



## BACKGROUND

Portugal has one of the highest levels of benzodiazepine's utilization at European level. This issue was highlighted on the latest *International Narcotics Control Board* report<sup>1</sup>, which advises Portugal to analyse the actual procedures on prescription and utilization of these drugs.

Benzodiazepine's use during long periods has been dissuaded, due to tolerance and dependence<sup>2</sup>. The chronic use of these drugs, beyond dependence, has effect on the level of psychomotor capacities and increases the risk of fractures and traffic accidents<sup>3</sup>.

Despite the recommendations for only 2 to 4 weeks in the treatment of anxiety and insomnia, it is observed that long periods of utilization are more common than desirable, especially in elderly people. The use of benzodiazepines has been associated not only to higher age groups, but also to feminine sex, high levels of unemployment and number of retired individuals<sup>4</sup>.

## OBJECTIVES

⇒ Analyse Portuguese benzodiazepine utilization and expenditure patterns at regional and national level.

⇒ Analyse the correlation between benzodiazepine utilization with factors known to affect the utilization of these drugs.

## METHODS

Cross-sectional descriptive study with an analytical component. Drug utilization data refers to Benzodiazepine's prescribed and dispensed in ambulatory to population covered by the National Health Service (NHS), from 1<sup>st</sup> January 2000 to 31<sup>st</sup> December 2004. In accordance with the WHO ATC classification index<sup>5</sup> they have the following codes: N05B (Anxiolytics) and N05C (Hypnotics and Sedatives). Utilization and expenditure indicators employed in the study are those recommended by EURO-MED-STAT<sup>6</sup>.

Utilization data was expressed in Defined Daily Dose (DDD), which correspond to the average maintenance dose in adults for the drug's main indication. In order to express consumption independently of the size of a region's population, DDD per 1000 inhabitants per day (DID) was used.

$$DID = \frac{Nr. \text{ of packages sold in a year (mg)} \times 1000 \text{ inhabitants}}{DDD \text{ (mg)} \times 365 \text{ days} \times \text{population}}$$

Expenditure was expressed in Retail Prices (RP), which includes the contribution of the NHS and of the user. The daily treatment cost (DTC) was also calculated using the formula  $DTC = RP/DDD$ , which gives the average cost of each active substance or drug class.

Analyses of correlation between benzodiazepine's utilization with factors known to affect the utilization of these drugs  
Pearson's correlation (with a level of significance of 0.05) was used to determine whether there was an association between drug's utilization, age structure, percentage of retired people and unemployed levels in health regions.

## RESULTS

### Decrease of 1.9% on benzodiazepine's utilization

94,70 DID in 2000 → 92,89 DID in 2004.

The utilization of anxiolytics was five times higher than the hypnotics in 2004:

↳ **Anxiolytics:** Increase of 3,1% (74,99 DID in 2000 → 77,32 DID in 2004);

Alprazolam showed the highest increase (26,3%) in the anxiolytics class. It was also the most prescribed active substance, followed by Lorazepam and Diazepam. These 3 substances represent 68% of anxiolytics utilization.

The use of intermediate duration anxiolytics increased (10,8%) while the use of long duration ones decreased (-8,3%).

↳ **Hypnotics:** Decrease of 23,0% (17,78 DID in 2000 → 13,69 DID in 2004);

Zolpidem has not followed the hypnotics class utilization's trend and presented a high increase (36,0%). Estazolam and Loprazolam were the substances with the lowest decrease in absolute utilization levels.

### Increase of 11,4% on benzodiazepine's expenditure

✓ Expenditure (RP) amounted over 56 millions euros in 2004.

✓ Anxiolytics were responsible for the greatest proportion of this growth (89,2%) and represent 77% of benzodiazepine's expenditure in 2004.

Expenditures have increased while benzodiazepine's utilization has decreased. The daily treatment cost (DTC) has increased (5,75%) during the period in study, even though the most used substances, as the Alprazolam, Lorazepam and Diazepam, have relatively low DTC.

### Regional analyses

↳ There were some asymmetries either on benzodiazepine's utilization level or on drug utilization pattern between regions in Portugal.

Alentejo presented the highest utilization level (104,26 DID) in 2004, but showed a high decrease rate, above the national average. Algarve had the lowest utilization level (64,27 DID) while Lisboa e Vale do Tejo (89,13 DID) had the lowest decrease either on absolute (-10,86 DID) or percentual values (-10,9%).

⇒ Faro, Bragança and Viana do Castelo were the sub-regions with the lowest utilization levels

⇒ Portalegre, Coimbra and Évora were the sub-regions with the highest utilization levels

These differences were not associated neither to age-structure (Figure 4), nor unemployment levels, nor percentage of retired people ( $p > 0.05$ )

For instance, Bragança, Évora and Beja present similar age structures but different consumptions levels.

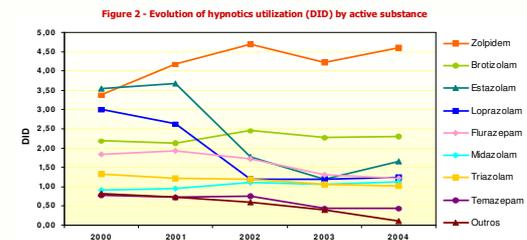
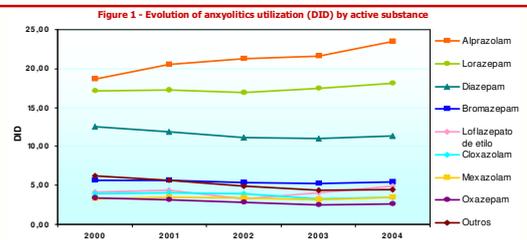


Table 1 - Evolution of benzodiazepine's expenditure (RRP) by therapeutic class

| THERAPEUTIC CLASS | 2000       | %     | 2004       | %     | Δ 2000-2004 | Impact in Δ 2000-2004 |
|-------------------|------------|-------|------------|-------|-------------|-----------------------|
| ANXIOLYTICS       | 38.466.001 | 75,6% | 43.616.023 | 77,0% | 13,4%       | 89,2%                 |
| HYPNOTICS         | 8.352.120  | 16,4% | 8.662.305  | 15,3% | 3,7%        | 5,4%                  |
| OTHERS            | 4.060.394  | 8,0%  | 4.376.321  | 7,7%  | 7,8%        | 5,5%                  |
| TOTAL             | 50.878.515 | 100%  | 56.654.648 | 100%  | 11,4%       | 100%                  |

Δ - Variation

Unit: euro

Figure 3 - Distribution of benzodiazepine's utilization (DID) in Portugal, 2004

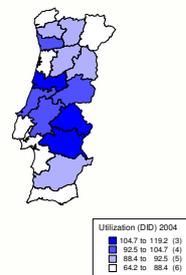
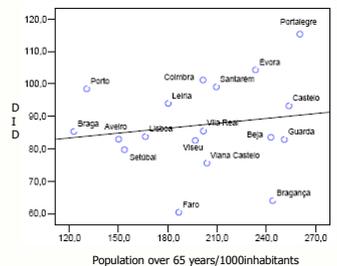


Figure 4 - Distribution of benzodiazepine's utilization (DID) and age structure in the sub-regions, 2003



## CONCLUSIONS

✓ Benzodiazepine's utilization in Portugal was considered of concern by *International Narcotics Control Board*. Therefore the stabilization on utilization, with even a small decrease, should be considered potentially positive.

✓ Expenditure has increased despite the reduction on the utilization's level. This fact means that DDD per inhabitants per day are more onerous.

✓ The asymmetries either on utilization's level or on drug utilization's pattern don't seem to be totally attributable to age-structure, unemployment levels nor to the percentage of retired people, as there wasn't a statistical significant relation between these variables.

✓ For this reason variations on Benzodiazepine's utilization in Portugal seem to be attributed to a combination of different factors, which emphasize the need of more initiatives conducted to health care professionals and patients, in order to diminish the chronic use of these drugs.

## REFERENCES

- 1 - International Narcotics Control Board: Report of the INCB for 2004. Available at [http://www.incb.org/en/nd\\_ar.htm](http://www.incb.org/en/nd_ar.htm)
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