Prescription of benzodiazepines and Z-drugs among older patients in primary care: a French, national, cohort study

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Key Messages

- 22% of GP consultations by older adults resulted in a prescription of benzodiazepine or a Z-drug.
- No GP characteristics were associated with BZD/ZD overprescription to older people.
- A greater chronic disease burden was associated with BZD/ZD overprescription
- Main limitation was the age of the data.

Abstract

Background: In France, general practitioners (GPs) prescribe benzodiazepines and Z-drugs (BZD/ZDs) widely, and especially to older adults. Several characteristics of patients and/or GPs linked to BZD/ZD overprescription have been described in the general population but not among older patients in primary care.

Objectives: To estimate the proportion of GP consultations by patients aged 65 and over that resulted in a BZD/ZD prescription, and determine whether any GP-related factors predicted BZD/ZD overprescription in this setting.

Methods: We analyzed sociodemographic and practice-related GP characteristics, and aggregated data on consultations recorded prospectively by 117 GPs in a database between 2000 and 2010. Next, we used logistic regression models to look for factors potentially associated with BZD/ZD overprescription (defined as an above-median prescription rate).

Results: The GPs' mean age at inclusion was 47.4 (7.1), and 87.9% were male. During the study period, the median [95% confidence interval] proportion of consultations with patients aged 65 and over resulting in a BZD/ZD prescription was 21.8% [18.1-26.1] (range per GP: 5–34.1%). In a multivariable analysis, a greater number of chronic disease (OR [95%CI] = 2.10 [1.22-3.64]), a greater number of drugs prescribed per consultation (5.29 [2.72-10.28]), and shorter study participation were independently associated with BZD/ZD overprescription.

Conclusions: BZD/ZD overprescription was associated with a greater chronic disease burden and the number of drugs prescribed per consultation but not with any sociodemographic or practice-related GP characteristics. Targeted actions are needed to help GPs limit their prescription of BZD/ZDs to older patients with multiple comorbidities and polypharmacy.

Word count: 249

Key words: Benzodiazepines; Hypnotics and sedatives; Inappropriate prescriptions; Aged; General practice; Cohort studies

Lay Summary

In France, general practitioners (GPs) prescribe benzodiazepines and Z-drugs (BZD/ZDs) widely, and especially to older adults. Even though BZD/ZDs may not have a favourable risk-benefit ratio in older patients, we lack data on GP-related factors that might influence BZD/ZD overprescription in our population. The objectives of the present study were to (i) estimate the proportion of GP consultations by patients aged 65 and over that resulted in a BZD/ZD prescription, and (ii) identify GP-related factors that were predictive of overprescription. To achieve this goal, we analyzed consultation notes registered by 117 GPs in a database curated by the *French Society of General Practice* between 2000 and 2010. About 22% of consultations by patients aged 65 and over resulted in a BZD/ZD prescription. With regard to the GPs, we did not find any sociodemographic or practice-related characteristics associated with overprescription. A greater chronic disease burden and the number of drug prescriptions (other than BZD/ZDs) per consultation was independently associated with overprescription. Targeted actions are therefore needed to help GPs limit their prescription of BZD/ZDs in older patients with multimorbidity and polypharmacy.

Word count: 2767

Background and objectives

Benzodiazepines (BZDs) and Z-drugs (ZDs) are prescribed widely worldwide[1,2,3,4] and in France in particular; the country ranks second in Europe in terms of *per capita* BZD/ZD consumption[5]. Indeed, the level of consumption is twice as high in France as in Europe overall, with respectively 50 and 25 daily dose deliveries (DDDs) per 1000 inhabitants[5]. In France, almost 90% of all BZD/ZDs are prescribed by general practitioners (GPs)[5].

It is well known that BZD/ZDs induce several non-negligible side effects – especially in older patients with multimorbidity[6,7,8,9]. The French National Health Authority (*Haute Autorité de Santé* (HAS)) reported that in 2007, two million people aged 65 or over had been prescribed a BZD/ZD[10]. Thus, in the last few years, the HAS has launched a number of actions intended to reduce the volume of BZD/ZDs prescribed. For example, the guidelines published in 2008 were designed to help GPs discontinue BZD/ZDs more easily when asked to renew a prescription for an older patient[11]. In 2012, a "pay for performance" (P4P) system for GPs was launched. The system currently includes three specific indicators: limitations on the duration of prescription for hypnotics and for BZD/ZDs (no more than 4 and 12 weeks, respectively), and a low prescription rate for psychotropic drugs and people aged 75 or over and who have not been diagnosed with a psychiatric disease. Furthermore, tetrazepam was definitively withdrawn from the market in 2013. Since 2017, the initiation and annual renewal of clonazepam prescriptions have been restricted to neurologists and paediatricians [12]. Despite these measures, the BZD/ZD prescription rate in France has fallen only slightly (from 83.6 DDDs per 1000 inhabitants in 2007 to 73.8 in 2015 [13]).

Although several studies have reported on patient and GP characteristics associated with BZD/ZD overprescription in the general population, this topic has not been addressed specifically in older patients. For example, patient characteristics reportedly associated with BZD/ZD overprescription are older age, chronic conditions, female gender, [14,15] and low socio-economic status[15]. A few studies have reported on GP characteristics associated with BZD/ZD overprescription, namely older age[15-18], male gender[15,16,17], low quality performance indicators[15], emotional proximity to the patient[17], prescription renewal without a consultation[17], not supervising trainee GPs[15,18], and the prescriber's own use of BZD/ZDs [18]. Although BZD/ZDs may not have a favourable benefit-risk ratio in older patients, we lack data on GP-related factors (i.e. sociodemographic, practice-related and consultation-related variables) that might influence BZD/ZD overprescription in this population. The present study's objectives were therefore to (i) estimate the proportion of consultations by patients aged 65 and over that resulted in a BZD/ZD prescription, and (ii) identify GP factors that predict BZD/ZD overprescription in this setting.

Methods

Study population and data collection

The study data were extracted from electronic medical records entered prospectively by French GPs into a database curated by the French Society of General Practice (*Societé Française de Médecine Générale* (SFMG), Issy-Les-Moulineaux, France). In 1993, the SFMG started to build a study cohort that ultimately comprised 117 volunteer GPs with complete data recorded in the database. The eligibility criteria for the GPs were membership of the SFMG and agreement to prospectively collect data on their routine daily practice from

January 1st, 2000, to December 31st, 2010. The data entered by the GPs were encrypted and anonymized before transfer to the central database. The SFMG cohort study's methodology has been described elsewhere[19].

Diseases and related health problems were coded using the Dictionary of Consultation Results (*Dictionnaire des Résultats de Consultation*), a nomenclature of standardized diagnoses with their corresponding codes from the International Classification of Diseases, 10th Revision, Clinical Modifications (ICD-10-CM) and that has been validated for use in France [20,21]. Prescriptions were coded according to the Anatomical Therapeutic Chemical Classification (WHO, 2006) (supplementary file Table S1). For the purposes of the present analysis, we retrospectively extracted data on the GPs' personal and practice-related characteristics and aggregated consultation data that had been correctly recorded in the SFMG database (i.e., with no missing information). The data were extracted in July 2016. The SFMG database was registered with the French National Data Protection Commission (*Commission nationale de l'informatique et des libertés* (Paris, France); registration number: 311668).

Outcome and predictors

The outcome (the BZD/ZD prescription rate) was defined as the proportion (as a percentage) of consultations with patients aged 65 during the study period that resulted in a BZD/ZD prescription. BZD/ZD overprescription was defined as an above-median prescription rate.

We assessed the following variables as possible GP-related predictors of BZD/ZD overprescription: sociodemographic variables (age, gender, and time since qualification as a physician); practice-related variables (billing over the standard fee, solo practice vs. group

practice, and practice location (urban area vs. rural area), and consultation-related factors (the total number of consultations per year, the total number of consultations with older patients per year, the number of consultations per patient (regardless of age), and number of consultations per older patient). For each GP, we also analyzed the number of psychiatric illness (consultation results), the number of chronic diseases (consultation results) (supplementary file, Table S2), and the number of drug prescriptions (other than BZD/ZDs) per consultation for older patients during the study period. The duration of participation in the SFMG cohort was also recorded.

Statistical analysis

Qualitative variables were described as the numbers (percentage), and quantitative variables were described as the mean (standard deviation (SD)) or the median [interquartile range (IQR)], as appropriate. The unit of analysis was the GP. The proportion of consultations resulting in a BZD/ZD prescription during the study period was calculated for each GP. This rate was dichotomized according to the median value, i.e. GPs were considered as below-median and above-median prescribers. The below-median vs. above-median prescribers' characteristics were compared using a chi-squared test, a Fisher's exact tests (for qualitative variables) or a Mann-Whitney test, as appropriate. Using univariate logistic regression models, we estimated unadjusted odds ratios (ORs) and their 95% confidence intervals (CIs). Variables with P values < 0.20 were then selected for multivariable analysis. Confounders and interactions were tested using bivariate models. Correlations were tested using Pearson's correlation coefficient or Cramer's V test, as appropriate. Adjusted ORs (aORs) and 95% CIs were estimated using multivariate logistic regression models. The use of aggregated

data for each GP prevented us from applying hierarchical data models. Lastly, we used a linear regression model to perform a sensitivity analysis and check the robustness of our findings; we considered the BZD/ZD prescription rate as a continuous variable. The results were estimated as regression coefficients (β) and 95% CI. All tests were two-sided, and the threshold for statistical significance was set to $P \leq 0.05$. Statistical analyses were performed using STATA software (version 12.0, StataCorp, College Station, TX, USA).

Results

Characteristics of the study population

Table 1 summarizes the characteristics of the 117 GPs; the mean age at inclusion was 47.4 years (7.1), 87.9% were men, 54.5% worked in group practices, and 54.7% worked in urban areas. The median time since qualification was 18 years [13-23], and the median length of participation in the SFMG cohort study was 6.32 years [3.9-10.9].

The median number of consultations per year and per GP was 3977 [2914-4843], including 669 [377-1010] with patients aged 65 and over. The median annual number of consultations per patient was 7 [4.5 -9.3] overall and 12.6 [9.2-18.7] for patients aged 65 and over. In the latter population, the median number of chronic diseases, psychiatric illnesses and drug prescriptions (other than for BZD/ZDs) were respectively 2.05 [1.53-2.64], 0.21 [0.14-0.27], and 4.16 [3.54-4.74] per consultation and per GP (Table 1).

Description of the BZD/ZD prescription rate

During the study period, the median BZD/ZD prescription rate for older patients was 21.8%, IQR [18.1-26.1], with a range per GP of 5% to 34.1%. The median prescription rate fell significantly over time (from 24% in 2000 to 18% in 2010; p=0.002; Figure 1).

Predictors of BZD/ZD overprescription

In a univariate analysis, consultation-related predictors (a greater number of chronic diseases, psychiatric illnesses and drug prescriptions (other than BZD/ZDs) per consultation and per GP) were significantly associated with BZD/ZD overprescription ($p \leq 0.05$), as was a below-median duration of GP participation in the study (<6.32 years, p=0.05). A non-significant trend in BZD/ZD overprescription were observed for male GPs (p=0.08) (Table2). No sociodemographic or practice-related GP factors were associated with the outcome.

Multivariate analysis

Given the strong correlations between the number of chronic diseases and the number of prescribed drugs per consultation, we built two multivariable models (Tables 3 and 4). The number of psychiatric illnesses was excluded from the multivariate analysis because it was collinear with the outcome. In a multivariable analysis, a greater number of chronic diseases per consultation (OR [95%CI] = 2.10 [1.22-3.64]), a greater number of drugs prescribed per consultation (5.29 [2.72-10.28]), and shorter study participation by the GP (less than 6.3 years) were independently and significantly associated with BZD/ZD overprescription (Table 3). Similar findings were observed in the linear regression sensitivity analysis (Table 4).

Discussion

Summary

About 22% of consultations by primary care patients aged 65 and over during the study period resulted in a BZD/ZD prescription. With regard to the GPs, we did not find any sociodemographic or practice-related characteristics associated with the overprescription of BZD/ZDs to patients aged ≥65. With regard to patient characteristics, a greater number of chronic diseases and a greater number of drug prescriptions (other than BZD/ZDs) per consultation were independently associated with BZD/ZD overprescription.

Strengths and weaknesses

The present study was (to the best of our knowledge) the first to have focused on GPs' prescribing practices for BZD/ZDs in people aged 65 and over. The study's other strengths included its design (a large cohort with exhaustive data collection), the national representativeness of the GP population about the mean age and the gender ratio during the study period (2000 to 2010), although GPs working in rural areas might have been under-represented [24], the standardized, long-term (10-year) data collection, and the sensitivity analysis (enhancing the robustness of our results).

Our study had some limitations. Firstly, the number of GPs was small, and a small number of their characteristics were recorded; for example, we did not know whether the GPs supervised trainee GPs. Secondly, we did not know whether a given BZD/ZD prescription was a new prescription or a renewal; our decision to consider the number of prescriptions per consultation might therefore have increased the outcome for patients with renewals.

Thirdly, we did not have data on the DDD; this prompted us to consider the median prescription rate – a less precise measure – in the study outcome. Given that a threshold for overprescription has never been defined in the literature data, we used the median value to identify the GPs who prescribed the most. Fourthly, our use of aggregated data prevented us from applying multilevel models and so might have resulted in a lack of power. Fifthly, participation in a study and membership of a scientific network might have influenced the GPs' attitude with regard to the prescription of Z-drugs; this might have led to underestimation of the prescription rate. Lastly, the age of the data (collected between 2000 and 2010) restricts our ability to extrapolate our finding. Although our population of GPs was representative of GPs in France at the time of the study, this is probably no longer the case.

Comparisons with the literature

In our study, about one in five patients aged 65 or over received a BZD/ZD prescription. This is consistent with other published data[21, 25]. As observed elsewhere in France and in the majority of European countries, we observed a significant decrease over time in BZD/ZD prescription; this might be due to greater experience, the application of a P4P system, and greater awareness of the BZD/ZDs' risk-benefit ratio.

A surprising finding was the narrow range of BZD/ZD prescription rates among GPs. This might be due to the nature of the study variables (aggregated data, and no individual DDD data) and suggests that GPs have similar prescription profiles. This may be partly explained by the selection of GPs from the *SFMG.*

Moreover, we did not find any sociodemographic or practice-related GP characteristics associated with BZD/ZD overprescription. Other studies have shown variously that male

gender (or, in contrast, female gender) [14,15,16,17], being older, and having more experience as a GP were linked to a higher BZD/ZD prescription rate [13,15]. However, the only GP-related factor to be significantly associated with BZD/ZD overprescription in our study was shorter participation in the cohort study. The latter finding may be due (at least in part) to the scientific network membership. With regard to gender, the non-significant trend observed (female gender: OR=0.34 [0.10-1.16], P=0.08) might have been due to a lack of power because only 14 of the participating GPs were female.

It is difficult to compare our present data with those of other studies, most of which assessed other drugs or did not focus on older adults. For example, a French cross-sectional study showed that frequent antidepressant prescribers were middle-aged, urban GPs with a moderate number of consultations, and fewer low-income patients and chronically ill patients[27].

Lastly, the main results of our multivariate analysis did not concern the GPs' personal characteristics but might reflect patient factors and/or aspects of the GP's medical activity during consultations. Indeed, a greater number of chronic diseases and a greater number of drug prescriptions were significatively associated with overprescription of BZD/ZDs. These outcomes might reflect multimorbidity and polypharmacy as well as the GP's medical practice (i.e., high prescription rates); when faced with a patient with multimorbidity, it might be difficult for GP to take time to deal with the issue of BZD/ZDs. In such a setting, it might be easier to prescribe a drug than a non-drug, patient-centred approach. Some studies found similar results regarding comorbidities and the risk of overprescription of BZD/ZDs for people aged 65 and over [28,29,30,31,32].

The results of qualitative studies prompted us to consider additional hypotheses. A GP might minimize the importance of a comorbidity if it is not the main problem[33] and might think that withdrawing a drug treatment would be worse for the patient[34]. GPs often report a lack of time; it would be easier to prescribe a BZD without exploring the patient's health problems in a holistic manner[16]. With regard to renewals,[34] discontinuation might be more difficult because the GP would have to discuss alternative therapeutic options for patients accustomed to long-term BZD/ZD treatment. Lastly, GPs underestimate their BZD/ZD prescription rate[16,35] - especially among older patients[36].

Some problems might come from patients indirectly. Indeed, some GPs report that discontinuing BZD/ZDs might harm the physician-patient relationship [33,34]. Prescribing these drugs might sometimes give the impression that the GP is delivering a solution[37] or is sympathetic towards with the patient[38]. The combination of a sense of powerlessness with the wish to relieve the patient's problem might prompt an inappropriate prescription[39] as a medical response to a biopsychosocial problem.

Implications

One simple way of trying to decrease the BZD/ZD prescription rate would be for the GP to write down the period of the time since treatment initiation in the consultation notes. It might be useful to have an alert in the prescribing software once a predefined period of the time has been exceeded. More broadly, it might be preferable to adopt a reflexive practice and consider a patient-centred approach (rather than a disease-centred approach) with (for example) close follow-up, patient education, the use of non-drug treatment option (e.g. meditation or cognitive behavioural therapy), and the provision of help with discontinuation

during dedicated consultations. From a pragmatic point of view, alternative options could be: training health professionals in cognitive behavioural therapies; knowing/creating professional websites to support patients in their understanding of therapeutic issues; creating a care plan in collaboration with the patient; providing adequate and sufficient time dedicated to primo-prescription of BZD/ZD; always combining them with a short initial prescription of BZD/ZD; and rapidly introduce non-drug techniques into the care plan.

Conclusion

About 22% of consultation by primary care patients aged 65 and over during the study period resulted in a BZD/ZD prescription. We did not find any sociodemographic or practice-related characteristics associated with BZD/ZD overprescription to patients aged 65 and over. However, a greater number of chronic diseases and a greater number of drug prescriptions (other than BZD/ZDs) per consultation were independently associated with overprescription. The study's main limitations were the age of the data, the absence of information about the DDD, and the lack of information on the potential renewal of some prescriptions. However, in light of our findings, targeted actions are needed to help GPs limit their prescription of BZD/ZDs to complex cases of older patients with multimorbidity and polypharmacy; possible actions may include the use of a reflexive practice, a patient-centred approach, and the consideration of alternative therapeutic options.

Declarations/acknowledgments

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ETHICS

The study data were handled confidentially in compliance with the requirements of the French Data Protection Agency (*Commission Nationale de l'Informatique et des Libertés*, CNIL, approval #311668

FUNDING

This study was funded by departmental resources.

CONFLICT OF INTEREST

Pascal CLERC and Julien LE BRETON are members of SFMG (society that have provided the database)

DATA AVAILIBILTY STATEMENT

A data availability statement was realized, using the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist for cohort studies.

References:

1. Bongue B, Laroche ML, Gutton S, Colvez A, Guéguen R, Moulin JJ, et al. Potentially inappropriate drug prescription in the elderly in France: A population-based study from the French National Insurance Healthcare system. Eur J Clin Pharmacol. 2011;67(12):1291–9.
2. Demyttenaere K, Bonnewyn A, Bruffaerts R, De Girolamo G, Gasquet I, Kovess V, et al. Clinical factors influencing the prescription of antidepressants and benzodiazepines:. Results from the European study of the epidemiology of mental disorders (ESEMeD). J Affect Disord. 2008;110(1-2):84–93.
3. Neutel CI, Skurtveit S, Berg C. What is the point of guidelines? Benzodiazepine and z-hypnotic use by an elderly population. Sleep Med [Internet]. Elsevier B.V.; 2012;13(7):893–7. [consulted 16/03/2016] Available from: http://dx.doi.org/10.1016/j.sleep.2011.12.014
4. Olfson M, King M, Schoenbaum M. Benzodiazepine use in the United States. JAMA psychiatry [Internet]. 2015;72(2):136–42. [consulted 16/03/2016] Available from: http://archpsyc.jamanetwork.com/article.aspx?articleid=2019955
5. ANSM, Etat des lieux de la consommation des benzodiazépines en France,2013; [consulted 24/07/2020). Available from: ansm.sante.fr/var/ansm_site/storage/original/application/3e06749ae5a50cb7ae80fb655dee103a.pdf
6. Bartlett G, Abrahamowicz M, Grad R, Sylvestre M-P, Tamblyn R. Association between risk factors for injurious falls and new benzodiazepine prescribing in elderly persons. BMC Fam Pract. 2009;10:1.
7. Bénard-Laribière A, Noize P, Pambrun E, Bazin F, Verdoux H, Tournier M, et al. Comorbidities and concurrent medications increasing the risk of adverse drug reactions: prevalence in French benzodiazepine users. Eur J Clin Pharmacol [Internet]. 2016; [consulted 10/06/2016] Available from: http://link.springer.com/10.1007/s00228-016-2044-y
8. Guillou-Landreat M, Grall-Bronnec M, Victorri-Vigneau C, Venisse JL. Sujets âgés et benzodiazépines: de la consommation à la dépendance. NPG Neurol - Psychiatr - Geriatr. 2008;8(46):9–16.
9. Laroche ML, Charmes JP, Merle L. Potentially inappropriate medications in the elderly: A French consensus panel list. Eur J Clin Pharmacol. 2007;63(8):725–31.
10. HAS, Benzodiazépines à demi vie longue chez le sujet âgé, janvier 2012. [Consulted 24/07/2020]. Available from: https://www.has-sante.fr/upload/docs/application/pdf/2012-05/3_ipc_bzd_demi_vie_long_sa_octobre_2011.pdf
11. HAS, Modalités d'arrêt des benzodiazépines et médicaments apparentés chez le patient âgé, 2008. [Consulted 22/07/2021]. Available: https://www.has-sante.fr/jcms/c_601509/fr/modalites-d-arret-des-benzodiazepines-et-medicaments-apparentes-chez-le-patient-age
12. ANSM, Rivotril® (clonazépam): Modification des conditions de prescription et de délivrance - Point d'information, 2011. [Consulted 24/07/2020]. Available from: **ansm.sante.fr/S-informer/Points-d-information-Points-d-information/Rivotril-**

R-clonazepam-Modification-des-conditions-de-prescription-et-de-delivrance-Point-d-information

13. ANSM, Etat des lieux de la consommation des benzodiazépines en France,2017; [consulted 09/07/2021). Available from: http://addictovigilance.aphp.fr/2017/05/23/ansm-rapport-benzodiazepines/
14. Bocquier A, Bezzou K, Nauleau S, Verger P. Dispensing of anxiolytics and hypnotics in southeastern France: Demographic factors and determinants of geographic variations. Fundam Clin Pharmacol. 2008;22(3):323–33.
15. Tsimtsiou Z, Ashworth M, Jones R. Variations in anxiolytic and hypnotic prescribing by GPs: A cross-sectional analysis using data from the UK Quality and Outcomes Framework. Br J Gen Pract. 2009;59(563):409–14.
16. Dybwad TB, Kjolsrod L, Eskerud J, Laerum E. Why are some doctors high-prescribers of benzodiazepines and minor opiates? A qualitative study of GPs in Norway. Family Practice. 1997. p. 361–8.
17. Bjorner T, Laerum E. Factors associated with high prescribing of benzodiazepines and minor opiates - A survey among general practitioners in Norway. Scand J Prim Health Care. 2003;21(2):115–20.
18. Verger P, Aulagnier M, Protopopescu C, Villani P, Gourrheux JC, Bouvenot G, et al. Hypnotic and tranquillizer use among general practitioners in south-eastern France and its relation to occupational characteristics and prescribing habits. Fundam Clin Pharmacol. 2004;18(3):379–85.
19. Rosman S et al, Gaining insight into benzodiazepine prescribing in General Practice in France: a data-based study, MC Fam Pract, 2011 May 11;12:28. doi: 10.1186/1471-2296-12-28.
20. Balestrieri M, Marcon G, Samani F, Marini M, Sessa E, Gelatti U, et al. Mental disorders associated with benzodiazepine use among older primary care attenders--a regional survey. Soc Psychiatry Psychiatr Epidemiol [Internet]. 2005 Apr;40(4):308–15. [consulted 16/03/2016] Available from: http://www.ncbi.nlm.nih.gov/pubmed/15834782
21. Clerc P, Duhot D, Gallais JL, Hebbrecht G, Martinez L, Raineri F. Dictionnaire des résultats de consultation en médecine générale. Révision 2010. Doc Rech en Médecine Générale Société Française Médecine Générale. 2010;66-70.
22. French Society of General Practice: Observatory of general practice (in French: Observatoire de médecine générale). SFMG, Issy les Moulineaux. 2006, (Accessed January 13, 2011), [http://omg.sfmg.org]
23. Bachmann CS, Berg EA, Spigset O, Slørdal L. Benzodiazepine-like hypnotics--attitudes and prescription practice among general practitioners. Tidsskr den Nor lægeforening Tidsskr Prakt Med ny række [Internet]. 2008 Jan 17;128(2):166–70. [consulted 16/03/2016] Available from: http://www.ncbi.nlm.nih.gov/pubmed/18202726
24. Conseil National de l'ordre des Médecins, Atlas de la démographie médicale en France, Janvier 2018. [Consulted 24/07/2020]; Available from: https://www.conseil-national.medecin.fr/sites/default/files/external-package/analyse_etude/hb1htw/cnom_atlas_2018_0.pdf

25. Canévet J-P, Bonnaud-Antignac A, Mollet V, Le Mauff P. Consommateurs de benzodiazépines au long cours : qu'en pensent leurs médecins généralistes prescripteurs ? Exercer. 2012;23(101):52–8.
26. Mercier A, Benichou J, Auger-Aubin I, Lebeau J-P, Houivet E, Van Royen P, et al. How do GP practices and patient characteristics influence the prescription of antidepressants? A cross-sectional study. Ann Gen Psychiatry [Internet]. 2015;14(3). [consulted 10/05/2016] Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=4308843&tool=pmcentrez&rendertype=abstract
27. Alvarenga JM. EA. Prevalence and sociodemographic characteristics associated with benzodiazepines use among community dwelling older adults : The Bambuí Health and Aging Study (BHAS). Rev Bras Psiquiatr. 2007;7–11.
28. Alvarenga JM, de Loyala Filho AI, Araujo Firmo JO, Lima-Costa MF, Uchoa E. A population based study on health conditions associated with the use of benzodiazepines among older adults (The Bambuí Health and Aging Study). Cad Saúde pública. 2009;25(3):605–12.
29. Fortin D, Préville M, Ducharme C, Hébert R, Allard J, Grégoire J-P, et al. Factors associated with short- and long-term use of benzodiazepines in the elderly from Quebec. Can J Aging [Internet]. 2005;24(2):103–13. [consulted 03/05/2016] Available from: http://www.ncbi.nlm.nih.gov/pubmed/16082614
30. Gleason PP, Schulz R, Smith NL, Newsom JT, Kroboth PD, Kroboth FJ, et al. Correlates and prevalence of benzodiazepine use in community-dwelling elderly. J Gen Intern Med. 1998;13(4):243–50.
31. Luijendijk HJ, Tiemeier H, Hofman A, Heeringa J, Stricker BHC. Determinants of chronic benzodiazepine use in the elderly: A longitudinal study. Br J Clin Pharmacol. 2008;65(4):593–9.
32. Voyer P, Cohen D, Lauzon S, Collin J. Factors associated with psychotropic drug use among community-dwelling older persons: A review of empirical studies. BMC Nurs. 2004;3:3.
33. Cook JM, Marshall R, Masci C, Coyne JC. Physicians' perspectives on prescribing benzodiazepines for older adults: A qualitative study. J Gen Intern Med. 2007;22(3):303–7.
34. Anderson K, Stowasser D, Freeman C, Scott I. Prescriber barriers and enablers to minimising potentially inappropriate medications in adults: a systematic review and thematic synthesis. BMJ Open [Internet]. 2014;4(12):e006544. Available from: http://bmjopen.bmj.com/content/4/12/e006544.full
35. Boixet M, Batlle E, Bolibar I. Benzodiazepines in primary health care: a survey of general practitioners prescribing patterns. Addiction [Internet]. 1996;91(4):549–56. [consulted 20/03/2016] Available from: http://www.ncbi.nlm.nih.gov/pubmed/8857380
36. Straand J, Rokstad K. General practitioners' prescribing patterns of benzodiazepine hypnotics: are elderly patients at particular risk for overprescribing? A report from the Møre & Romsdal Prescription Study. Scand J Prim Health Care [Internet]. 1997;15(1):16–21. [consulted 16/03/2016] Available from: http://www.ncbi.nlm.nih.gov/pubmed/9101618

37. Parr JM, Kavanagh DJ, Young RM, McCafferty K. Views of general practitioners and benzodiazepine users on benzodiazepines: A qualitative analysis. Soc Sci Med. 2006;62(5):1237–49.
38. Rogers A, Pilgrim D, Brennan S, Sulaiman I, Watson G, Chew-Graham C. Prescribing benzodiazepines in general practice: a new view of an old problem. Prescr Benzodiazepines Gen Pract. 2015;11(2):181–98.
39. Collin J, Damestoy N LR. La construction d'une rationalité : les médecins et la prescription de psychotropes aux personnes âgées. Sci Soc Sante. 1999;17(2):31–52.

Figures legend

FIGURE 1: Median BZD/ZD prescription rate per year during the study period (2000-2010)