# Prevalence of Outpatient Use of Medicines by the Elderly Population in Portugal: A Cross-Sectional Study

# Prevalência da Dispensa de Medicamentos em Ambulatório na População Idosa em Portugal: Um Estudo Transversal

Ana CARMONA ARAÚJO✉[1,2], Elisabete FERNANDES[1], Inês FRANCO RUIVO[3], Maria do Céu MACHADO[4], António FARIA VAZ[1,5], Cláudia FURTADO[1,6]

**ABSTRACT**

**Introduction:** Like in other countries, the age pyramid in Portugal has been changing considerably, with a substantial increase in the size of the older population and a significant reduction in the number of young people. With aging, co-occurrence of several conditions becomes frequent, often leading to the use of multiple medications (polypharmacy). Polypharmacy in the older population is particularly relevant considering the physiological changes of the ageing process, which increase the risk of drug interactions, poor adherence to treatment, and adverse drug reactions, especially in the oldest-old population (85 years or older). As the size of the older population is likely to increase significantly, it is important to characterize the pattern of medicines' use by the elderly while also identifying cases of polypharmacy in order to obtain evidence that can be used to develop specific measures to tackle the high prevalence of use and its associated risks. To this end, the aim of this study was to characterize medication use by older individuals in Portugal.
**Methods:** Cross-sectional study with data from the National Health System's Control and Monitoring Center on reimbursed medicines that were pre-scribed and dispensed to individuals aged 65 years or older in 2019 in all community pharmacies of the Portuguese mainland. We performed a demographic and geographic analysis of the data by international nonproprietary name and therapeutic group. The number of reimbursed packages and the number of reimbursed packages *per capita* were the metrics used (data from Instituto Nacional de Estatística).
**Results:** A higher consumption of medicines was observed in women, increasing with age, except in the oldest olds, in which the sex difference tended to shrink. Use *per capita* showed an opposite trend, with the oldest-old men surpassing the oldest-old women (mean reimbursed packages: 55.5 in men *versus* 55.1 in women). In women, consumption was led by cardiovascular medicines (31%), followed by central nervous system medications (30%) and antidiabetics (13%); in men, 37% of TOP 10 consumption was due to cardiovascular medications, antidiabetics (16%) and drugs for benign prostatic hypertrophy (14%).
**Conclusion:** In the elderly, there were sex differences in the pattern of medicines' use, and there were also significant age-related differences in 2019. To the best of our knowledge, our study is the first nationwide analysis of reimbursed medicines' consumption data in the elderly, which is essential to characterize the use of medicines in this age group in Portugal.
**Keywords:** Aged; Drug Prescriptions; Outpatients; Portugal

**RESUMO**

**Introdução:** À semelhança de outros países, a pirâmide etária em Portugal tem sofrido alterações profundas, com um expressivo aumento na dimensão da população idosa. A multimorbilidade que surge com o envelhecimento leva, frequentemente, à utilização concomitante de vários medicamentos. A polimedicação é particularmente importante no idoso devido às alterações fisiológicas associadas ao processo de envelhecimento, que aumentam o risco de interações medicamentosas, de fraca adesão à terapêutica e de reações adversas à medicação, em particular nos indivíduos muito idosos (85 ou mais anos). Dado que a dimensão da população idosa poderá aumentar significativamente, importa caracterizar o padrão de consumo de medicamentos pelos idosos, identificando também os casos de polifarmácia, de forma a gerar-se evidência que permita o desenvolvimento de medidas específicas de combate à elevada prevalência de utilização e riscos associados. Assim, o objetivo desta análise preliminar foi determinar a prevalência e caracterizar o padrão de utilização de medicamentos pelos idosos em Portugal, desagregando por faixa etária, sexo e localização geográfica.
**Métodos:** Estudo transversal com dados relativos aos medicamentos comparticipados e dispensados nas farmácias comunitárias de Portugal Continental em 2019, aos utentes com mais de 65 anos. Efetuou-se análise descritiva demográfica e geográfica, por denominação comum internacional e grupo terapêutico. A utilização foi estudada através do número de embalagens comparticipadas dispensadas e número de embalagens comparticipadas dispensadas *per capita* (dados do Instituto Nacional de Estatística).
**Resultados:** Observou-se uma dispensa superior nas mulheres, a qual foi aumentando com a idade, à exceção dos idosos 85+, nos quais a diferença tendeu a diminuir. No que diz respeito ao número de embalagens comparticipadas dispensadas *per capita*, a tendência foi inversa, com os homens muito idosos a ultrapassarem as mulheres 85+ (média de embalagens: 55,5 nos homens *versus* 55,1 nas mulheres). Nas mulheres, os medicamentos mais consumidos foram os do foro cardiovascular (31%), seguidos dos prescritos para o sistema nervoso central (30%) e antidiabéticos (13%). Nos homens, o *ranking* foi liderado também pelos medicamentos para o aparelho cardiovascular (37%); contudo, em segundo lugar surgem os antidiabéticos (16%), seguidos dos medicamentos para a hiperplasia benigna da próstata (14%).
**Conclusão:** Existiram diferenças de sexo e idade relevantes no padrão de dispensa de medicamentos comparticipados nos idosos portugueses em 2019. Esta é a primeira análise publicada de âmbito nacional à dispensa de medicamentos em idosos, sendo essencial para caracterizar o perfil de utilização de medicamentos pelos seniores em Portugal.
**Palavras-chave:** Doentes em Ambulatório; Idoso; Portugal; Prescrição de Medicamentos

1. Direção de Informação e Planeamento Estratégico. Autoridade Nacional do Medicamento e Produtos de Saúde, I.P. (INFARMED). Lisboa. Portugal.
2. Instituto de Investigação do Medicamento (iMed.ULisboa). Faculdade de Farmácia. Universidade de Lisboa. Lisboa. Portugal.
3. NOVA School of Science and Technology. Universidade NOVA de Lisboa. Lisboa. Portugal.
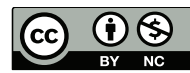4. Faculdade de Medicina. Universidade de Lisboa. Lisboa. Portugal.
5. Comissão de Ética para a Saúde. Administração Regional de Saúde de Lisboa e Vale do Tejo. Lisboa. Portugal.
6. NOVA National School of Public Health. Universidade NOVA de Lisboa. Lisboa. Portugal.
✉ **Autor correspondente:** Ana Araújo. anacarmonaaraujo@yahoo.com

## INTRODUCTION

Increasing comorbidities have been found, related to the increased life expectancy and population ageing, reflected in an increase in the prescription and dispensing of medication in addition to a higher likelihood of polymedication (concomitant administration of at least five drugs),[1,2] as well as higher demand for healthcare services. This study was aimed at assessing the prevalence of use of the different medicines/therapeutic groups by the elderly population.

In fact, ageing is related to an impairment in liver metabolism and renal filtration and excretion capacity, as well as a reduction in body water and muscle mass, in addition to the effects on homeostasis. The pharmacokinetics and pharmacodynamics of different medicines could be affected by these physiological processes, reducing the metabolite excretion and an increased risk of drug interactions and adverse reactions.[3] In addition, elderly patients are frequently excluded from clinical trials, so there is lower evidence in this population, increasing the uncertainty of a benefit-risk ratio.[4]

The relevance of the subject has accounted for several studies on polymedication,[1,5] the use of potentially inappropriate medicines[2,6] and the added value of medication review processes.[7] However, literature is somewhat scarce when it comes to characterising the use of medicines by elderly patients, focused on identifying the mostly used pharmacotherapeutic classes[8-11] and the differences between genders[10,12] and age groups.[8,9,11]

A progressive increase in the average number of medicines has been found, from 1.9 in < 65 age group, to 7.4 in the 80 - 84 age group, followed by a more significant reduction in the 95+ age group, (an average of 2.8 medicines per elderly patient) in the study by Onder *et al.*[8] on the dispensing of medication to the elderly patients in Italy (2013). The Italian Medicines Agency (AIFA) report on the use of medicines by Italian elderly patients in 2019[9] has also found an increase in consumption up to the age of 84, with a decrease in the older age groups.

Johnell *et al.*[10] have found that, on average, female patients were prescribed more medicines than male patients in a sample of the Swedish population aged 75 - 89, in line with what was found by Auvray and Sermet[11] in the French population aged +65. However, in the study by Onder et al[8], a higher prevalence of prescribed medicines between the ages of 65 and 94 has been found, which was reversed from the age of 95 onwards.

Proton pump inhibitors were the mostly prescribed medicines to patients 65+, followed by anticoagulants, in the Onder's study.[8] In the study by Auvray and Sermet[11] on the year 2000, cardiovascular drugs were mostly consumed by this group of patients, as described in the 2019 AIFA report.[9] A predominance in the use of cardiovascular drugs (56.8% of the patients in the study were treated with renin-angiotensin-system modulators, and 52% with statins) was also found by a Portuguese study on polymedication in patients aged 65+.[13]

The relevance of the analysis of the use of medicines by the 65+ population is reinforced by the fact that it is estimated that from 2016 to 2070, the rate of the European Union population aged 65+ will increase from 19% to 29%, particularly in the age group 80+, which is expected to increase from 5% to 13%.[14]

Portuguese data are in line with these, currently with a resident 65+ population of 2.2 million, that could reach 3.0 million by 2080. The ageing index in Portugal will almost double, from 159 to 300 elderly people per 100 young people in 2080, due to the combined result of the decrease in the young population and the increase in the elderly population.[14] The old-age dependency ratio grew from 28.6 in 2010 to 31.3 in 2015, and is expected to reach 67.0 in 2060.[16] As regards healthy ageing, and considering the 'Number of healthy life years at 65' (HLY) indicator, the Portuguese scenario seems to be different from other European countries. In 2015, this indicator, created under the European Health 2020 policy, was of seven years for men and five years for women, well below the European average of 9.4 years for both genders.[17]

Cerebrovascular diseases, cancer, dementia, and mental disorders (e.g., depression), diabetes mellitus, osteoarticular diseases and accidents (significantly related to hearing and vision impairment) have been found as the most prevalent pathologies affecting the elderly.[3] In fact, sense organ diseases and osteoarticular diseases (low back pain and neck pain) were found as the most prevalent in 2016 data, affecting patients of both genders and aged 70+. Male patients in this age group are usually affected by diabetes, cerebrovascular disease and Alzheimer's and other neurodegenerative diseases, while Alzheimer's and other neurodegenerative diseases and mental disorders ranked third and fourth in female patients, followed by oral diseases.[15]

According to the 2019 data from the National Statistics Institute (*Instituto Nacional de Estatística* - INE), most deaths from diseases of the circulatory system have occurred in people aged 65+, accounting for 91.5% of all deaths from this cause.[18] Diseases of the circulatory system have caused 33,624 deaths, the leading cause of death (29.9% of all deaths), affecting mostly female patients (100:83). A mortality rate of 324.9 per 100,000 people related to diseases of the circulatory system has been found, the highest within the past 10 years.[19] Cerebrovascular diseases caused the death of 10,975 people, 93.6% of whom were aged 65+ and 82.5% were aged 75+, leading to an average 9.3 years of potential life lost.[19] The impact of

circulatory system diseases was reflected in the use of medicines, with these class of medicines having the greatest weight in expenditure and use in Portugal. However, little is known about the distribution of this use by age group.

Therefore, this analysis was aimed at assessing the prevalence and characteristics of the use of medicines by patients aged 65+ in mainland Portugal during 2019. The analysis was broken down by age group and gender, by therapeutic group and International Nonproprietary Name (INN), and in terms of the geographical location of dispensing (district).

## METHODS
### Data source

This was a cross-sectional study of the outpatient medicines market in mainland Portugal, using information collected from the National Health Service Monitoring and Control Center (*Centro de Monitorização e Controlo do Serviço Nacional de Saúde* - CMCSNS) on medicines prescribed and dispensed with reimbursement by community pharmacies in mainland Portugal to patients aged 65+, during 2019. The database contains information on all packs of medicines that were reimbursed and dispensed in community pharmacies in mainland Portugal, regardless of where the prescription originated from (primary care, social sector, and hospital outpatient prescription), at both the public and private sectors.

### Methodology

The following variables were analysed: age, gender, dispensing location (district), international non-proprietary name (INN) and therapeutic class of medicines. The 2021 version of the international Anatomical Therapeutic Chemical classification system (ATC) - level 3 - developed by the WHO Collaborating Centre for Drug Statistics Methodology was used. The ATC classification, based on anatomical, therapeutic, and chemical classification criteria, is hierarchically organised, starting from a general classification, at the level of the organ (level 1), to the most specific level of chemical classification of the substance (level 5). Level 3, considered in our analysis, as well as level 4, is a more frequently pharmacological or therapeutic subgroup.

The number of reimbursed packs and the number of reimbursed packs dispensed *per capita*, using population data provided by the INE were analysed. It is worth mentioning that the dispensing of medicines does not necessarily mean these were consumed by patients, since the dispensing of medicines is a proxy for the actual use/consumption of medicines. It is also worth mentioning that non-reimbursed prescription medicines and non-prescription medicines were excluded from this analysis, since only dispensed packs reimbursed by the National Health Service

(SNS) were included in the data source. As regards age groups, 10-year intervals were defined between the ages of 65 and 85, while a single 'very elderly' age group was considered (85+).

Based on these variables, a demographic (age group and gender) and geographical (by district of dispensing) characterisation was carried out, and the pharmacotherapeutic groups and the most used substances were also identified.

The differences between gender and age groups in the dispensing of medicines *per capita* for each pharmacotherapeutic group, district and INN were analysed using a generalised linear model and hypothesis tests (ANOVA). The strength and direction of the association between dispensing of medicines *per capita* by therapeutic group, district and INN, and age group, were obtained using Spearman's correlation tests, with a positive value meaning that dispensing of medicines *per capita* increases with increasing age group, with a stronger correlation the closer the correlation coefficient is to 1. All the statistical analyses were carried out using the R Project for Statistical Computing software (v. 4.1.2).

As a study including data aggregated by age group, using a database containing only anonymised data, no ethics committee approval was required.

## RESULTS

In 2019, around 92.9 million packs of reimbursed medicines were dispensed to patients aged 65+ living in mainland Portugal, representing 56% of the overall dispensed medicines throughout the year, which were prescribed within the healthcare system and reimbursed by the SNS. According to data, there is a decrease in the number of dispensed packs with increasing age, following the pattern of a reduction in the number of elderly patients in the higher age groups. However, the number of dispensed packs *per capita* has increased with the patients' age - from 35 packages in the 65 - 74 age group to 55.3 in the 85+ group.

In addition, there was a gender difference in the overall dispensing of medicines, showing that female patients consumed more than male, a difference that have worsened with age (Fig. 1). However, looking at *per capita* dispensing, there was a reversal of this difference in patients aged 85+, with male patients consuming more than female (annual average of 55.5 packs for male *vs.* 55.1 for female patients). A total of 34.3 packs of medicines were consumed in 2019 by male patients aged 65 - 74, compared to 35.5 annual packages by female patients within the same age group (Fig. 1).

### Geographical characteristics of dispensing

Evora (47.8 packs per elderly patient), Coimbra (46.6) and Santarem and Leiria (both with 46.1 packs per elderly

patient) were the districts with the highest dispensation of reimbursed medicines per elderly patient. Statistically significant differences in *per capita* dispensation of reimbursed medicines were found in 10 of the 18 districts of mainland Portugal (Aveiro, Braga, Coimbra, Guarda, Leiria, Lisboa, Portalegre, Porto, Santarem and Setubal) ($p < 0.001$, except Coimbra and Santarem - $p < 0.01$) between the second age group (75 - 84) and the third (85+), while when comparing the first age group (65 - 74 years) with the second and third, the differences in *per capita* dispensation of reimbursed medicines were all statistically significant ($p < 0.001$) (Table 1). At a national level, *per capita* dispensation was higher among female patients (average of 43.1 packs) than among male (average of 41.0 packs). However, there are some districts in which elderly male patients have consumed more packs *per capita* than female patients: Faro (34.2 *vs.* 33.5); Viana do Castelo (45.4 *vs.* 44.2) and Vila Real (43.3 *vs.* 42.5), showing statistically non-significant differences ($p = 0.311$, $p = 0.281$ and $p = 0.27$, respectively).

The highest medicine consumption by the very elderly was found in the district of Setubal (62.1 packs *per capita*), especially by female patients (63.8 packs *per capita*), with Leiria ranking second (62.7 packs). Among very elderly male patients, Braga was the district with the highest consumption (61.6 packs *per capita*), followed by Porto (61.2 packs *per capita*).

A positive correlation between *per capita* dispensation and age groups has been found (very strong for age groups 65 - 74 and 75 - 84: $\rho = 0.8058$, $p < 0.0001$; strong for age groups 75 - 84 and 85+: $\rho = 0.7131$, $p < 0.01$; moderate for age groups 65 - 74 and 85+: $\rho = 0.3657$, $p = 0.1356$).

**Characteristics of the use by therapeutic area**

Considering the 10 pharmacotherapeutic classes (top 10) mostly used by patients aged 65-74, antidyslipidaemic agents (3.7 million packs) represented 18% of the dispensation of reimbursed packs in top 10, non-insulin antidiabetics (3.5 million packs) represented 17% and antithrombotic agents (2 million packs) represented 9%. In total, medicines used in cardiovascular disorders accounted for 41% of the 10 mostly used pharmacotherapeutic classes in 2019 and 21% of total dispensation to patients aged 65 - 74, with around 20.9 million reimbursed packs dispensed.

A change in the consumption patterns has been found in the 85+ age group: antithrombotic drugs were the most used (16% of the top 10, representing 1.3 million packs), followed by antidyslipidaemic agents (12%, corresponding to 989,775 packs). It should also be noted that central nervous system medicines (anxiolytics, antidepressants, antipsychotics, and opioid analgesics) represented 35% of the top 10 dispensed medicines to the very elderly, the double of those dispensed to less elderly users (18%). Cardiovascular medicines accounted for 28% of the top 10 most used pharmacotherapeutic classes, compared to 41% among younger patients.

Significantly different patterns of use have been found when disaggregating by gender and considering the 10 most used pharmacotherapeutic classes. In fact, male patients mostly used medicines for cardiovascular diseases (37% of the top 10), followed by antidiabetics (16%) and medicines for the treatment of benign prostatic hyperplasia - 14% (Fig. 2). Antidiabetics represented the highest consumption *per capita* by younger elderly people, followed by medicines used to treat benign prostatic hyperplasia among
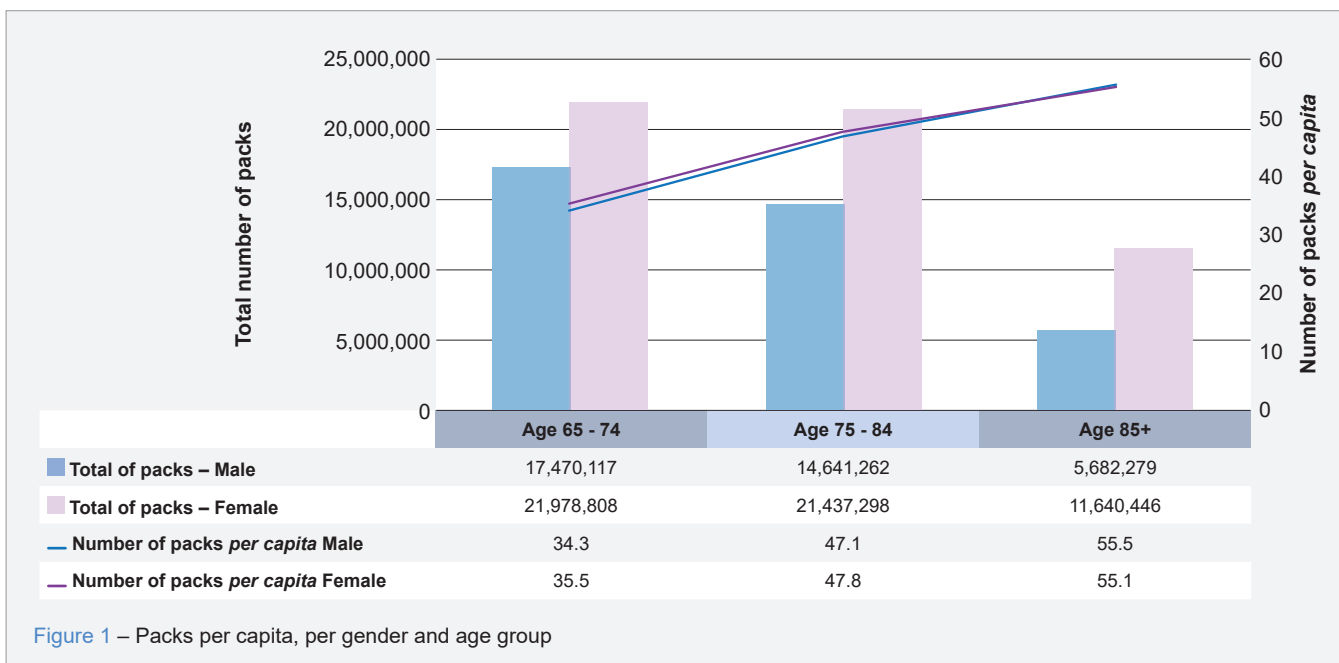


| | Age 65 - 74 | Age 75 - 84 | Age 85+ |
|---|---|---|---|
| Total of packs – Male | 17,470,117 | 14,641,262 | 5,682,279 |
| Total of packs – Female | 21,978,808 | 21,437,298 | 11,640,446 |
| Number of packs *per capita* Male | 34.3 | 47.1 | 55.5 |
| Number of packs *per capita* Female | 35.5 | 47.8 | 55.1 |

Figure 1 – Packs per capita, per gender and age group

Table 1 – Packs *per capita*, per district and age group

| | District | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Aveiro | Beja | Braga | Bragança | Castelo Branco | Coimbra | Évora | Faro | Guarda | Leiria | Lisbon | Portalegre | Porto | Santarém | Setúbal | Viana do Castelo | Vila Real | Viseu |
| No. packs per capita 65 - 74 (I1) | 35.4 | 32.3 | 37.2 | 32.6 | 37.2 | 38.8 | 38.8 | 29.2 | 33.8 | 37.3 | 31.6 | 37.7 | 35.9 | 38.1 | 34.3 | 38.7 | 37.4 | 38.0 |
| No. packs per capita 75 - 84 (I2) | 49.8 | 42.5 | 51.6 | 40.8 | 48.5 | 51.9 | 53.7 | 37.6 | 45.4 | 52.2 | 43.7 | 48.8 | 49.0 | 50.6 | 47.6 | 49.2 | 47.4 | 50.1 |
| No. packs per capita ≥ 85 (I3) | 58.1 | 45.7 | 62.0 | 41.3 | 49.4 | 58.7 | 58.0 | 40.4 | 54.0 | 61.7 | 52.6 | 57.6 | 59.5 | 58.6 | 62.1 | 51.0 | 48.1 | 54.6 |
| p-value (I1 - I2) | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
| p-value (I1 - I3) | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.01 | < 0.001 | < 0.001 | < 0.001 | < 0.001 |
| p-value (I2 - I3) | < 0.001 | 0.101 | < 0.001 | 0.825 | 0.769 | < 0.01 | 0.062 | 0.15 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.001 | < 0.01 | < 0.001 | 0.518 | 0.665 | 0.055 |

the very elderly (5.2 packs *per capita*), more significant with advancing age, especially from the 65 - 74 age group (2.3 packs *per capita*) to the next age group (4.0 packs *per capita*).

As regards female patients, a high consumption of cardiovascular medicines was also found (31% of the top 10), with antidyslipidaemic agents leading the way: 3.1 reimbursed packs *per capita* by the 65 - 74 age group, and 3.6 reimbursed packs *per capita* by the 75 - 84 age group. A change in the pattern of use has been found among very old female patients, with antithrombotic medicines leading (3.9 reimbursed packs *per capita*), followed by central nervous system (CNS) medicines (accounting for 30% of the top 10, in contrast to 11% among male patients), namely anxiolytics, sedatives and hypnotics, as well as antidepressants and opioid analgesics, followed by antidiabetics, accounting for 11% of the top 10.

These gender differences in the dispensation *per capita* of some therapeutic classes are statistically significant, particularly regarding antidepressants (2.6 *vs.* 1.2 packs *per capita* by female *vs.* male patients, *p* < 0.001), opioid analgesics (1. 5 *vs.* 0.7 packs, *p* < 0.01), anxiolytics (2.4 *vs.* 1.3 packs, *p* < 0.01) and antidepressants (5 *vs.* 0.7 packs, *p* < 0.01), anxiolytics (2.4 *vs.* 1.3 packs, *p* < 0.01) and antithrombotic agents (2.3 *vs.* 3.0 packs, *p* < 0.05).
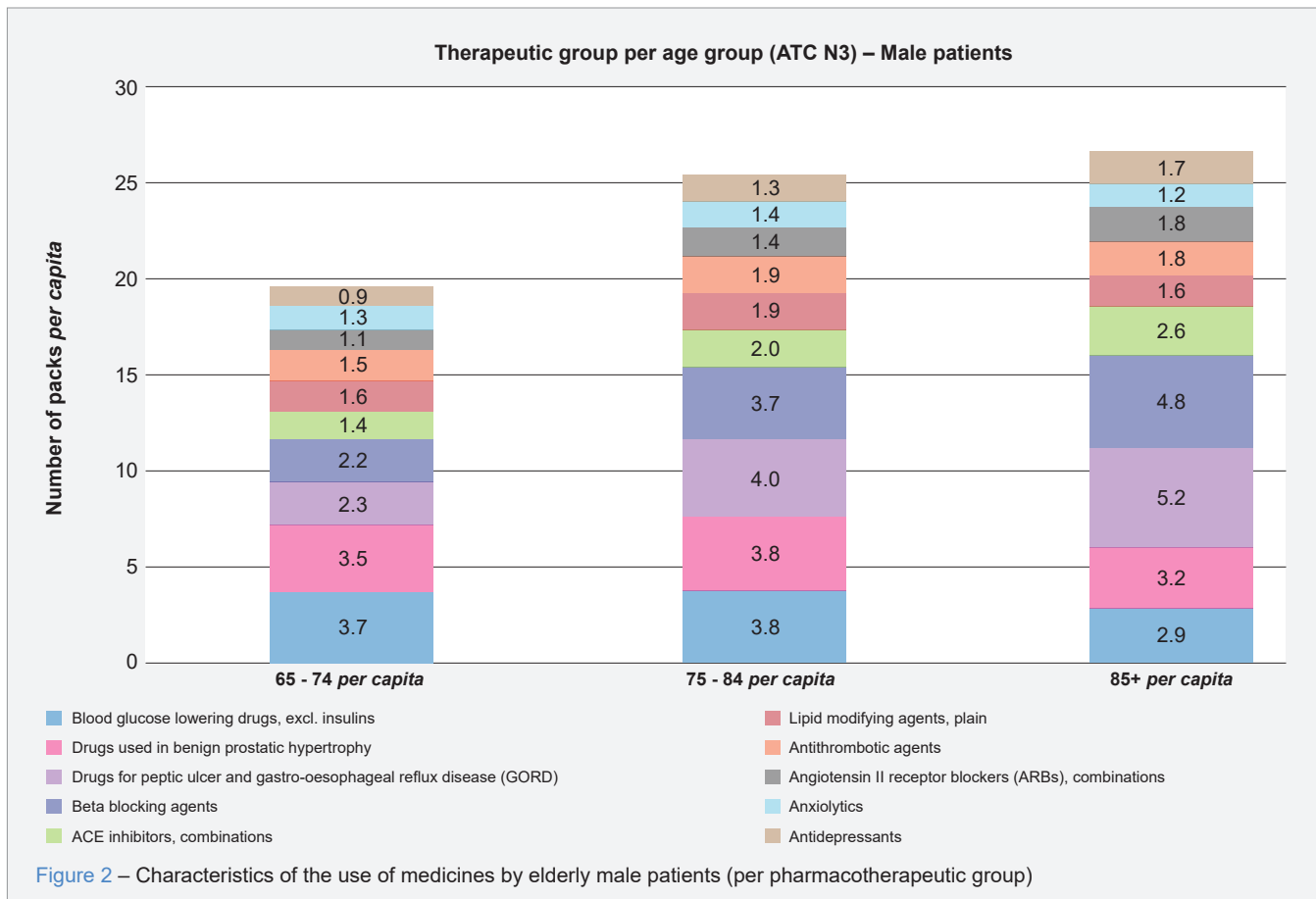
It was also found that the use of antithrombotic drugs has significantly increased with age, from 1.4 reimbursed packs *per capita* in the 65 - 74 age group, to 2.7 reimbursed packs *per capita* in the next age group, increasing to 3.9 reimbursed packs *per capita* in very old women (Fig. 3). In the generalised linear analysis that was carried out, these differences in *per capita* consumption of antithrombotic agents at the extremes of the age range (65 - 74 and 85+) proved to be statistically significant (*p* < 0.001), as did the dispensing of opioid analgesics (*p* < 0.05), with the consumption of 1.1 packs *per capita* in the least elderly women, and 2.2 packs *per capita* in the oldest age group.

A positive correlation, regardless of gender, between *per capita* dispensation and age was also found (very strong for the 65 - 74 and 75 - 84 age groups: ρ = 0.9541, *p* < 0.0001; very strong for the 75 - 84 and 85+ age groups: ρ = 0.88, *p* < 0.001; strong for the 65 - 74 and 85+ age groups: ρ = 0.77, *p* < 0.01).

### Characterisation of use by INN

INNs used to treat dyslipidaemia (atorvastatin and simvastatin - 3.1 and 2.0 million reimbursed packs, respectively) and diabetes mellitus (metformin - 2.3 million reimbursed packs) ranked first in top 10. The beta-adrenergic blocker bisoprolol ranked fourth, with 1.8 million packs dispensed in 2019, followed by acetylsalicylic acid used as an antithrombotic agent (1.7 million packs reimbursed), and paracetamol (1.6 million packs reimbursed).

A higher dispensation of tamsulosin (17% *vs.* 12%) and a lower dispensation of statins - atorvastatin + simvastatin (19% *vs.* 28%) have been found when comparing male patients 85+ with the less elderly (65 - 74 years), while metformin, that ranked second in top 10 INNs among less elderly men, did not rank in the top 10 by

Figure 2 – Characteristics of the use of medicines by elderly male patients (per pharmacotherapeutic group)

older men.

Conversely, furosemide did not rank in top 10 by the least elderly; however, it ranked second by male patients aged 85+ (15% of the top 10).

Statins also ranked first in the list regarding older female patients (28% of the top 10 INNs), followed by metformin (13%). Paracetamol, as well as its combination with the opioid tramadol, both accounted for 16% of the top 10 dispensations; in total, the dispensation of CNS medicines (paracetamol, tramadol + paracetamol and alprazolam) accounted for 24% of the top 10 (Table 2).

Furosemide was mostly used (15% of the top 10 dispensations) by female patients aged 85+, while paracetamol (11%), the combination tramadol + paracetamol (10%), betahistine (9%) and quetiapine (11%) accounted for 41% of the top 10 INNs by older female patients (Table 2).

Considering the INNs included in the top 10 (atorvastatin, metformin, simvastatin, bisoprolol, acetylsalicylic acid as an antithrombotic agent, paracetamol, furosemide, pantoprazole, tramadol + paracetamol and omeprazole), only the differences in dispensation *per capita* of tramadol + paracetamol between genders, and between the extremes

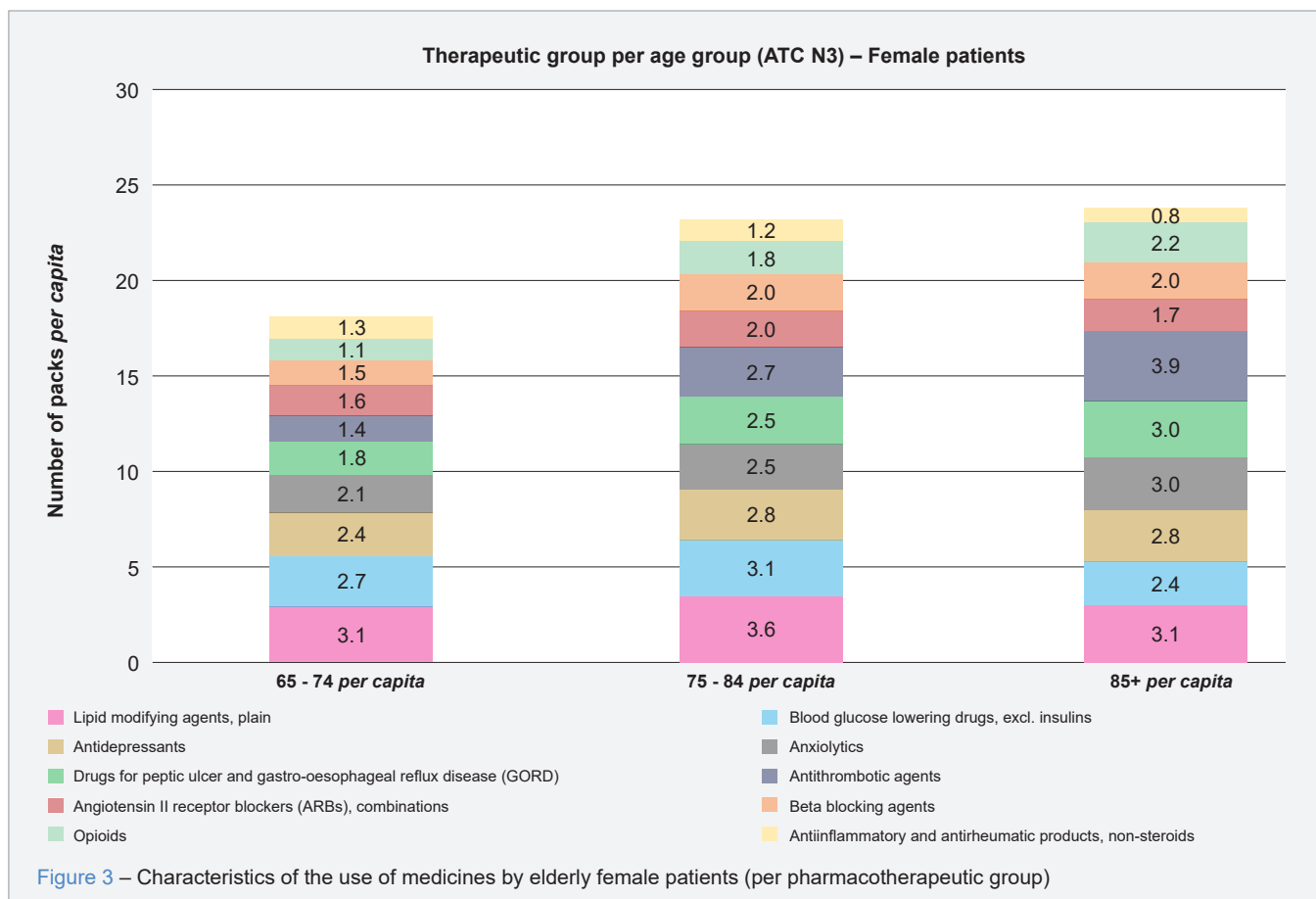of age, were considered statistically significant ($p < 0.05$).

There was also a very strong positive correlation, regardless of gender, between dispensation *per capita* and age ($\rho = 0.98$, $p < 0.0001$, for the 65 - 74 and 75 - 84 age groups; $\rho = 0.91$, $p < 0.001$, for the 75 - 84 and 85+ age groups; $\rho = 0.83$, $p < 0.01$, for the extremes of age).

**DISCUSSION**

The results of this study have shown that the dispensation of reimbursed medicines was higher in female patients, both in terms of absolute consumption and dispensation *per capita*, which is in line with data from the 2014 National Health Survey,[20] in which more than 60% of female patients have described the consumption of prescription medicines, while 48.6% was found in male patients. However, our data were not in line with what was found by two Italian studies,[8,9] in which a higher consumption of medicines has been found in Italian male, compared to female patients.

In our study, gender differences in terms of the average number of reimbursed packs dispensed *per capita* have decreased with increasing age and dispensing *per capita* by patients aged 85+ was even higher in male patients (55.5

**Therapeutic group per age group (ATC N3) – Female patients**



Figure 3 – Characteristics of the use of medicines by elderly female patients (per pharmacotherapeutic group)

*vs.* 55.1 reimbursed packs). A gender difference was also found in terms of dispensing patterns, in line with other studies.[10,12] As expected, considering that cerebrovascular diseases are the most prevalent pathology affecting Portuguese elderly patients, a significant dispensing of cardiovascular medicines was found in both genders (37% in men and 31% in women), which is in line with the AIFA study,[9] in which eight out of 10 elderly patients were treated with at least one cardiovascular medicine. However, we found that the dispensation of CNS medication (namely benzodiazepines, antidepressants, and opioid painkillers) was higher in female (30%) when compared to male patients (11%), which is also in line with what was described by the AIFA report, showing a higher prevalence of use of antidepressants and painkillers in female patients (antidepressants: 19.3% *vs.* 10.6%; painkillers; 17.1% *vs.* 11.5%). This is due to the fact that female patients more frequently present with anxiety disorders and depression.[21] Similarly, female patients more frequently present with musculoskeletal disorders, often associated with severe chronic pain, contributing to the greater use of opioids.[22] A closer monitoring is required due to the high use of psychotropic drugs by elderly female

patients, considering that the elderly are more susceptible to the adverse effects of CNS agents.

A higher dispensation of medicines was found in the Northern region, followed by the Lisbon Metropolitan Area (*Área Metropolitana de Lisboa* - AML), Central region, Alentejo, and Algarve, in line with the 2014 National Health Survey,[20] probably related to the greater accessibility to medicines in the Northern region and AML.

The profile of medicine use by the elderly found in our study is partially in line with what has been described by other authors, namely Wastesson *et al.*,[5] who described the pattern of use in Swedish patients aged 75+, showing that cardiovascular drugs (antihypertensives and statins) and blood drugs (antithrombotic agents) were also among the top 10. It should be noted that the use of hypnotics and sedatives (ATC N05C) predominated in this study, while anxiolytics (ATC N05B) predominated in our study, reflecting the different pattern in the Nordic countries that had already been identified in a previous analysis conducted by Infarmed.[23] Even though the analysis by Onder *et al.*[8] has involved a more specific therapeutic grouping level, some common aspects can be found, namely the presence of

Table 2 – Most used INN by elderly patients in Mainland Portugal, per gender and age group

| | Age 65 - 74<br>INN (no. packs; %) | Age 75 - 84<br>INN (no. packs; %) | Age 85+<br>INN (no. packs; %) |
|---|---|---|---|
| **Male** | Atorvastatin (613,904; 16%) | Tamsulosin (452,357; 15%) | Tamsulosin (182,726; 17%) |
| | Metformin (561,441; 15%) | Atorvastatin (374,243; 12%) | Furosemide (166,085; 15%) |
| | Tansulosin (439,696; 11%) | Acetylsalicylic acid (349,422; 12%) | Acetylsalicylic acid (117,306; 11%) |
| | Acetylsalicylic acid (437,567; 11%) | Metformin (340,357; 11%) | Simvastatin (100,973; 9%) |
| | Simvastatin (436,489;11%) | Simvastatin (339,814; 11%) | Clopidogrel (100,792; 9%) |
| | Bisoprolol (308,388; 8%) | Furosemide (255,608; 9%) | Pantoprazole (86,883; 8%) |
| | Gliclazide (269,676; 7%) | Clopidogrel (250,835; 8% | Atorvastatin (86,435; 8%) |
| | Clopidogrel (268,194; 7%) | Bisoprolol (216,537; 7%) | Paracetamol (81,936; 8%) |
| | Alopurinol (252,380; 7%) | Alopurinol (211,430; 7%) | Alopurinol (75,969; 7%) |
| | Pantoprazole (238,523; 6%) | Pantoprazole (210,141; 7%) | Omeprazole (75,369; 7%) |
| **Female** | Atorvastatin (655,757; 15%) | Simvastatin (554,979; 14%) | Furosemide (345,200; 15%) |
| | Simvastatin (606,654; 14%) | Atorvastatin (509,139; 12%) | Paracetamol (248,134; 11%) |
| | Metformin (548,019; 13%) | Metformin (418,033; 10%) | Simvastatin (239,923; 11%) |
| | Levothyroxine sodium (399,359; 9%) | Acetylsalicylic acid (408,626; 10%) | Acetylsalicylic acid (227,808; 10%) |
| | Alprozolam (380,393; 9%) | Tramadol + Paracetamol (391,084; 10%) | Omeprazole (207,547; 9%) |
| | Omeprazole (379,304; 9%) | Paracetamol (386,214; 9%) | Beta-histine (204,464; 9%) |
| | Bisoprolol (368,862; 8%) | Omeprazole (375,350; 9%) | Tramadol + Paracetamol (203,337; 9%) |
| | Paracetamol (342,910; 8%) | Furosemide (372,348; 9%) | Lorazepam (197,429; 9%) |
| | Acetylsalicylic acid (341,447; 8%) | Beta-histine (350,236; 9%) | Pantoprazole (191,031; 8%) |
| | Pantoprazole (329,110; 8%) | Pantoprazole (343,347; 8%) | Quetiapine (185,285; 8%) |

different cardiovascular and blood therapeutic subclasses in the top 10 of the Italian dispensing.

However, as far as the CNS is concerned, benzodiazepines were excluded from the Italian analysis as these are not reimbursed, so preventing from making any comparison regarding this therapeutic class, with a very relevant use by the Portuguese elderly patients, as described in a study by Infarmed.[23] In fact, Portugal ranked as the third OECD country with the highest chronic consumption of benzodiazepines in 2017, (65 DDD per 1,000 population/day).[24] The antithrombotic agent acetylsalicylic acid, which in our study ranked fourth in the overall dispensation in both genders, is the most consumed INN in the study carried out by Wastesson *et al*.[5] while furosemide, with a very significant dispensing mainly in more elderly male patients in this analysis, ranked fifth in that study.

Our study has some limitations that should be taken into account when interpreting the results, namely the fact that a database of dispensed reimbursed medicines was used, leaving out the dispensing of non-reimbursed or over-the-counter medicines (which represented 17% of the total market for outpatient medicines in Portugal in 2019).[25] In addition, the dispensing of medicines may not correspond to their use, and it is not known whether users actually consume the medicines they buy at the pharmacy. Finally, the 'number of packs' metric used in the study does not take their size into account, since small packs are considered equivalent to larger packs, and vice versa, resulting in a possible over- or underestimation of use. The most appropriate metric for studies on the use of medicines is the Defined Daily Dose (DDD), assigned by the WHO Collaborating Centre for Drug Statistics Methodology. However, a significant number of the INNs analysed do not have a DDD assigned, so using this metric would lead to the exclusion of a significant part of the use of medicines by the elderly population. On the other hand, this study has the advantage of covering the entire population that purchased reimbursed medicines in community pharmacies in mainland Portugal.

A preliminary analysis was included in this study, aimed at assessing the pattern of use of reimbursed medicines by the elderly population in Portugal, based on dispensation data covering the entire population living in mainland Portugal. To our knowledge, it is the first study in Portugal on this subject with this scope.

These results should be further analysed to understand whether the dispensation levels may be the result of inappropriate prescribing/use of medicines. In fact, by using dispensing data at the user level, it will allow the

characterisation of the individual use and also the identification of the most frequent drug combinations in the elderly as well as polymedication, which is one of the main issues in this age group, due to the associated multimorbidity.

## CONCLUSION

More than half of the reimbursed medicines consumed in Portugal in 2019 were used by elderly patients, with a higher consumption *per capita* by female patients in the lower age groups compared to male patients, a difference that faded with increasing age, with a similar dispensation *per capita* by the very elderly for both genders. There were significant gender and age differences in the pattern of medicine consumption among the Portuguese elderly patients in terms of pharmacotherapeutic groups, INNs, and dispensing districts, which should be considered when developing and implementing specific measures against the high prevalence of medicine use among the elderly and the associated risks.

## AUTHOR CONTRIBUTION

ACA, EF: Study Conception, planning, data collection, analysis, and interpretation. Writing of the manuscript and approval of the final version.

IFR: Statistics, review, and approval of the final version.

MCM, AFV: Critical review of the manuscript and approval of the final version.

CF: Study conception and planning, critical review of the manuscript and approval of the final version.

## HUMAN AND ANIMAL PROTECTION

The authors declare that this project complied with the regulations that were established by the Ethics and Clinical Research Committee, according to the 2013 update of the Helsinki Declaration of the World Medical Association.

## CONFLICTS OF INTEREST

The authors declare that there were no conflicts of interest in writing this manuscript.

## DATA CONFIDENTIALITY

The authors declare that they have followed the protocols of their work centre on the publication of patient data**.**

## FINANCIAL SUPPORT

The authors declare that there was no financial support in writing this manuscript.

## REFERENCES

1. Carmona-Torres JM, Cobo-Cuenca AI, Recio-Andrade B, Laredo-Aguilera JA, Martins MM, Rodríguez-Borrego MA. Prevalence and factors associated with polypharmacy in the older people: 2006-2014. J Clin Nurs.2018;27:2942-52.
2. Unutmaz GD, Soysal P, Tuven B, Isik AT. Costs of medication in older patients: before and after comprehensive geriatric assessment. Clin Interv Aging. 2018;13:607-13.
3. Mosca C, Correia P. O medicamento no doente idoso. Acta Farm Port. 2012;1:75-81.
4. Committee for Medicinal Products for Human Use. Reflection paper on physical frailty: instruments for baseline characterisation of older populations in clinical trials. EMA/CHMP/778709/2015, European Medicines Agency, 2018. [cited 2022 May 09]. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-physical-frailty-instruments-baseline-characterisation-older-populations-clinical_en.pdf.
5. Wastesson JW, Cedazo Minguez A, Fastbom J, Maioli S, Johnell K. The composition of polypharmacy: a register-based study of Swedes aged 75 years and older. PLoS One. 2018;13:e0194892.
6. Suzuki Y, Sakakibara M, Shiraishi N, Hirose T, Akishita M, Kuzuya M. Prescription of potentially inappropriate medications to older adults. A nationwide survey at dispensing pharmacies in Japan. Arch Gerontol Geriatr. 2018;77:8-12.
7. Hurmuz MZ, Janus SI, van Manen JG. Changes in medicine prescription following a medication review in older high-risk patients with polypharmacy. Int J Clin Pharm. 2018;40:480-7.
8. Onder G, Marengoni A, Russo P, Degli Esposti L, Fini M, Monaco A, et al. Advanced age and medication prescription: more years, less medications? A nationwide report from the Italian Medicines Agency. J Am Med Dir Assoc. 2016;17:168-72.
9. The Medicines Utilisation Monitoring Centre. National report on medicines use in older adults in Italy. Year 2019. Rome: Italian Medicines Agency (AIFA); 2021.
10. Johnell K, Weitoft GR, Fastbom J. Sex differences in inappropriate

drug use: a register-based study of over 600,000 older people. Ann Pharmacother. 2009;43:1233-8.
11. Auvray L, Sermet C, Consommations et prescriptions pharmaceutiques chez les personnes âgées. Un état des lieux. Gerontol Soc. 2002;25:13-27.
12. Venturini CD, Engroff P, Ely LS, Zago LF, Schroeter G, Gomes I, et al. Gender differences, polypharmacy, and potential pharmacological interactions in the elderly. Clinics. 2011;66:1867-72.
13. Simões PA, Santiago LM, Maurício K, Simões JA. prevalence of potentially inappropriate medication in the older adult population within primary care in Portugal: a nationwide cross-sectional study. Patient Prefer Adherence. 2019;13:1569-76.
14. Comissão Europeia. The 2018 Ageing Report. Institutional Paper 065. 2017. [cited 2022 May 11]. Available from: https://economy-finance.ec.europa.eu/publications/2018-ageing-report-underlying-assumptions-and-projection-methodologies_en.
15. Ministério da Saúde. Retrato da Saúde, Portugal. 2018. [cited 2022 May 05]. Available from: https://www.sns.gov.pt/wp-content/uploads/2018/04/RETRATO-DA-SAUDE_2018_compressed.pdf.
16. Instituto Nacional de Estatística. Projeções de População Residente – 2015-2080. 2017. [cited 2022 May 12]. Available from: https://www.ine.pt/xportal/xmain?xpid=INE&xpgid=ine_destaques&DESTAQUESdest_boui=277695619&DESTAQUESmodo=2&xlang=pt.
17. Organização Mundial da Saúde. European Health Report 2018. 2018. [cited 2022 May 05]. Available from: https://www.euro.who.int/__data/assets/pdf_file/0003/380478/HEALTH_REPORT_HIGHLIGHTS_2018_EN.PDF.
18. Instituto Nacional de Estatística. Estatísticas da Saúde 2019. 2021. [cited 2022 May 26]. Available from: https://www.ine.pt/xportal/xmain?xpid=INE&xpgid=ine_publicacoes&PUBLICACOESpub_boui=257483090&PUBLICACOESmodo=2.
19. Instituto Nacional de Estatística. Causas de morte 2019 (dados provisórios). 2021. [cited 2022 May 26]. Available from: https://www.ine.pt/ngt_server/attachfileu.jsp?look_parentBoui=484469261&att_

display=n&att_download=y.

20. Instituto Nacional de Estatística. Inquérito Nacional de Saúde 2014. 2016. [cited 2022 Jun 10]. Available from: https://www.ine.pt/xportal/xmain?xpid=INE&xpgid=ine_publicacoes&PUBLICACOESpub_boui=263714091&PUBLICACOESmodo=2.

21. Conselho Nacional de Saúde. Sem mais tempo a perder – Saúde mental em Portugal: um desafio para a próxima década. 2019. [cited 2022 Jun 02]. Available from: http://www.cns.min-saude.pt/wp-content/uploads/2019/12/SEM-MAIS-TEMPO-A-PERDER.pdf.

22. United Nations. World Drug Report 2017. Global overview of drug demand and supply - latest trends, cross-cutting issues. 2017. [cited 2022 Jul 01]. Available from: https://www.unodc.org/wdr2017/en/drug-demand-and-supply.html.

23. Ramos I. Utilização de benzodiazepinas e análogos. Infarmed;2017. [cited 2022 Jun 15]. Available from: http://www.infarmed.pt/documents/15786/2219894/Utiliza%C3%A7%C3%A3o+de+Benzodiazepinas+e+an%C3%A1logos/adb100fa-4a77-4eb7-9e67-99229e13154f.

24. OECD/European Union. Health at a Glance: Europe 2020: State of Health in the EU Cycle. 2020. [cited 2022 Jun 02]. Available from: https://www.oecd-ilibrary.org/social-issues-migration-health/health-at-a-glance-europe-2020_82129230-en.

25. Infarmed. Relatório do Infarmed "Medicamentos não sujeitos a receita médica – monitorização das vendas fora das farmácias". 2019. [cited 2022 May 11]. Available from: https://www.infarmed.pt/web/infarmed/profissionais-de-saude/utilizacao-e-despesa/relatorios/mnsrm.