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Geographic variations in the use of anxiolytics and hypnotics

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Abstract

Objective. To examine geographic variations in the dispensing of anxiolytics and hypnotics (AX-HY) and their determinants at the canton level in southeastern France.

Materials and methods. Data came from the 2005 outpatient database of the southeastern France general health insurance fund, covering more than 70% of the population. We calculated the annual age-adjusted prevalence rates of subjects filling prescriptions for AX-HY at least once (to measure "overall use") and at least six times ("chronic use"), assessed geographic variations with the extremal quotient and weighted coefficient of variation, and conducted simple and multiple linear regression analysis to study their determinants.

Results. Prevalence rates of overall and chronic AX-HY use were respectively 15.5% and 5.9% and varied significantly between cantons, by a factor of 3-4. The prevalence of mental illness and that of chronic illness were independently and positively associated with overall and chronic use; unemployment rates and mean family income were positively associated only with overall use. Density of general practitioners did not explain geographic variations.

Conclusions. These results provide a basis for targeting interventions to reduce AX-HY use and promoting appropriate discontinuation. Future studies should examine trends in those geographic variations.

Key words. Psychotropic Drugs, Small-Area Analysis, Socioeconomic Factors, Hypnotics and Sedatives, Anti-Anxiety Agents

Introduction

Anxiolytics and hypnotics (AX-HY) are the most commonly used psychotropic drugs in Europe in general and especially in France, where the annual prevalence rate of its use in 2000 (19%) was nearly double that the average of other European countries (10%) [1-3]. In France, these drugs are mainly prescribed by general practitioners (GPs) [4] and are often prescribed or used inappropriately: treatment often does not match the patient's actual diagnosis [3], and the length of treatment often exceeds recommended durations. Indeed, about 5% of the French population uses AX-HY chronically [3, 5]. These reports are particularly worrisome since benzodiazepines may cause dependence and side effects [6-11].

AX-HY use varies between French administrative regions, ranging from 16% to 21% for AX and from 8% to 12% for HY [12, 13]. Such geographic differences are of concern to policy-makers since they may represent either excessive levels of unnecessary care or undertreatment, perhaps due to difficulties in access to health services. Priority areas for intervention could be better identified if these variations were better described and their determinants more completely understood [14-16]. To the best of our knowledge, few studies have focused on geographic variations of AX-HY use and its determinants, except for one study in France [13] and another in Northern Ireland [17]. The latter showed that geographic variations in the prevalence of benzodiazepines use were highly associated with the proportions of elderly people and of women in the area [17]. Studies of geographic variations in utilization of other mental health services or drugs (e.g., acute psychiatric admissions, psychostimulants, antidepressants, and

opioid analgesics) suggest that several factors besides demography may explain them. Specifically, they include social factors, such as poverty, socioeconomic deprivation, social fragmentation, individual isolation, and concentration of minority ethnic groups [18-21], as well as the supply and geographic proximity of health care services [18, 19, 22]. As far as we know, the prevalence of chronic diseases has not been taken into account in previous published articles analysing AX-HY use geographic variations, although epidemiological evidence shows substantial comorbidity between chronic physical diseases and mental disorders [23].

In this article, we use the reimbursement database of the southeastern France regional health insurance fund (PACA-CNAMTS) to: 1) describe geographic variations of the prevalence of AX-HY dispensing at a canton level, and 2) identify canton characteristics (demographic and socioeconomic factors, GP density, prevalence of chronic illnesses) associated with the prevalence of AX-HY dispensing.

Materials and methods

Data on dispensing of anxiolytics and hypnotics

As in other French studies of psychotropic drug use [13, 24, 25], data came from the outpatient reimbursement database of the general health insurance fund of southeastern France (PACA-CNAMTS). This fund covers salaried employees in trade and industry, who account for more than 70% of the population in France as a whole and in southeastern France in particular [26].

This database includes all instances in which prescribed drugs were dispensed by community pharmacies. It does not include any prescriptions dispensed by public hospital pharmacies. Each time a prescribed drug is dispensed by a community pharmacy, information on the drug dispensed (barcode) and the patient identification number (by means of a "smart" or chip card issued by the health insurance authorities) are recorded and electronically sent to the general health insurance fund. Pharmacies may not give the patient treatment for more than one month at a time. Physicians can prescribe a treatment for a longer duration, if they so specify on the prescription. In that case, patient must come back each month to the pharmacy with the prescription to get a one-month treatment (prescription refills).

For this study, data included each occasion on which anxiolytics (N05C according to the European Pharmaceutical Marketing Research Association — EphMRA — classification) and nonbarbiturate hypnotics (N05B1-N05B2) were dispensed in 2005 (Appendix 1). A unique beneficiary identifier that preserves the patient's anonymity linked all events related to the same patient. Data on patients included: gender, five-year age group (from 0-4 to 95 years or older), and code of the canton of residence. We also knew if subjects were covered by the public supplementary health insurance program ("CMUC") or were exempt from copayments because of a long-term illness (the "ALD" program providing 100% reimbursement for chronic or long-term disease).

For each canton, we calculated the 2005 period prevalence of AX-HY dispensing as the ratio of individuals with at least one delivery of an AX or HY in 2005

(regardless of the location of the pharmacy or of the prescriber) to the number of people covered by the general health insurance fund and residing in that canton at the end of 2005. We also calculated the prevalence of patients who received an AX or HY at least six times, used as a proxy for chronic use [3]. Age-adjusted prevalence was calculated for men and women separately with the direct standardisation method and with the most recent census data (1999) for the French population as the reference (five-year age groups).

Unit of analysis

Cantons were chosen as the geographic units for this analysis because they were the smallest units for which individual-level health insurance data were available that ensured subjects' anonymity. A French canton is a subdivision of a district ("département", of which there are 96 in metropolitan France) and is essentially an electoral district.

Southeastern France is divided into 159 cantons. The PACA-CNAMTS database included 4,548,171 subjects in 2005. Canton of residence was unknown for 142,125 subjects (3.1%). The number of subjects per canton ranged from 144 to 826,901. One canton included fewer than 500 subjects and was not included in the canton-level analysis because the expected number of AX-HY users was less than five [27]. The regression analysis finally included 4,405,902 subjects from 158 cantons.

Explanatory variables

We defined explanatory variables on the basis of aggregate data at canton level, derived from different sources.

- Social and demographic data

Social and demographic data were derived from the 1999 decennial population census (from the National Institute of Statistics and Economical Studies, INSEE), the most recent available at the canton level. Data included in the analysis were: population density (per km²), fraction of the population in four age classes (younger than 20 years, 45-59 years, 60-74 years, 75 years or older), and percentages of elderly people living alone and of single-parent families.

- Socioeconomic data

Also derived from the most recent census were data related to occupational category (we noted the proportions of manual workers, office workers, and managerial and professional employees), unemployment rate, and proportions of subsidized housing, and housing without indoor toilets, bathtubs or showers (henceforth referred to as inadequate housing). We also used data on means-tested benefits, including income support for people older than 25 years-old ("RMI") and for single-parent families ("API"), and the public supplementary health insurance program ("CMUC"), all of which are standard deprivation indicators in France; we used the proportion of claimants in each canton in 2001-2002. We could calculate the aged-adjusted proportion only for CMUC (in 2005). We also included the mean annual family income in 2001 for each canton, provided by the tax authorities.

- General practitioner density

Rates of GPs per 100,000 persons in 2001 were calculated for each canton based on information from the French general health fund database.

- Prevalence of chronic illness

In France, people who suffer from chronic illnesses (e.g., cancer, cardiovascular, or respiratory diseases, or diabetes) can be exempted from any copayments for medical bills by the "long term-illness" (ALD) program, if their illness is on the ALD list. Individual ALD coverage is recorded in the health insurance database. We used information from the PACA-CNAMTS database and aged-adjusted rates of ALD beneficiaries in each canton in 2005 as an indicator of chronic morbidity [28, 29].

To assess mental illness, we determined age-adjusted proportions of subjects with at least one filled prescription for an antipsychotic agent (N05A1-N05A9 according to the EphMRA classification) in 2005 and used it as a proxy for the prevalence of severe mental illness [30, 31]. Antipsychotics are prescribed not only for psychotic patients, but also frequently for patients with major depression, anxiety, and dementia [32]. Thus the prevalence of antipsychotic use should not be interpreted as a proxy for psychotic diseases specifically.

Statistical analysis

We calculated descriptive statistics of the variation in the prevalence of AX-HY deliveries according to age and gender. We also calculated the Pearson correlation coefficient between the global prevalence of AX-HY use and of chronic use.

At the canton level, all prevalence rates are reported with their 95% confidence intervals [33]. These intervals were not calculated at the regional level because the numerators and denominators were so high.

We measured variation between cantons with the extremal quotient (EQ) and the weighted coefficient of variation (COV), two statistics often used in small-area analyses [27]. The EQ is the ratio of the highest rate to the lower rate. The weighted COV is the ratio of the standard deviation of the rates (among cantons) to the mean rate (among cantons) weighted by the population in each canton. We compared the calculated values for the EQ and the weighted COV to the estimated 95th percentile tables generated by Diehr et al. (1990) [27].

We analysed age-adjusted prevalence by canton of AX-HY deliveries with simple and stepwise multiple linear regression (entry threshold: $p<0.20$; exit threshold: $p<0.05$) to study its potential determinants separately in men and women. The explanatory variables related to population age and density were forced in the model. We used the Kolmogorov-Smirnov test to test the normal distribution of the dependent variables (threshold: $p=0.05$) and used the standard "R^2" to measure the fit of each model (larger values represent a higher percentage of explained variance). The statistical analysis used SPSS software (version 14.0; SPSS Inc., Chicago, IL).

Results

Descriptive results

Of the 4,406,046 people included in the regional health insurance database, 684,006 (15.5%) had a prescription for an AX or HY filled at least once in 2005 (12.6% for AX, and 6.9% for HY); 258,731 (5.9%) had at least six deliveries of such drugs in 2005. Prevalence rates increased with age and were higher for women than for men (19.8% vs 10.9% for AX and 7.7% vs 3.9% for HY),

regardless of age group (Figure 1). Of subjects with at least six deliveries in 2005, mean length between two consecutive refills was 34.9 ± 11.3 days.

Age-adjusted prevalence of AX-HY deliveries varied by canton, from 7.3% [5.6-9.3] to 25.2% [23.9-26.5] for women (EQ = 3.4; weighted COV = 0.114), and from 4.8% [3.4-6.5] to 14.7% [14.1-15.3] for men (EQ = 3.0; weighted COV = 0.111). The age-adjusted prevalence of chronic AX-HY use varied from 2.5% [1.2-4.3] to 9.9% [9.0-10.8] for women (EQ = 3.9; weighted COV = 0.164) and from 0.8% [0.1-2.6] to 6.1% [4.2-8.5] (EQ = 8.0; weighted COV = 0.179) for men. All EQ and weighted COV values were outside of the 95th percentile values estimated by Diehr et al. [27] and thus indicate statistically significant geographic variations between cantons (Figure 2).

All aged-adjusted dispensing rates followed a Gaussian distribution, according to the Kolmogorov-Smirnov test. The Pearson correlation coefficient between the prevalence of AX-HY deliveries and the prevalence of chronic use was high for both men and women (respectively $r = 0.753$, $p < .0001$, and $r = 0.835$, $p < .0001$).

Factors associated with the prevalence of AX-HY use by cantons

Among women, the prevalence of subjects with chronic illness and of people using antipsychotics, unemployment rates, mean family income, and the percentage of subsidized housing were each positively and independently associated with the prevalence of AX-HY dispensing (Table I). The results were similar for men, except that the significant association with subsidized housing rate disappeared (Table II). 'R^2' was 0.497 for women and 0.533 for men.

The prevalence of chronic use of AX-HY among women at the canton level was strongly and positively associated with the prevalence of antipsychotic use and of subjects with chronic illness, the proportion of the population aged 45-59 years, and the proportion of subsidized housing. It was negatively associated with the proportion of inadequate housing and of the population aged 60-74 years (Table I). Among men, it was also positively associated with the prevalence of antipsychotic use and of subjects with chronic illnesses, but not with the proportion of subsidized housing. As among women, it was also negatively associated with the percentage of inadequate housing (Table II). 'R^2' was 0.518 for women and 0.474 for men.

Discussion

Our results confirm the high prevalence of AX-HY use in southeastern France: 15.5% of the population had a prescription for AX-HY filled at least once in 2005. We cannot rule out the possibility that the true proportion of AX-HY users is slightly higher than our results since a small proportion of AX-HY might have been delivered without medical prescription. The proportion we found in our study is slightly lower than that observed in 2000 from the same source [13]: it was then 20.3% for AX and 10.4% for HY. This suggests a decrease in the prevalence of AX-HY use, also suggested by the results of the French sample of the European Study on the Epidemiology of Mental Disorders (ESEMeD) [3]. The introduction in the mid-1990s of new antidepressants, such as selective serotonin reuptake inhibitors (SSRIs), may have changed the patterns of psychotropic drug prescription. SSRIs may have replaced AX-HY in some cases, especially for the

treatment of several anxiety disorders [34], even though the combination of AX-HY and SSRIs is also common [35, 36].

Clinical guidelines on the use of anxiolytics and hypnotics were not published in France until December 2006 [37, 38], rather late compared with other European countries [39-42]. This, in combination with a variety of other factors (such as generally high rate of drug demand and use in France, and fee-for-service payments), might have contributed to the high prevalence of the use of AX-HY in France [43].

As previously reported in the literature [44], we observed that use of AX-HY was more frequent among women than men. This may result from a higher prevalence of depression and anxiety in women [45], gender differences in psychological complaints and care-seeking [46], or differences in physicians' attitudes and practices according to patient gender [47, 48]. The prevalence of AX-HY use increased substantially with age, and the prevalence of chronic use reached 25% among women aged 80 years or older in our study. This result is quite worrisome since a recent meta-analysis showed that the benefits of these drugs in people older than 60 years may not justify the increased risks [49], which are worsened by frequent multiple drug prescriptions in this population.

Our findings add to existing evidence of significant geographic variations in health behaviors and health service utilization. Prevalence of AX-HY use varied significantly between cantons, even after we adjusted for age, by a factor on the order of three or four (8 for chronic use in men). These variations are consistent with those observed for psychostimulant use among children at county and state

levels in the USA [20, 50] and antidepressant use in adults at a regional council level in New Zealand [51].

We found in both sexes that the prevalences of antipsychotic use and chronic morbidity at the canton level were the two major independent determinants of the rate of AX-HY use, including chronic use. AX-HY are frequently coprescribed with antipsychotic drugs, especially among patients with schizophrenia or schizoaffective disorders, who often have comorbid psychiatric disorders including anxiety disorders and major depression [52, 53]. There is also strong evidence of comorbidity between common mental disorders (such as depression or anxiety) and other physical health conditions (including coronary heart disease, stroke, diabetes, and obesity) even if their interactions are complex: severe chronic physical illnesses are associated with an increased risk of mental disorders; inversely, mental illnesses can also indirectly increase the risk of chronic diseases because they can modify health behaviors (smoking, alcohol use, and other health habits, all of which are strong risk factors for disease) and treatment compliance [23, 54, 55].

Dispensing of AX-HY was highest in cantons where both unemployment and mean family income were high and thus suggests strong socioeconomic disparities. Explanations for these results may involve individual and neighborhood environment factors. Evidence of an association between AX-HY use and individual socioeconomic characteristics is contradictory, with some studies suggesting negative associations between AX-HY use and education levels or income or employment [56-58] while others suggest positive

associations with the same characteristics [59, 60]. There is also evidence that neighborhood environment affects mental health and thus probably AX-HY use, independently of individual socioeconomic factors: the neighborhood environment may influence strong determinants of mental health, such as social cohesion, stress factors and the resources available to individuals to cope with these factors [61, 62].

Prevalence of AX-HY use, including chronic use in women, was positively associated at the canton level with the proportion of subsidized housing. In France, multiple dwelling units, located in urban or peri-urban areas, account for most subsidized housing, and one third were constructed in the 1960-70s. More than half of all tenants feel their neighborhood is unsafe, and one third of them complain about inadequate noise-proofing [63]. These conditions may worsen anxiety and sleeplessness and this could lead some people to use AX-HY.

We also found that prevalence of AX-HY use at the canton level was not associated with GP density in the multiple models, contrary to previous studies targeting other types of medications (such as psychostimulants and opioid antalgics); those reports showed higher rates of use in areas with a high density of physicians [22, 50]. The smaller range of GP density in southeastern France — relatively high and consistent — than in other regions or countries may explain this result [64]. This finding also suggests that qualitative aspects of the available medical services, more than quantitative elements, need to be taken into account in explaining the geographic variations of AX-HY use. Relevant factors may include GPs' personal and professional characteristics and their attitudes and

practices, as suggested in other health fields [50, 65, 66]. We are not aware of any intervention conducted in southeastern France at canton level to improve benzodiazepine prescription. Until recently, GPs were free to take — or not take — continuing medical education courses on health topics of their choice. This probably contributed to some heterogeneity in prescription practices [36].

Finally, the prevalence of chronic AX-HY use in our study was strongly associated with the prevalences of antipsychotic use and chronic morbidity. Contrary to overall use prevalence, it was not associated with unemployment rates or income levels. This is consistent with previous results showing that factors associated with long-term use of AX-HY differ from those associated with any use [59]. Age, disability, and mental and somatic illnesses appear to be the strongest determinants of chronic benzodiazepine use [67-69].

Like other studies analyzing pharmaceutical reimbursement data, our study has some limitations. It is based on the database of the French general health insurance fund, which does not cover farmers, tradespeople, shopkeepers, professional occupations and other self-employed workers. As far as we know, little information is available on psychotropic drug use in these groups. One study observed a higher annual prevalence of AX-HY use among general practitioners — classified as self-employed workers — than in the general population [70]. However, evidence on the association between AX-HY use and socioeconomic groups remains still contradictory [56-60]. Consequently, our results cannot be considered as representative of the regional population as a whole.

The database does not include reimbursements for drugs dispensed by public hospitals. A study of 91 hospitalized patients showed that 46% of them had been prescribed an AX or HY during their hospitalization [71]. GPs often, however, continue AX or HY treatment initially prescribed in hospitals.

Moreover, data from the health fund database do not provide information about the medical reasons for prescriptions, or about whether purchasers take the drugs as prescribed or at all.

Finally, in this study, sociodemographic characteristics and GP density were derived from data corresponding to calendar years different from that for AX-HY deliveries (respectively 1999, 2001 and 2005). Data available on unemployment rate and GP density at different geographic levels suggest that differences between cantons did not vary substantially during the period 1999-2005 however [72, 73].

Conclusion

Our study showed that the prevalence of AX-HY use in the general population in southeastern France exceeds 15%. The finding that more than one third of consumers use AX-HY chronically is disquieting in view of the side effects of benzodiazepines. Our results revealed variation on the order of 3-4 in the prevalence of AX-HY dispensing at the canton level. Differences in the prevalence of mental and chronic illness were the major determinants of these geographic variations of AX-HY use in southeastern France, especially for chronic use. Moreover, we found that overall prevalence of AX-HY use was higher in cantons where both unemployment and mean family income were high.

These results provide a basis for public health decision-makers. In particular, they may help them to set priorities in targeting a variety of interventions. These might include better information to the local general population and health care professionals about the side effects of benzodiazepines and therapeutic alternatives to them, to reduce the number of new AX-HY treatments and thus the risk of dependence. Continuing medical education for GPs should also include the guidelines for stopping AX-HY treatment. Future studies are needed to examine trends in geographic variations in the use of AX-HY, better disentangle their individual and contextual determinants and evaluate public health action in this field.

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Table I: Determinants of the prevalence of overall and chronic AX-HY use among women at the canton level (n=158). Southeastern France general health fund, 2005

	AX-HY dispensed at least once		Chronic use of AX-HY	
	Simple regression	Multiple regression[a]	Simple regression	Multiple regression[a]
	β	β	β	β
Social and demographic characteristics				
Population density	1.10 ***	-0.00	0.44 **	0.05
% <20 years	0.18 *	0.01	0.03	-0.05
% 45-59 years	0.11	0.08	0.03	0.08 *
% 60-74 years	-0.02	-0.03	-0.01	-0.07 *
% >75 years	-0.13	0.01	0.00	0.05
% elderly living alone	0.01		0.01	
% single-parent families	0.13 *		0.06 *	
Socioeconomic characteristics				
% manual workers	0.09 *		0.06 **	
% office workers	0.12 *		0.05 *	
% managerial and professional employees	0.19 **		0.03	
Unemployment rate	0.27 ***	0.16 **	0.10 ***	
Mean annual income per family	0.21 *	0.35 ***	-0.02	
% “RMI” recipients	0.60 ***		0.23 ***	
% “API” recipients	0.06		0.05 **	
Aged-adjusted % “CMUC” recipients	0.44 ***		0.20 ***	
% inadequate housing	-0.88 ***		-0.30 **	-0.37 ***
% subsidized housing	0.18 ***	0.10 ***	0.08 ***	0.04 **
Availability of health services				
Rate of FPs	1.92		2.64	
Prevalence of chronic illness				
Aged-adjusted % “ALD” recipients	0.61 ***	0.36 **	0.40 ***	0.25 ***
Aged-adjusted % of users of antipsychotics	2.05 ***	1.24 **	1.13 ***	0.65 ***
		R^2 = 0.497		R^2 = 0.518

[a] Adjusted for population age and density

* p<.05

** p<.01

*** p<.001

Table II: Determinants of the prevalence of overall and chronic AX-HY use among men at canton-level (n=158). Southeastern France general health fund, 2005

	AX-HY dispensed at least once		Chronic use of AX-HY	
	Simple regression	Multiple regression[a]	Simple regression	Multiple regression[a]
	β	β	β	β
Social and demographic characteristics				
Population density	0.65 ***	0.10	0.28 *	0.03
% <20 years	0.12 **	0.02	0.01	-0.01
% 45-59 years	0.06	0.03	0.02	0.05
% 60-74 years	-0.02	-0.01	0.10	-0.04
% >75 years	-0.10	-0.04	0.03	0.07
% elderly living alone	-0.01		-0.01	
% single-parent families	0.06 *		0.05 *	
Socioeconomic characteristics				
% manual workers	0.06 *		0.02	
% office workers	0.03		0.03	
% managerial and professional employees	0.14 ***		0.03	
Unemployment rate	0.17 ***	0.12 ***	0.06 **	
Mean annual income per family	0.14 **	0.23 ***	-0.00	
% "RMI" recipients	0.38 ***		0.15 ***	
% "API" recipients	0.02		0.01	
Aged-adjusted % "CMUC" recipients	0.29 ***		0.13 ***	
% inadequate housing	-0.60 ***		-0.24 **	-0.38 ***
% subsidized housing	0.10 ***		0.05 ***	
Availability of health services				
Rate of FPs	-3.26		0.85	
Prevalence of chronic illness				
Aged-adjusted % "ALD" recipients	0.41 ***	0.30 ***	0.28 ***	0.18 ***
Aged-adjusted % of users of antipsychotics	1.45 ***	1.02 ***	0.90 ***	0.63 ***
		R^2 = 0.533		R^2 = 0.474

[a] Adjusted for population age and density

* p<.05

** p<.01

*** p<.001

Figure 1: Proportion of subjects with AX-HY prescriptions filled either once or at least six times, according to gender and age. Southeastern France general health fund, 2005

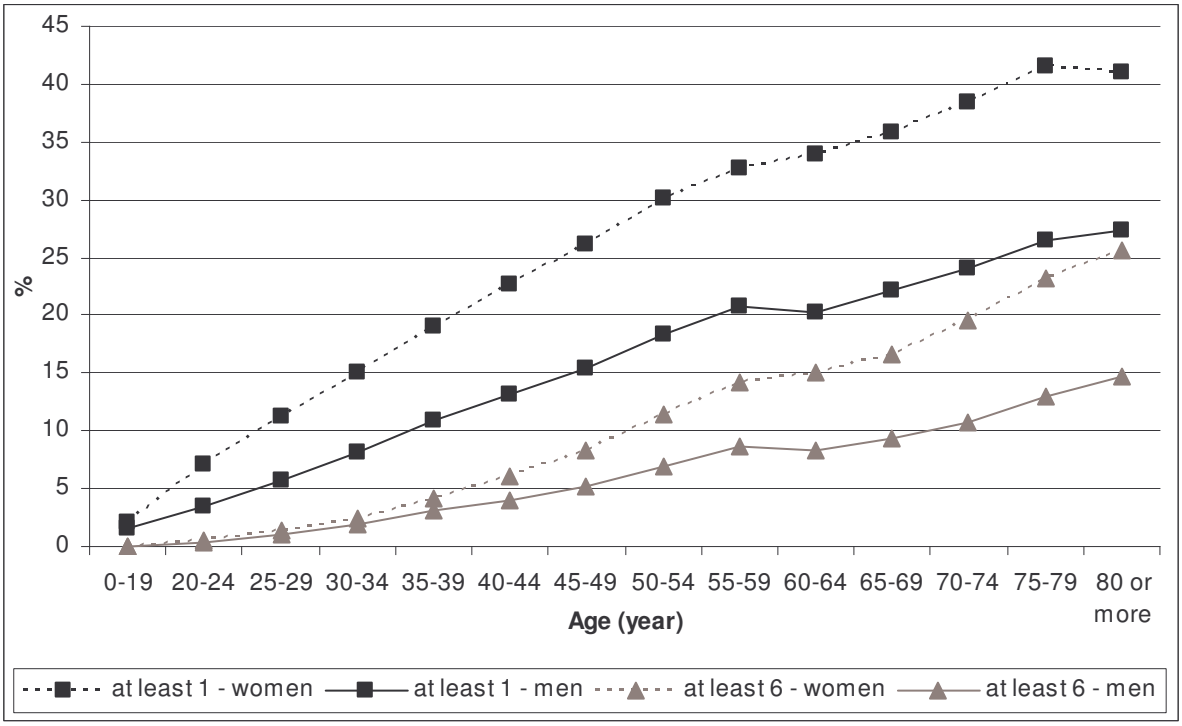
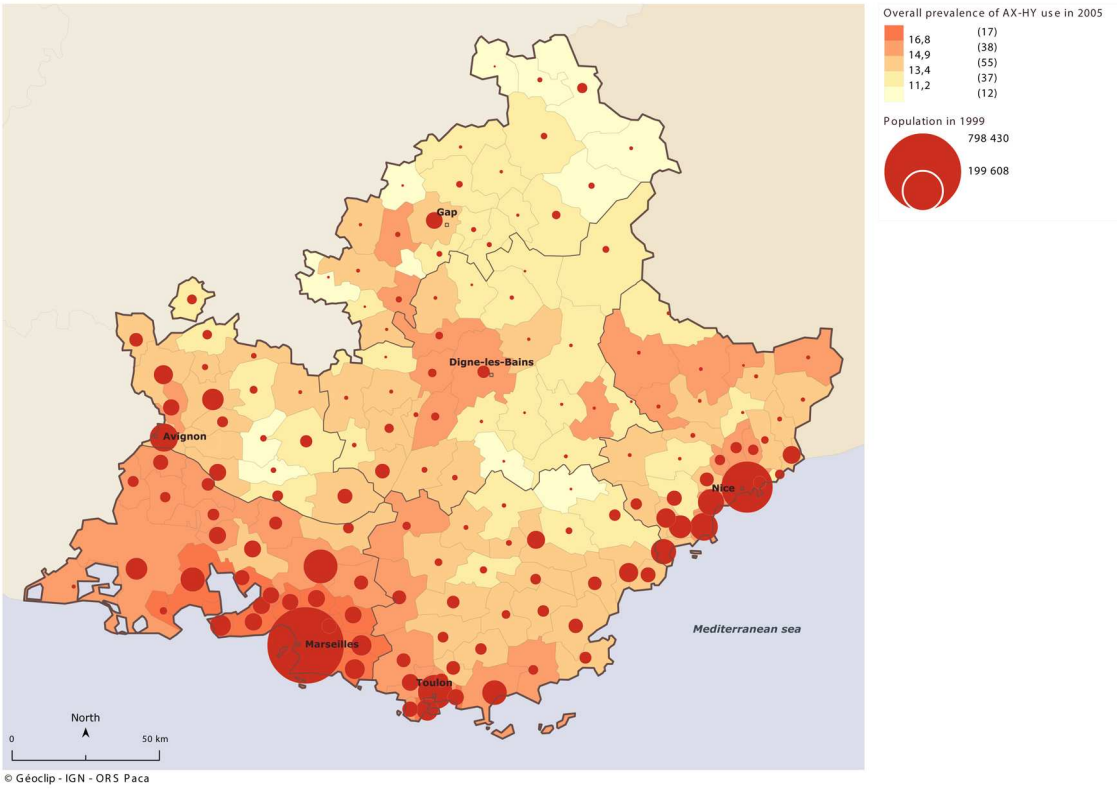


Figure 2: Age-adjusted prevalence of AX-HY use at canton-level (%) (Southeastern France general health fund, 2005), and population (INSEE, census 1999)



Appendix 1: List of anxiolytics and nonbarbiturate hypnotics included in the study according to their proprietary (brand) name

Anxiolytics	Nonbarbiturate hypnotics
ALPRAZOLAM ARROW (0.25 MG, 0.50 MG)	FLUNITRAZEPAM RPG (1 MG)
ALPRAZOLAM BIOGARAN (0.25 MG, 0.50 MG)	HALCION (0.125 MG)
ALPRAZOLAM EG (0.25 MG, 0.50 MG)	HAVLANE (1 MG)
ALPRAZOLAM G GAM (0.25 MG, 0.50 MG)	IMOVANE (3.75 MG, 7.5 MG)
ALPRAZOLAM GNR (0.25 MG, 0.50 MG)	MEPRONIZINE
ALPRAZOLAM IREX (0.25 MG, 0.50 MG)	MOGADON (5 MG)
ALPRAZOLAM MERCK (0.25 MG, 0.50 MG)	NOCTAMIDE (1 MG, 2 MG)
ALPRAZOLAM RATIOPHARM (0.25 MG, 0.50 MG)	NOCTRAN
ALPRAZOLAM RPG (0.25 MG, 0.50 MG)	NORMISON (10 MG, 20 MG)
ALPRAZOLAM SANDOZ (0.25 MG, 0.50 MG)	NUCTALON (2 MG)
ALPRAZOLAM TEVA (0.25 MG, 0.50 MG)	ROHYPNOL (1 MG)
ALPRAZOLAM WINTHROP (0.25 MG, 0.50 MG)	STILNOX (10 MG)
ALPRAZOLAM ZYDUS (0.25 MG, 0.50 MG)	ZOLPIDEM ARROW (10 MG)
ANXYREX (6 MG)	ZOLPIDEM BIOGARAN (10 MG)
ATARAX (100 MG)	ZOLPIDEM EG (10 MG)
ATARAX (100 MG/2 ML)	ZOLPIDEM G GAM (10 MG)
ATARAX (25 MG)	ZOLPIDEM GNR (10 MG)
ATARAX SIROP (1/200 ML)	ZOLPIDEM IREX (10 MG)
BROMAZEPAM ARROW (6 MG)	ZOLPIDEM IVAX (10 MG)
BROMAZEPAM BIOGARAN (6 MG)	ZOLPIDEM MERCK (10 MG)
BROMAZEPAM EG (6 MG)	ZOLPIDEM QUALIMED (10 MG)
BROMAZEPAM G GAM (6 MG)	ZOLPIDEM RATIOPHARM (10 MG)
BROMAZEPAM GNR (6 MG)	ZOLPIDEM RPG (10 MG)
BROMAZEPAM IREX (6 MG)	ZOLPIDEM SANDOZ (10 MG)
BROMAZEPAM IVAX (6 MG)	ZOLPIDEM TEVA (10 MG)
BROMAZEPAM MERCK (6 MG)	ZOLPIDEM WINTHROP (10 MG)
BROMAZEPAM QUALIMED (6 MG)	ZOLPIDEM ZYDUS (10 MG)
BROMAZEPAM RATIOPHARM (6 MG)	ZOPICLONE ARROW (7.5 MG)
BROMAZEPAM RPG (3 MG)	ZOPICLONE BIOGARAN (7.5 MG)
BROMAZEPAM RPG (6 MG)	ZOPICLONE EG (7.5 MG)
BROMAZEPAM TEVA (6 MG)	ZOPICLONE G GAM (7.5 MG)
BROMAZEPAM WINTHROP (6 MG)	ZOPICLONE GNR (7.5 MG)
BROMAZEPAM ZYDUS (6 MG)	ZOPICLONE IREX (7.5 MG)
BUSPAR (10 MG)	ZOPICLONE IVAX (7.5 MG)
BUSPIRONE G GAM (10 MG)	ZOPICLONE MERCK (7.5 MG)
BUSPIRONE MERCK (10 MG)	ZOPICLONE QUALIMED (7.5 MG)
COVATINE (50 MG)	ZOPICLONE RATIOPHARM (7.5 MG)
DIAZEPAM RATIOPHARM (2 MG, 5 MG, 10 MG)	ZOPICLONE RPG (7.5 MG)
EQUANIL (250 MG, 400 MG)	ZOPICLONE SANDOZ (7.5 MG)
EQUANIL (400 MG/5 ML)	ZOPICLONE TEVA (7.5 MG)
LEXOMIL 6 MG	ZOPICLONE WINTHROP (7.5 MG)
LORAZEPAM MERCK (1 MG, 2.5 MG)	ZOPICLONE ZYDUS (7.5 MG)
LYSANXIA (10 MG)	
LYSANXIA (15 MG/ML)	
MEPROBAMATE RICHARD (200 MG)	
NORDAZ (7.5 MG, 15 MG)	

NOVALM (400 MG)
NOVAZAM (10 MG)
QUIETILINE (6 MG)
SERESTA (10 MG, 50 MG)
TEMESTA (1 MG, 2.5 MG)
TRANXENE (5 MG, 10 MG, 20 MG, 50 MG)
TRANXENE (20 MG/2 ML)
TRANXENE (50 MG/2.5 ML)
URBANYL (5 MG, 10 MG, 20 MG)
VALIUM ROCHE (2 MG, 5 MG, 10 MG)
VALIUM ROCHE (10 MG/2 ML SOL INJ)
VALIUM ROCHE (10 MG/ML SOL BUV)
VERATRAN (5 MG, 10 MG)
VICTAN (2 MG)
XANAX (0.25 MG, 0.50 MG)