or neck problems or receive any treatment for them at any time during the past 12 months?
Did you still have frequent or severe headaches or receive any treatment for them at any time during the past 12 months?
Did you still have (any other) chronic pain or receive any treatment for it during the past 12 months?

Box 2

Drugs included in the category of antidepressants and benzodiazepines

Antidepressants	**Tricyclic antidepressants:** Amitriptyline, clomipramine, doxepin, imipramine, lofepramine, melitracen, nortriptyline, opipramol, tianeptine, trimipramine **Selective Serotonine Reuptake Inhibitor (SSRI)** Citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline **All other antidepressants** Ademethionine, dibenzepin, dosulepin, maprotiline, medifoxamine, mianserin, milnacipran, mirtazapine, moclobemide, nefazodone, oxitriptan, reboxetine, st john's wort, tranylcypromine, trazodone, tryptophan, venlafaxine, viloxazin
Benzodiazepines	Alprazolam, bentazepam, bromazepam, brotizolam, chlordiazepoxide, clobazam, clorazepate, clotiazepam, cloxazolam, delorazepam, diazepam,

Box 2 (*continued*)

Benzodiazepines	dipotassium clorazepate, estazolam, ethyl loflazepate, etizolam, flunitrazepam, flurazepam, halazepam, ketazolam, loprazolam, lorazepam, lormetazepam, medazepam, midazolam, nitrazepam, nordazepam, oxazepam, pinazepam, potassium clorazepate, prazepam, quazepam, temazepam, tofisopam, triazolam

diazepines) was modelled using logistic regression. Statistically significant main effects and interactions were identified by stepwise logistic regression using the likelihood ratio test to delineate the most important predictors. Based on the crude prevalence estimates, the following factors were initially considered: gender, age, employment, education, living condition, help seeking, PPS, chronic somatic disorders, MDE, dysthymia, anxiety disorder. Among these factors, significant factors examined through stepwise logistic regression were retained in the final logistic regression analysis to study the relative influence on the three outcomes of interest: (i) use of antidepressants, (ii) use of benzodiazepines, and (iii) use of antidepressants and/or benzodiazepines in the previous 12-month prior to the interview. All statistical calculations were performed using Stata Statistical Software (2003).

3. Results

3.1. Antidepressants/benzodiazepines use

Table 1 provides the overall prevalence (%) of AD/BZD use according to sociodemographical and clinical

Table 1
Prevalence (%) of antidepressants and benzodiazepines use by sociodemographic and clinical factors

		Antidepressants	Benzodiazepines	Antidepressants and/or benzodiazepines
Demographic group	Demographic category	% (SE)	% (SE)	% (SE)
Sample	All respondents	4.38 (.00)	9.17 (.00)	11.68 (.00)
Sex	Male	2.81 (.00)	6.85 (.01)	8.48 (.01)
	Female	5.83 (.00)	11.33 (.01)	14.65 (.01)
Age	18–24	1.36 (.00)	3.73 (.01)	4.45 (.01)
	25–34	2.85 (.00)	4.95 (.01)	6.92 (.01)
	35–49	5.06 (.01)	8.38 (.01)	11.03 (.01)
	50–64	5.74 (.01)	10.78 (.01)	14.07 (.01)
	65+	5.05 (.01)	15.29 (.01)	18.25 (.01)
Education	0–4	5.98 (.01)	14.10 (.01)	16.86 (.01)
	5–8	4.20 (.01)	10.20(.01)	12.44 (.01)
	9–12	4.53 (.01)	5.77 (.00)	9.21 (.01)
	13+	3.09 (.00)	7.27 (.01)	8.97 (.08)
Living conditions	Living alone	4.64 (.00)	10.81 (.00)	13.58 (.01)
	Living with someone	4.30 (.00)	8.68 (.00)	11.11 (.00)
Employment	Employed	3.28 (.00)	6.64 (.00)	8.55 (.00)
	Other	5.60 (.00)	12.24 (.01)	15.36 (.01)
Help seeking	No	2.33 (.02)	7.38 (.02)	8.91 (.00)
	Yes	35.91 (.02)	36.72 (.02)	54.24 (.02)
Painful physical symptoms (PPS)	No	2.96 (.00)	7.06 (.00)	8.66 (.01)
	Yes	7.79 (.01)	14.25 (.01)	18.93 (.01)
Chronic somatic disorder	No	3.41 (.00)	5.57 (.00)	7.59 (.01)
	Yes	5.29 (.00)	12.56 (.01)	15.53 (.01)
MDD	Never	2.61 (.00)	7.54 (.00)	9.07 (.00)
	Lifetime, no 12 months	9.86 (.01)	14.54 (.01)	20.17 (.01)
	12 months	29.95 (.02)	33.85 (.02)	48.33 (.02)
Anxiety disorder	Never	2.98 (.00)	7.60 (.00)	9.36 (.00)
	Lifetime, no 12 months	8.34 (.01)	13.84 (.02)	18.58 (.02)
	12 months	17.39 (.02)	23.52 (.02)	32.95 (.03)
Dysthymia	Never	3.75 (.00)	8.44 (.00)	10.65 (.00)
	Lifetime, no 12 months	14.12 (.02)	21.30 (.02)	29.22 (.02)
	12 months	27.72 (.05)	33.19 (.04)	46.38 (.04)

factors. Overall, 4.38% (SE=0.00) of the total sample reported having taken ADs during the 12 months prior to the interview. This was about half of those who reported having used BZDs (9.17%, SE=0.00) during the same period. In total, 11.68% (SE=0.00) had used either ADs or BZDs, implying that approximately four in ten of those who used ADs also took BZDs. As expected, the crude prevalence estimates revealed that a diagnosis of MDE, anxiety disorder and dysthymia was associated with more prevalent use of these medications. For instance, almost half of the respondents with a CIDI diagnosis of MDE (48.33%, SE=0.02) took ADs or BZDs in the past one year prior to the interview. In contrast, 9.07% (SE=0.00) of the respondents without any episode of MDE took either or both of these medications. Other clinical factors such as pain or the presence of a chronic somatic disorder also had positive associations with the use of antidepressants or benzodiazepines.

Beyond clinical factors, the use of the medications was also more prevalent among those who were female, older, less educated, not employed, or living alone. Notably, 'help-seeking for emotional problems' seemed to have a particularly strong association with the use of ADs and BZDs. More than half of the help seekers (54.24%, SE=0.02) used ADs and/or BZDs in the previous 12 months, while only 8.91% (SE=0.00) of non-help seekers reported having used these medications.

Tables 2a and 2b further illustrate the differentiating effect of 'help seeking for emotional or mental health problems' on the prescription of psychotropic medication in the investigated population. In the respondents without MDE, without dysthymia and without anxiety disorders (12 month as well as lifetime prevalence), AD and BZD use was reported by 1.46% and 5.91% respectively in non-help seeking subjects while this was 19.59% and 31.36% respectively in help seeking subjects. Help seeking significantly increased the use of ADs and BZDs in subjects with a lifetime or 12-month prevalence of MDE, dysthymia or anxiety disorders. AD and BZD use was higher in respondents with a 12-month prevalence than in respondents with a lifetime prevalence of MDE or dysthymia. However, in anxiety disorders antidepressant or benzodiazepine use was more comparable in respondents with a 12-month or lifetime prevalence.

A more detailed look at Tables 2a and 2b gives some more interesting findings. First, in the non-help seeking population (with or without MDE, dysthymia or anxiety disorder) BZDs were used more commonly than ADs. Second, in help seeking respondents with a 12-month prevalence of MDE or of an anxiety disorder, BZDs were used as commonly as ADs. Third, in help seeking respondents with a lifetime prevalence of MDE, dysthymia or an anxiety disorder, BZDs were used less commonly than ADs.

3.2. Multivariate analysis

Since several sociodemographic and clinical factors were found to have an influence on the use of ADs and BZDs, multivariate logistic analysis was therefore conducted to assess the relative importance of each factor. The results with the odds ratio (OR) and 95% confidence interval (CI) are shown in Table 3. 'Help seeking for emotional or mental health problems' was the most important predictor of the use of ADs or BZDs, especially of the use of ADs. Help seekers were much more likely to use ADs than non help seekers in the previous 12 month (adjusted OR: 13.58, 95% CI: 9.88–18.68). Help seekers also used BZDs more often than non-help seekers (adjusted OR: 5.17, 95% CI: 3.92–6.83).

Several sociodemographic variables were associated with medication use. Age was associated with the use of ADs as well as with the use of BZDs. During the past one year, respondents above 65 years old were approximately five times more likely to have used ADs and/or BZDs than the respondents who were 18–24 years old (adjusted OR: 5.42, 95% CI: 3.29–8.92).

Female gender was not associated with the use of ADs though it was marginally associated with the use of BZDs (adjusted OR: 1.27, 95% CI: 1.02–1.59). Education was also associated only with the use of BZDs. In terms of years of schooling, more educated individuals were less likely to use BZDs. Employment was a marginally

Table 2a
% of subjects with help seeking or no help seeking within each category (e.g. within No MDE subjects, within lifetime MDE subjects and within 12 month prevalence subjects)

	No MDE, no dysthymia no anxiety	No MDE	MDE lifetime	MDE 12 months	No dysthymia	Dysthymia lifetime	Dysthymia 12 months	No anxiety	Anxiety lifetime	Anxiety 12 months
No help seeking	97.02%	96.27%	85.76%	61.55%	94.60%	83.15%	67.58%	95.75%	89.62%	75.62%
Help seeking	2.98%	3.73%	14.24%	38.45%	5.40%	16.85%	32.42%	4.25%	10.38%	24.38%

Table 2b
% of individuals being prescribed antidepressants or benzodiazepines during the last 12 months

	No MDE, no dysthymia no anxiety	No MDE	MDE lifetime	MDE 12 months	No dysthymia	Dysthymia lifetime	Dysthymia 12 months	No anxiety	Anxiety lifetime	Anxiety 12 months
No help	1.46%	1.67%	4.84%	16.39%	2.13%	6.45%	11.12%	1.81%	3.85%	8.57%
seeking	*5.91%*	*6.50%*	*11.84%*	*22.71%*	*6.90%*	*19.02%*	*22.87%*	*6.43%*	*10.88%*	*17.79%*
Help	19.59%	26.67%	40.11%	51.67%	32.22%	51.96%	62.33%	29.36%	47.10%	44.77%
seeking	*31.36%*	*32.01%*	*30.75%*	*51.68%*	*35.33%*	*36.68%*	*54.69%*	*34.06%*	*39.32%*	*41.29%*

Antidepressants — %/12 months (SE ranging from 0.00 to 0.07).
Benzodiazepines — %/12 months (SE ranging from 0.00 to 0.07). Data shown in italics.

significant predictor for the use of ADs and/or BZDs (adjusted OR: 1.28, 95% CI: 1.005–1.63). Its predictive utility was however not significant in predicting either the use of ADs or BZDs alone.

Several clinical variables were associated with medication use. A diagnosis of mood or anxiety disorders (as well 12-month as lifetime prevalence) was associated with a more prevalent use of ADs and BZDs. The use of psychotropic medication in the past one year was higher in respondents with a 12-month diagnosis than with a lifetime diagnosis of MDE. It is interesting to notice that anxiety disorders showed a different pattern: the use of

Table 3
Logistic regression analysis on sociodemographic and clinical factors associated with the prescription of antidepressants/benzodiazepines/both

		Antidepressants	Benzodiazepines	Antidepressants and/or benzodiazepines
Demographic group	Demographic category	Adjusted OR [a] (95%CI)	Adjusted OR [b] (95%CI)	Adjusted OR [c] (95%CI)
Gender	Male	–	1.00 (reference)	1.00 (reference)
	Female	–	1.27 (1.02–1.59)	1.26 (1.02–1.55)
Age	18–24	1.00 (reference)	1.00 (reference)	1.00 (reference)
	25–34	2.19 (1.12–4.27)	1.39 (0.80–2.41)	1.75 (1.06–2.91)
	35–49	3.81 (2.04–7.10)	2.30 (1.40–3.78)	2.77 (1.73–4.43)
	50–64	4.74 (2.52–8.93)	2.94 (1.78–4.88)	3.52 (2.20–5.63)
	65+	6.52 (3.36–12.66)	4.86 (2.88–8.20)	5.42 (3.29–8.92)
Education	0–4	–	1.00 (reference)	–
	5–8	–	0.69 (0.52–0.92)	–
	9–12	–	0.45 (0.33–0.62)	–
	13+	–	0.79 (0.58–1.07)	–
Employment	Employed	–	–	1.00 (reference)
	Other	–	–	1.28 (1.005–1.63)
Help seeking	No	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Yes	13.58 (9.88–18.68)	5.17 (3.92–6.83)	8.57 (6.56–11.20)
Painful physical symptoms	No	1.00 (reference)	1.00 (reference)	1.00 (reference)
(PPS)	Yes	1.99 (1.48–2.68)	1.60 (1.28–1.90)	1.80 (1.46–2.21)
Chronic somatic disorder	No	–	1.00 (reference)	1.00 (reference)
	Yes	–	1.50 (1.18–1.90)	1.36 (1.08–1.70)
MDD	Never	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Lifetime, no 12 months	2.04 (1.48–2.82)	1.29 (1.01–1.65)	1.34 (1.07–1.68)
	12 months	5.00 (3.39–7.36)	2.82 (2.09–3.81)	3.87 (2.88–5.21)
Anxiety disorder	Never	1.00 (reference)	1.00 (reference)	1.00 (reference)
	Lifetime, no 12 months	1.71 (1.16–2.51)	1.40 (1.003–1.94)	1.50 (1.12–2.02)
	12 months	2.13 (1.40–3.25)	1.85 (1.32–2.59)	2.24 (1.61–3.11)
Dysthymia	Never	–	–	1.00 (reference)
	Lifetime, no 12 months	–	–	1.64 (1.24–2.17)
	12 months	–	–	1.19 (0.76–1.86)

[a] Age, help seeking, PPS, MDD, and anxiety disorder were included in the final analysis for the use of antidepressants.
[b] Gender, age, education, help seeking, PPS, somatic disorder, MDD and anxiety disorder were included in the final analysis for the use of benzodiazepines.
[c] Gender, age, employment, help seeking, PPS, somatic disorder, MDD, anxiety disorder, and dysthymia were included in the final analysis for the use of antidepressants and/or benzodiazepines.

psychotropic medication in the past one year was comparable among respondents with a 12 month prevalence or a lifetime prevalence of anxiety disorders. Individuals with a diagnosis of MDE in the preceding 12 months were approximately five times more likely to use ADs than those who had never had MDE in their lifetime (adjusted OR: 5.00, 95% CI: 3.39–7.36). Meanwhile, individuals with an anxiety disorder in the preceding 12 months were approximately twice more likely to use BZDs than those without any such history (adjusted OR: 1.85, 95% CI: 1.32–2.59). A diagnosis of 12-month MDE was associated with the use of BZDs (adjusted OR: 2.82, 95% CI: 2.09–3.81) and a diagnosis of 12–month anxiety disorder was also a predictor of the use of ADs (adjusted OR: 2.13, 95% CI: 1.32–2.59). In the multivariate analysis, the presence of a dysthymia diagnosis did no longer have predictive utility for the use of either ADs or BZDs.

With regards to PPS and chronic somatic disorders, individuals who had PPS were approximately twice more likely to use ADs than those without while the presence of chronic somatic disorders was not a significant factor on the use antidepressants. Both PPS and chronic somatic disorders were however significantly associated with the use of BZDs.

4. Discussion

The present study, as a part of the ESEMeD project, investigated the factors associated with the use of ADs or BZDs in a general European adult population. The present results confirm that psychotropic medications are commonly prescribed medications. Indeed, 11.68% of the respondents in these 6 European countries had used ADs and/or BZDs during the last one year.

The main finding in the present study is the suboptimal relation between formal DSM-IV diagnosis and prescription or use of psychotropic medication. Indeed, on the one hand, antidepressants were used only by a minority of respondents with a 12-month prevalence of MDE, confirming the previously published finding that many patients suffering from common mental disorders are not treated with psychotropic medication (Wang et al., 2005; Alonso et al., 2004). On the other hand, a number of respondents used antidepressants without ever having fulfilled criteria for a formal DSM-diagnosis of MDE. Indeed, seeking help for emotional problems appeared to be a more important predictor for the use of ADs/BZDs than a formal diagnosis of MDE: although only 6.4% of the total sample had consulted a formal health service for their mental health in the previous year (Alonso et al., 2004), more than half among these help seekers used either ADs or BZDs in the past 12 months in our study.

The finding that 'seeking help' for emotional problems is a more powerful predictor for the use of psychotropic medication than a formal DSM-IV diagnosis could be due to several factors. First, the mental health problems that help seekers had might have been at sub-clinical levels that did not fulfill a formal DSM-IV diagnosis of mood or anxiety disorder. Physician and patient factors could contribute to this suboptimal match between diagnosis and prescription. It has indeed been reported that diagnoses of anxiety and/or mood disorder established by general practitioners in primary care settings had only a partial concordance with those based on structured interviews using the National Institute of Mental Health Diagnostic Interview Schedule (DIS) (Füredi et al., 2003). But it has also been suggested that prevalence indeed is something different than perceived need: in the National Comorbidity Study 45.2% of people who sought help did not have a discernable mental disorder during the previous twelve months (Mechanic, 2003). Such people often place high value on medications (and psychotherapy) as a way of managing difficult life problems. Some observers derogate such people by calling them 'the worried well' but the absence of measured disorder does not prove the absence of need (Freeman, 2005). Second, sleep problems could be the reason for taking antidepressants. A study performed in the UK indeed showed that 27.6% of subjects taking antidepressants report that sleep problems rather than anxiety or depressive symptoms were the reason for taking antidepressants and in the same study 14.3% of subjects taking psychotropic medication only had insomnia complaints (i.e. they did not report any psychiatric symptoms) (Ohayon et al., 1998). Third, antidepressants could have been prescribed for other licensed indications like premenstrual dysphoric disorder (Freeman, 2005) or for neuropathic pain (Saarto and Wiffen, 2005).

ADs are more commonly used in respondents with a 12-month prevalence of MDE than in respondents with a lifetime prevalence of MDE, but this difference is more pronounced in non-help seeking than in help seeking subjects (4 times more versus 1.20 times more). Most international guidelines recommend 6 to 9 months continuation treatment with ADs for a major depressive episode: therefore, the finding that 40% of help-seeking respondents with a lifetime MDE still use antidepressants could be due to maintenance treatment (in order to prevent recurrences) or to continued treatment by clinical feeling rather than evidence-based guidelines or just by the patient's or physician's fear of stopping the medication (Bauer et al., 2002).

Another remarkable finding is that in non-help seeking respondents (with or without a diagnosis of MDE, dysthymia or anxiety disorder), BZDs were used more commonly than ADs while in help seeking subjects with a 12 month prevalence of these disorders BZDs were used as commonly as ADs and in help seeking subjects with a lifetime prevalence BZDs were used less commonly than ADs. This interesting finding suggests that in help seeking subjects with a 12-month prevalence of MDE, dysthymia or anxiety disorders, physicians often add BZDs to ADs (in about half of the patients) but that due to awareness of addictive properties or of cognitive side effects of BZDs, the latter are no longer co-prescribed in the more long-term treatment of these disorders.

Individuals with MDE were also slightly more likely to use BZDs (33.85%) than ADs (29.95%).

Individuals with anxiety disorders were also slightly more likely to use BZDs (23.52%) than ADs (17.39%).

The use of ADs and BZDs was also attributed to other clinical and sociodemographic factors beyond a diagnosis of mood or anxiety disorder. Although several studies have already examined the influence of these factors either in the context of general population or primary care settings, the present paper to our knowledge is the first study that investigates an influence of 'help seeking' alongside these factors on the use of ADs or BZDs in the general European population. Indeed, the present investigation found a positive association between the use of ADs/BZDs and the presence of PPS or somatic disorders. PPS but not somatic disorders were associated with a more frequent use of ADs while both are associated with a more frequent use of BZDs. The impact of PPS and somatic disorders co-occurring with mental disorders has not been conclusive in the literature. Previous studies conducted in the 1980s and 90s were more likely to report a negative association between pain or medical illness and the use of ADs/BZDs (Bellantuono et al., 1989; Marino, 1993; Kisely et al., 2000). But findings on the relation between physical illness and use of ADs / BZDs from a more recent study by Ohayon et al. however were consistent with the finding in our study (Ohayon et al., 2002).

Another notable finding in the present study was that adjusted odds ratios showed only a few sociodemographic factors associated with the use of ADs and BZDs. After adjusting for the concurrent influence of other factors, the associations between age and the medication use remained significant. Consistent with other studies, the use of ADs and BZDs was more prevalent among older individuals. Contrary to previous studies (Wells et al., 1985; Koenig et al., 1987), the use of ADs in our study was not more prevalent among the females. The use of BZDs was however more prevalent among females although this finding was marginally significant. Education was also associated with the use of BZDs, but not with the use of ADs. Such similar findings were in fact reported by Joukamaa et al. (1995). Their study reported that only age and marital status, but not female gender, were associated with the prescription of psychotropic drugs. These results emerged only after adjusting for other factors such as the presence of mental health diagnosis as in the case of the present investigation. This suggests that sociodemographic factors (other than age) might have been confounded with other factors such as a diagnosis of the mood or anxiety disorder.

This study has a few limitations that might hamper interpretation of the results of this cross-sectional examination. First, in assessing the use of antidepressants and benzodiazepines, in spite of the using of booklet with pictures, a possible recall bias could have been occurred. Second, the response rate of the sample was moderate. Although weighting strategies were used to optimize the representativity of the study, it is possible that our results were biased. It is however unclear in which direction these limitations could have influenced the reported use of psychotropics.

5. Summary

Less than one third of subjects with a 12 month prevalence of MDE had been taking ADs. But 'seeking help for emotional or mental health problems' was a more important predictor of the use of ADs (and of BZDs) than a formal DSM-IV psychiatric diagnosis suggesting that usage of ADs is often not always according to the licensed indication. Individuals with co-occurring PPS were more likely to take ADs and individuals with PPS or a somatic disorder were more likely to take BZDS in the past 12 months. Among sociodemographic variables, age had the strongest positive linear relationship with the use of ADs or BZDs. The present data illustrate the complex relation between 'caseness for a disorder', 'seeking help' and 'taking psychotropic medication'.

Role of funding source

The EU funding and the GSK funding (see also Acknowledgements) did not interfere with the design, the analysis or the preparation of the manuscript.

Conflict of interest

The authors declare that they do not have a conflict of interest in submitting this manuscript.

Acknowledgements

The ESEMeD survey included in this report were carried out in conjunction with the World Health Organization World Mental Health (WMH) Survey Initiative. We thank the WMH staff for assistance with instrumentation, fieldwork, and data analysis. These activities were supported by the United States National Institute of Mental Health (R01MH070884), the John D. and Catherine T. MacArthur Foundation, the Pfizer Foundation, the US Public Health Service (R13-MH066849, R01-MH069864, and R01 DA016558), the Fogarty International Center (FIRCA R01-TW006481), the Pan American Health Organization, Eli Lilly and Company, Ortho-McNeil Pharmaceutical, Inc., GlaxoSmithKline, and Bristol-Myers Squibb. A complete list of WMH publications can be found at http://www.hcp.med.harvard.edu/wmh/. The ESEMeD project was funded by the European Commission (Contracts QLG5-1999-01042; SANCO 2004123), the Piedmont Region (Italy), Fondo de Investigación Sanitaria, Instituto de Salud Carlos III, Spain (FIS 00/0028), Ministerio de Ciencia y Tecnología, Spain (SAF 2000-158-CE), Departament de Salut, Generalitat de Catalunya, Spain, and other local agencies and by an unrestricted educational grant from GlaxoSmithKline. More information on this study can be found on http://www.epremed.org. There are no conflicts of interest or commercial products related to this study.

References

Allgulander, C., Nasman, P., 1991. Regular hypnotic drug treatment in a sample of 32, 679 Swedes: associations with somatic and mental health, inpatient psychiatric diagnoses and suicide, derived with automated record-linkage. Psychosom. Med. 53, 101–108.

Alonso, J., Angermeyer, M., Bernet, S., et al., 2004. Use of Mental Health Services in Europe: results from the European Study on epidemiology of mental disorders (ESEMeD) project. Acta Psychiatr. Scand. vol.109 (suppl 420), 47–54.

Alonso, J., Ferrer, M., Romera, et al., 2002. The European study of the epidemiology of mental disorders (ESEMeD/MHEDEA 2000) project: rationale and methods. Int. J. Methods Psychiatr. Res. vol.11, 55–67.

Bauer, M., Whybrow, P.C., Angst, J., Versiani, M., Moller, H.J., 2002. World federation of societies of biological psychiatry task force on treatment guidelines for unipolar depressive disorders. Part 1: Acute and Continuation Treatment of Major Depressive Disorder. World J. Biol. Psychiatry 3 (1), 5–43. Part 2: Maintenance Treatment of Major Depressive Disorder and Treatment of Chronic Depressive Disorders and Subthreshold Depressions. World J. Biol. Psychiatry 3 (2), 69–86.

Bellantuono, C., Arreghini, E., Adami, M., et al., 1989. Psychotropic drug prescription in Italy. A Survey in General Practice. Soc. Psychiatry Psychiatr. Epidemiol. vol. 24, pp. 212–218.

Freeman, E.W., 2005. Effects of antidepressants on quality of life in women with premenstrual dysphoric disorder. Pharmacoeconomics 23 (5), 433–444.

Füredi, J., Rozsa, S., Zambori, J., Szadozky, E., 2003. The role of symptoms in the recognition of mental health disorders in primary care. Psychosomatics 44 (5), 402–406.

Joukamaa, M., Sohlman, B., Lehtinen, V., 1995. The prescription of psychotropic drugs in primary health care. Acta Psychiatr. Scand 92, 359–364.

Kessler, R.C., Ustun, T.B., 2004. The World Mental Health (WMH) survey initiative version of the World Health Organization (WHO) composite international diagnostic interview (CIDI). Int. J. Methods Psychiatr. Res. vol. 13, 93–121.

Kisely, S., Linden, M., Bellantuono, C., et al., 2000. Why are patients prescribed psychotropic drugs by general practitioners? Results of an international study. Psychol. Med. 20, 1217–1225.

Koenig, W., Rüther, E., Filipiak, B., 1987. Psychotropic drug utilization patterns in a metropolitan population. Eur. J. Clin. Pharmacol. vol. 32, 43–51.

Linden, M., Lecrubier, Y., Bellantuono, C., et al., 1999. The Prescription of Psychotropic Drugs by Primary Care Physicians: An International Collaborative Study 19, pp. 132–140.

Marino, S., 1993. Health and social predictors of psychotrophic prescription in general practice. Int. J. Soc. Psychiatry vol. 39, 167–176.

Mechanic, D., 2003. Is the prevalence of mental disorders a good measure of the need for services? Health aff. 22 (5), 8–20.

Mojtabai, R., 1999. Prescription patterns for mood and anxiety disorder in a community sample. Psychiatr. Serv. 50 (12).

Nielsen, M.W., Hansen, E.H., Rasmussen, N.K., 2004. Patterns of psychotropic medicine use and related diseases across educational groups: national cross-sectional survey. Eur. J. Clin. Pharmacol. 60, 199–202.

Ohayon, M.M., Lader, M.H., 2002. Use of psychotropic medication in the general population of France, Germany, Italy, and the United Kingdom. J. Clin. Psychiatry. 63, 817–825.

Ohayon, M.M., Caulet, M., Priest, R.G., Guilleminault, C., 1998. Psychotropic medication consumption patterns in the UK general population. J. Clin. Epidemiol. 51 (3), 273–283.

Olfson, M., Marcus, S.C., Pincus, H.A., Zito, J.M., Thompson, J.W., Zarin, D.A., 1998. Antidepressant prescribing practices of outpatient psychiatrists. Arch. Gen. Psychiatry 55, 310–316.

Paulose-Ram, R., Jonas, B.S., Orwig, D., Safran, M.A., 2004. Prescription psychotropic medication use among the U.S. adult population: results from the third National Health and Nutrition Examination Survey, 1988–1994. J. Clin. Epidemiol. 57, 309–317.

Saarto, T., Wiffen, P.J., 2005. Antidepressants for neuropathic pain. Cochrane Database Syst. Rev. 20 (3) CD005454.

Stata Statistical Software, 2003. Statacorp. College Station, Texas.

Wang, P.S., Lane, M., Olfson, M., Pincus, H.A., Wells, K.B., Kessler, R.C., 2005. Twelve month use of mental health services in the U.S.: Results from the National Comorbidity Survey Replication (NCS-R). Arch. Gen. Psychiatry. 62, 629–640.

Wells, K.B., Kamberg, C., Brook, R., et al., 1985. Health status sociodemographic factors and the use of prescribed psychotropic drugs. Med. Care vol. 23, 1295–1300.