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Modelling Spanish anxiolytic consumption: economic, demographic and behavioral influences.

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Abstract

Anxiolytics (AX) are the psychotropic drugs prescribed for the treatment of anxiety and insomnia for 2-4 weeks. For longer periods of consumption (>1 month) may lead to the development of tolerance or addiction. Its prescription was 16% of the total pharmaceutical expenditure in Spain in 2007. This paper deals with the development of a mathematical model describing the dynamic of the addiction to AX for the case study of the Spanish region of Castellón. The reasons believed to cause the development of addicts to AX are: the economic situation, the marriage termination and the social contact. The simulations performed to forecast the addicts rate for the period 2010-2014 showed an increase from 6% in 2010 to 14% in 2014 with a fluctuation about 2% between the possible economic scenarios. Finally, the analysis of sensitivity of the rate of addicts to the fluctuation of the social contact parameters was performed, letting us estimate its impact on the pharmaceutical expenditure.

1 Introduction

Of all psychotropic drugs (antidepressants, antipsychotics, anxiolytics (AX) and analgesics opioid group), the most prescribed medications are AX belonging to the group of benzodiazepines [1] N05B, code defined as the classification system Anatomical Therapeutic Chemical (ATC). The main causes of

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the prescription of AX by the general practitioners (GP) of Primary Health Care Centers (PHCC) are the presence of anxiety and/or insomnia [2], [3]. The causes of the emergence of these diseases may be the presence of chronic diseases [4], or social, economic and demographic variables [1].

In Spain, the consumption of AX has increased significantly since the 90's. In fact, in 2007, it represented the 16% of the total pharmaceutical expenditure. In 2009, 15.5% of Spanish population consumed AX in a regular bases. The public expenditure of it summed up over 200 million Euros.

These drugs are only suitable for short-term treatment (between 15-30 Defined Daily Doses (DDD)$\approx$1 month). However, several studies show that GP often prescribe treatments for longer, which increases the risk of patients developing tolerance and physical or psychological addiction [5]. The consequences of developing drug dependence may lead to brain damage resulting in poor concentration, reduced ability to react, memory loss, and accidents. It should seek alternative therapies to psychopharmacology, to reduce not only the economic cost, but also the social cost [6].

Also several studies have been developed in analyzing the ability of patients who have taken sedatives for over a year to reduce and eliminate their consumption [7], [8].

Recent studies show how the consumption of AX increases with the age of the patients consumption is more common in female than in men [9], in singles, divorced or widowed than married [10] and in situation of unemployment [11], in general people who show lower levels of well-being. Also, the social contact could play an important role in all levels of consumption of AX, as occurs with other addictive behavior (nicotine, shopping, food) [12], [13]. Previous studies [12], [13] develop discrete mathematical models considering that social contact may spread from one person to another by the interaction of individuals [14].

The aim of this paper is to develop a mathematical model to predict addictive behaviours to AX by social contact. For this purpose, the population of the study is grouped into three levels according to their level of AX consumption: incidental user, regular user and long-term user (those who have developed addiction). This will lead us to estimate the social effects, the pharmaceutical expenditure, and possible public health recommendations. The paper is organized as follows. The first section is an introduction; second develops the mathematical model and presents the hypotheses and sources of information considered; the third section shows the results obtained from different economical scenarios simulated. Finally, the main conclusions are showed.

2 Method

2.1 Information sources

The study population in this work is made up of subjects who were registered as inhabitants in the Census of the province of Castellón in the Autonomous Community of Valencia (Spain) and also were registered in the Population-based Information System (SIP) in the province of Castellón in 2009 and 2010. The region of study was selected because of the implementation of the electronic prescription system (RELE system) at the end of 2008. Let us note that each inhabitant is provided a SIP number to be identified within the National Health System.

Information about the prescription of AX at PHCC in the province of Castellón in 2009 and 2010 was provided by the DGF (the Regional Valencian Government's General Pharmacy Management). Data was already codified according to the Organic Law 15/1999 on the Protection of Personal Data.

The two databases analyzed (one from 2009, the other from 2010) consisted of 597,844 rows and 591,804 rows respectively and 5 columns embracing the code of each person, their gender, age, number and cost of DDD of AX prescribed.

2.2 Mathematical model and hypotheses

To build the mathematical model, the population is divided into three subpopulations according to the AX (number of DDD) prescribed by year [9]: A: long-term users (more than 180DDD)≈more than 6 months); R: regular users (31-180DDD≈2-6 months); I: incidental users (1-30 DDD)≈1 month). The subpopulation of incidental consumers (I) includes all people that have never consumed for the period considered or they have done just occasionally.

The total population (P) at any time n is expressed as follows:

$$P_n = I_n + R_n + A_n \,.$$

The dynamic of the population can be described by the following system of difference equations (n, time in years):

$$\begin{aligned}
I_{n+1} - I_n &= \beta(I_n + R_n + A_n) - d_1 I_n - \alpha I_n + \gamma_1 R_n + \gamma_2 A_n - \mu_1 I_n A_n - \psi I_n \,, \\
R_{n+1} - R_n &= -d_2 R_n + \alpha I_n - \alpha R_n - \gamma_1 R_n + \gamma_1 A_n + \mu_1 I_n A_n - \mu_2 R_n A_n + \psi I_n - \psi R_n \,, \\
A_{n+1} - A_n &= -d_3 A_n + \alpha R_n - \gamma_1 A_n - \gamma_2 A_n + \mu_2 R_n A_n + \psi R_n \,.
\end{aligned}$$

The model was built following the assumptions of previous studies of social contagious [12], [13]. The values of all parameters were estimated from different sources of information and hypothesis with the exception of the transit rates (μ_1, μ_2) that were adjusted by the model.

The parameters of the model are:

- β, birth rate of the population, where $\beta = 0.00107$ of Castellón for 2009 [16], according to INE (Spanish Institute of Statistics). We consider the birth rate forecasted by INE for the period [2011,2014].
- d_i, mortality rate by categories of AX consumption (i=1,2,3). We used INE information about the mortality rates by age intervals. We adjusted the mortality rate of each category of AX to their age proportion. Let us be $d_1 = 0.024038$, $d_2 = 0.0355799$, $d_3 = 0.0276696$. [16].
- γ_1, rate of recovery of addictive consumers to regular consumers or transit of regular consumers to incidental consumer through a therapy of discontinuation of AX. We estimated this parameter following studies [7], [8], [17] related to the discontinuation of AX prescription through interventions (letter, therapy, etc) as $\gamma_1 = 0.015$. The recovery process is determined by the primary action of the GP who has to diagnose the patient's addiction defining a therapy and secondly the patient who has to admit his illness.
- γ_2, rate of recovery of addictive consumers that become incidental consumers after therapy (change of medication) with other substances. We assumed that addicts aged less than 50 years old could become incidental consumers if other medication substance different from AX replaces their AX prescription. The parameter is estimated as follows: we know from our database that the proportion of addicts aged less than 50 years old over the total number of addicts (26.66%), while we assume that the proportion of addicts younger than 50 years old whose medication changes (3%). Due to the average rate of success of the new medication (55%) [18], this way, $\gamma_2 = 0.2666 \times 0.03 \times 0.55 = 0.0043989$.
- α, rate of unemployed people that consume AX. Where $\alpha = 0.0273$ in 2010. This rate is considered independently of the level of consumption. We assume that the 20% of unemployed people in Castellón (23.96% (forth trimester 2010)) older than 35 years old (57% population of Castellón) [16]) increases the consumption of AX, becoming a regular or long-term consumer. ($\alpha = 0.2 \times 0.2396 \times 0.57$).
- ψ, rate of marriage termination (divorce, separation, annulment). As a result they develop stress and mental disorders becoming regular users and addictive users over time [15]. It was considered constant for all categories of consumption. $\psi = 0.000355$. We estimated as follows: we assume that the 15% of the total employed people of Castellón in 2009 (76.04% of population), who terminated their marriage (3.1175%; average rate in the Valencian Community for the period 2006-2009 [16]) transit to a higher level of AX consumption [15]. This way, $\psi = 0.7604 \times 0.15 \times 0.031175 = 0.000355$.

– μ_1, transit rate of incidental consumers to regular consumers due to "*social contact*" (incidental user regular user).
– μ_2, transit rate of regular users to long-term consumers due to "*social contact*".(regular user addicts). We consider the social contact influence is higher in regular consumers than in incidental ones, $\mu_1 < \mu_2$. It is assumed that no consumer transits from incidental to addict consumer.

Once the parameters were estimated, and the social contact parameters μ_1 and μ_2 are adjusted by the model using the data from the databases, as in [12], [13], we forecast the consumption of AX assuming different economic scenarios for next four years (2011-2014), considering this period of time appropriate due to the available sources of information of the parameters trying to minimize the error of the estimations.

2.3 Economic scenarios

Different simulations are developed considering that the value of α evolves during the next four years assuming different economic scenarios [19].

- **Scenario L**: the economic crisis will remain for at least 5 years (long-term recovery)
- **Scenario V**: the economic recovery will happen in one year and half (short-term recovery)
- **Scenario** $\sqrt{}$: at first there will be a little relapse, the second year the economic situation will suffer a recovery and then will remain constant.
- **International Monetary Fund (IMF) Scenario** [20]: a strong recovery for the first year, and then a constant recovery (unemployment rate decreases a 1% per year) for next 4 years.
- **Optimistic Scenario**: the unemployment rate decreases over time.

With the aim of analyzing exclusively the social contact effect, we simulate different values for μ_1, μ_2 between the interval $[1/2\mu, 3/2\mu]$, while the rest of parameters remain constant.

3 Results

The first row of table 1 shows the composition of the population by categories of AX consumers for 2010. The 88% of total population were incidental consumers in 2010, while the long-term consumers resulted to be slightly higher (6.22%) than the regular consumer category (5.42%). The average pharmaceutical expenditure of each patients' category was: 1 Euros for the case of

incidental consumers, 100 Euros for the regular consumer category and 643.66 Euros a long-term consumer in 2010.

The value of the parameters μ_1 and μ_2 were obtained: $\mu_1 = 6.598 \times 10^{-21}$ and $\mu_2 = 6.365 \times 10^{-6}$. The results obtained show how the rate of transit of incidental to regular consumers due to their "*social contact*" is almost null.

The prediction shows an increase of the number of long-term consumers of AX for all economic scenarios, (table 1). In fact, the mathematical model forecasts about 13-14% of the total population of Castellón will be addicted to the consumption of AX in 2014, while this subpopulation was about 6.22% in 2010. The results between economic scenarios fluctuate about 2% in 2014. Figure 1 shows the differences between economic scenarios for long-term consumers.

Year	**Subpopulation**	**L**	**V**	$\sqrt{\ }$	**IMF**	**Optimistic**
2010	I	522,857	522,857	522,857	522,857	522,857
	R	32,112	32,112	32,112	32,112	32,112
	A	36,835	36,835	36,835	36,835	36,835
2011	I	502,233	502,827	502,827	506,091	505,735
	R	38,172	37,614	37,614	34,550	34,884
	A	43,590	43,553	43,553	43,353	43,375
2012	I	482,753	484,448	485,019	490,773	491,127
	R	40,167	38,779	38,251	33,883	33,448
	A	53,269	52,969	52,926	51,576	51,654
2013	I	464,292	468,074	469,159	476,681	478,184
	R	38,537	35,827	35,034	30,904	29,543
	A	65,581	64,533	64,247	60,946	60,805
2014	I	446,741	453,462	453,950	463,522	466,731
	R	34,204	30,235	30,404	26,725	24,358
	A	79,733	77,039	76,398	70,653	69,827

Table 1
Forecast of consumers of AX by subpopulation and economic scenario.

Then, we estimated the public healthcare expenditure derived from the prescription of AX for next four years and different economic scenarios considering the average expenditure for each category is constant for each year and equivalent to the 2010 cost. This implies we assume there is not inflation effect and also there are not healthcare policies to reduce the Pharmacological Budget (i.e. Generics use, co-payment, etc). Figure 2 shows the increasing trend of

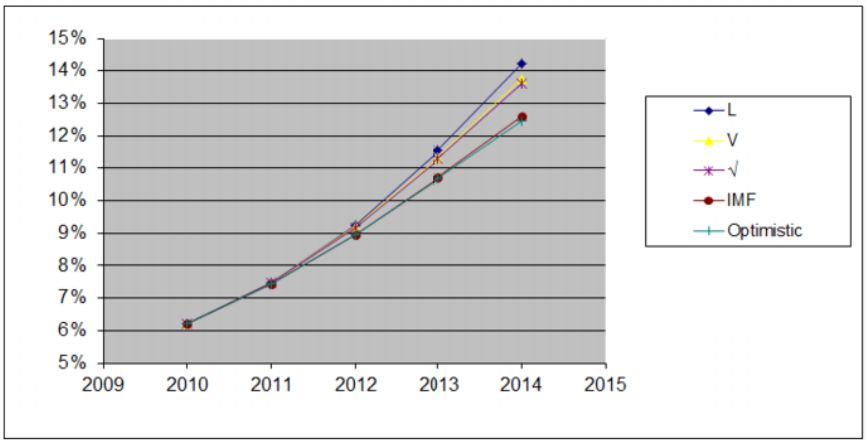

Fig. 1. Development of the percentage of long-term consumers of AX by economic scenarios.

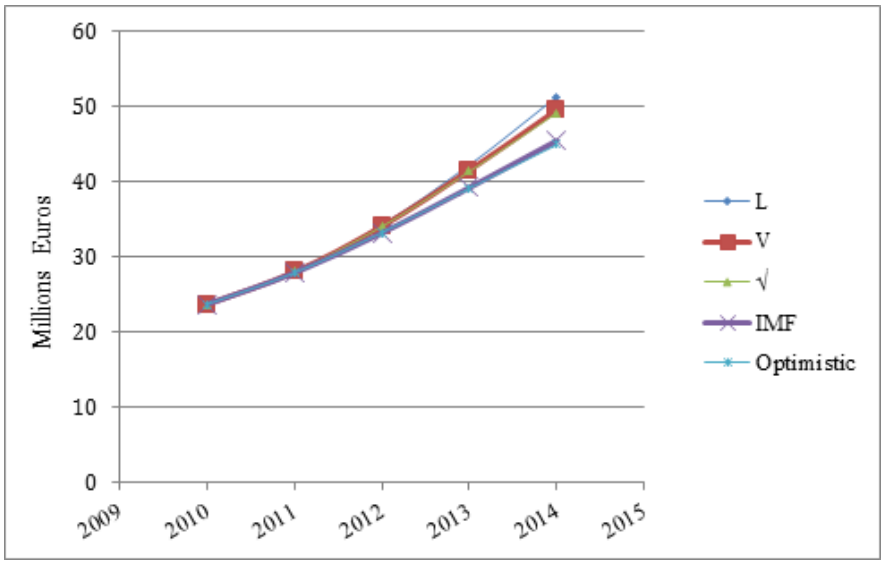

Fig. 2. Development of the Public AX expenditure for the period 2011-2014 in Castellón.

the AX expenditure which will over double in four years, since data shows an increase from about 23 million Euros to over 51 million Euros in 2014 in the worst possible scenario (Scenario L) or close to 45 million Euros in the best alternative (Optimistic Scenario).

Finally we analyze the sensitivity of the percentage of addicts to the fluctuation of the social contact parameters μ_1, μ_2 between the interval $[1/2\mu, 3/2\mu]$. The simulations were made assuming all parameters are constant and the rate of unemployment was estimated as the average rate of unemployment of all possible economic scenarios considered for each year (Scenario L, V, $\sqrt{\ }$, IMF, Optimistic). Since there are two social contact parameters μ_1, μ_2 with different fitting values, we will simulate each parameter μ_1, μ_2 considering the other one remains constant.

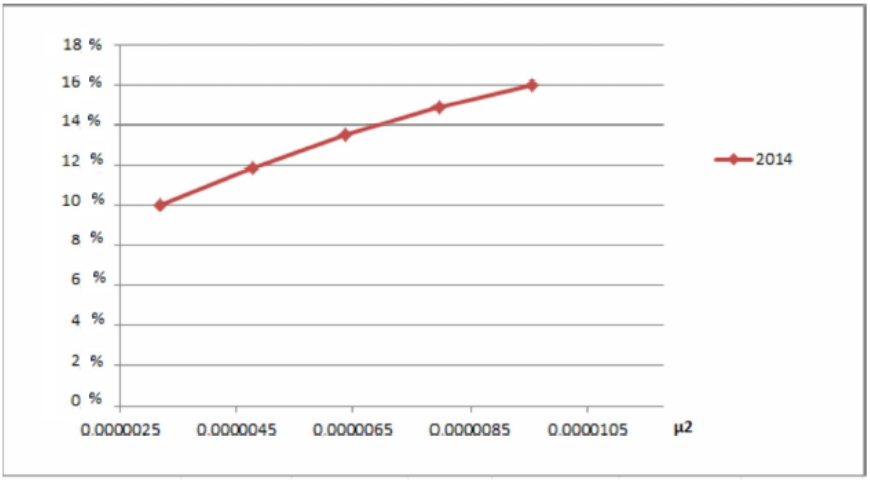

Fig. 3. Analysis of sensitivity of the number of addicts to the change of the parameter μ_2.

The sensitivity of the percentage of addicts to the oscillation of μ_1, was almost null, since the subpopulation of addicts practically remain constant for all possible economic situation. However, as figure 3 shows, a decrease or increase of the parameter μ_2 of 50%, produces an oscillation from 10% to almost 16% of the AX addicts rate, respectively, what would mean in economic terms a public expenditure over 57 million Euros ($3/2\mu_2$), or 36 million Euros ($\mu_2/2$).

4 Conclusions

The paper presents a prospective model to forecast the level of consumption of AX for the next four years (2011-2014) in the province of Castellón considering as main variables that can influence the AX consumption: the social contact, the economic situation, and the marital termination.

The mathematical model let us to predict the future number of regular and addicts to AX, and as a result the volume of DDD prescribed and their public expenditure.

Considering the demographic, economic and cultural similarities between provinces, this can be applied to any Spanish province or the whole country. For the particular case of Castellón, the percentage of consumers will double from 2010 to 2014. As consequence, the public expenditure of AX will increase for all possible economic scenarios, measured through the rate of unemployment.

The results obtained should be considered as a valuable source of information for Public Authorities in order to control and reduce the AX prescription

by GP through different policies, mainly alternative therapies to the pharmacological ones since the results obtained show how the GPs' prescribing patterns are not in accordance with recommended dosage and duration of AX treatment.

On the other hand, the social contact plays an important role in the development of addiction of AX as already other studies [12], [13] show. We have observed an important oscillation of the percentage of addicts when the social contact rate (μ_2) fluctuates. This fact shows the relevance of the Public Authorities to educate the population about the effects of the addiction to AX in order to prevent the population in risk (low self-esteem) to become addicts.

Finally, as limitations of our study we could name the non-consideration of* the interaction between the variables of the model (i.e. effect of divorced people is considered as a static variable and not as a dynamic; the interaction between: mortality rate and divorce, unemployment rate and mortality, or unemployment and birth).

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