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Original Research

Prescribing pattern of antihypertensive drugs in two European cohorts: a population-based database study

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Abstract

Background: Antihypertensive drugs play a crucial role in reducing cardiovascular morbidity and mortality. Variability in prescribing patterns constitutes a major challenge for current healthcare systems. This study aimed to compare patterns of use of antihypertensives in general practice in two southern European populations.

Methods: Observational study. Data on antihypertensive drugs consumption in primary care setting (2016) were obtained from pharmacy refill records in Campania (Italy) and Aragon (Spain). Prescribing rates and the number of defined daily doses [DDD]/1,000 inhabitants/day (DID) were calculated, and the Drug Utilization 90% (DU90%) approach used to reveal differences in prescribing patterns in both regions.

Results: Antihypertensive prescribing rates in Campania and Aragon were 250.8 (95%CI: 250.2-251.3) and 201.7 (95%CI: 200.9-202.5) users/1,000 inhabitants/year. Overall consumption was of 310.1 and 256.8 DID, respectively. Spanish users, especially women and the elderly, consumed a greater volume of diuretics. Conversely, other therapeutic subgroups were more consumed in Campania. However, the most prescribed subgroups accounted for comparable proportions of the total consumption in each region.

Conclusions: Both prescribing rates and intensity of antihypertensive use were higher in Campania. Pharmacy refill records in cross-national comparisons allow to know the factors influencing variability in prescribing habits with a view to improving prescribing quality.

Key words: Drug utilization study, hypertension, international comparison, pharmacoepidemiology.

1. Introduction

Hypertension is a major cardiovascular (CV) risk factor for cardiac, cerebrovascular, and renal diseases and death [1]. In European countries, the prevalence of hypertension in the adult population ranges from 30–50%, and will likely increase as a consequence of population ageing and current lifestyles [2]. Given their demonstrated effects in controlling blood pressure, antihypertensive drugs play a crucial role in reducing CV morbidity and mortality [3]. However, a recent large international study [4] found that blood pressure was uncontrolled in over 50% of individuals receiving antihypertensive treatment. Inappropriate choices of drugs or therapeutic regimens may lead to poor patient adherence, consequently contributing to suboptimal disease control [5]. Furthermore, even within areas with comparable prevalence of arterial hypertension, prescribed treatments can vary widely depending on place of residence [6]. Variability in prescribing patterns and drug consumption, and its consequences in terms of effectiveness, safety, equity, and social efficiency of medical interventions, thus constitutes a major challenge for current healthcare systems [7].

High quality pharmacy claims data, when available and accessible, represents a useful and reliable data source for the monitoring of drug utilization at the population level [8]. Moreover, the availability of comparable data on drug use across different regions allows cross-national comparisons, which can serve as a stimulus to improve the quality of prescribing and to identify target population groups when designing relevant interventions [9,8].

In the present study, we used pharmacy claims data from two southern European populations, Campania (Italy) and Aragon (Spain). The primary healthcare systems of Spain and Italy share many common features: both are predominantly funded with public money, healthcare is managed at the regional government level, and

copayment fees apply to similar segments of the respective populations. The health expenditure per capita is similar: 2,502 euros in Italy and 2,374 euros in Spain [10]. Citizens covered in both countries are assigned a General Practitioner (GP) who is responsible for them and collates a large body of data on each individual patient. The duration of a medical consultation in both countries, and consequently the time to examine, listen to, and diagnose patients and to recommend pharmacological and/or nonpharmacological treatment, is also similar: 7 minutes in Spain and 5-7 minutes in Italy.

This study aimed to compare the patterns of use of antihypertensive drugs in general practice in Campania and Aragon.

2. Patients and methods

2.1. Study design and data sources

This observational study examined the pattern of use of antihypertensive drugs in primary care settings in Campania (southern Italy) and Aragon (northeastern Spain). Data were obtained from two administrative healthcare databases: the Campania Regional Database and the Information System for Medication Consumption in Aragon. Drug-utilization data obtained from both these databases have been used in previous studies [11,12]. The Italian database records data on drugs dispensed by community pharmacies in Campania and reimbursed by the Local Health Authority of Campania Region. The database records the following information for each prescription: anonymous patient code; date of dispensation; Anatomical Therapeutic Chemical (ATC) code; number of Defined Daily Doses (DDD); and number of packages dispensed. This information is matched by record-linkage analysis to the civil registry to collect demographic information (i.e., age and sex) on all residents recorded in the database. Permission to use this information for the present study was granted by the relevant authority. The Spanish database records information on all drugs prescribed using an official medical prescription and purchased at pharmacies in Aragon under the coverage of the Aragon Health Service. Each entry in the database corresponds to one prescription and includes the following information: anonymous patient code; sex; date of birth; date of dispensation; ATC code; number of DDDs; and number of packages dispensed. Access to this information was granted by the Aragon Health Sciences Institute. Neither of the two databases include information on prescriptions provided by private practices, in-hospital consumption, or drugs purchased without a prescription.

2.2. Study populations

The study populations consisted of all individuals in the respective regions covered by the corresponding public health systems, representing about 99% of the inhabitants. The Italian population studied corresponded to individuals living in four Local Health Units in the region of Campania, and accounts for 60% of the total population of Campania (hereinafter referred to as Campania). On January 1, 2016, the populations of Campania and Aragon were approximately 3.4 million and 1.3 million people, respectively. . We included all individuals from these populations who were prescribed and subsequently filled a prescription for at least one antihypertensive drug during 2016.

2.3. Drug exposure measurement

Drugs were identified according to the ATC/DDD system [13] developed by the World Health Organization (2018). Drugs included in the present study were those indicated in current European guidelines [14] for the initiation and maintenance of antihypertensive treatment: diuretics (thiazides [C03A], chlorthalidone [C03BA04], and indapamide [C03BA11]); beta-blockers (C07); calcium antagonists (C08); drugs affecting the renin-angiotensin system (including angiotensin-converting-enzyme [ACE] inhibitors [C09A, C09B] and angiotensin receptor blockers [C09C, C09D]). It should be noted that the public health services of both regions reimburse the cost of all antihypertensive drugs (i.e., the proportion of drugs analyzed with respect to the total consumed should be almost 100%).

Following the economic crisis, a copayment for medication prescriptions was instituted in Spain: since 2012, pensioners are required to pay a 10% copayment, with a specific limit dependent on their incomes, while copayments for those under 65 years of age are established according to three income-tested levels. Exemptions are available for the long-term unemployed and for non-contributory pensioners. A copayment system has also been implemented for medicines in Italy. In the Campania region a fixed copayment was implemented in 2009 in order to limit public spending and improve the appropriateness of drug prescription. Exemptions are applied to those of over 65 years of age, as well as low-income groups, pregnant women, and those with severe disabilities or specific medical conditions.

2.4. Data analysis

Baseline characteristics of both populations were analysed and compared. The utilization of antihypertensive drugs was determined by estimating prescribing rates and the intensity of drug use, and by characterizing the specific medications prescribed. The total prescribing rate (number of individuals per 1000 inhabitants who received at least one prescription for an antihypertensive drug in one year), both unadjusted and adjusted for age using the direct method and the standard European population, were estimated, as well as corresponding 95%

confidence intervals (CI). Prescribing rates by age and sex were also determined for both study populations. The intensity of drug use or exposure was determined as the number of DID (DDD/1,000 inhabitants/day) by pharmacological subgroup, sex, and age group. Finally, an analysis using the drug utilization 90% (DU90%) approach of Bergman et al. [15] was performed. This method groups drugs into chemical subgroups, and then ranks them according to the number of DID and the number and type of substances comprising the upper 90%. For each region, the most prescribed chemical subgroups were identified and compared.

3. Results

In 2016, 848,581 individuals in Campania (250.8 per 1,000 inhabitants per year [95%CI: 250.2-251.3]) and 263,958 individuals in Aragon (201.7 per 1,000 inhabitants per year [95%CI: 200.9-202.5]) were prescribed an antihypertensive drug. Adjustment for age using the direct method revealed rates of 192.6 and 130.6 per 1000 inhabitants per year in Campania in Aragon, respectively. Prescribing rates in both regions increased with age. Rates for those over 80 years of age were 802.6 (95%CI: 798.1-807.0) in Campania and 699.2 (95%CI: 694.1-704.3) in Aragon. Stratification by sex revealed a significantly higher prescribing rate for women (262.4 [95%CI: 261.7-263.2]) than men (238.4 [95%CI: 237.7-239.1]) in Campania. Sex-related differences were also observed in Aragon, where the prescribing rate was 206.9 (95%CI: 205.8-208.0) for women and 196.4 (95%CI: 195.4-197.5) for men. For all age groups and both sexes, the prescribing rate was significantly higher in Campania than Aragon (Figure 1). The results obtained for women in the middle-aged groups were particularly striking. For instance, the prescribing rate for women aged 40-59 years was 249.4 (95%CI: 248.1-250.8) in Campania versus 122.1 (95%CI: 120.5-123.6) in Aragon. The equivalent rates for women aged 60-79 was 693.9 (95%CI: 691.0-696.7) in Campania and 496.0 (95%CI: 492.2-499.8) in Aragon.

Table 1 shows the characteristics of the populations in each of the regions studied. In Campania, women accounted for 53.8% of those prescribed antihypertensive drugs, while individuals aged >60 years accounted for 65.5%. In Aragon, 51.8% of antihypertensive drug users were women while 76.3% were aged >60 years. In Campania 27.8% of those prescribed antihypertensive drugs received at least 12 packages of medication and the average number of packages per user was 16.1. In Aragon 19.7% of users purchased at least 12 packages during the study year, and the average number of packages per user was 14.0. In Campania 52.3% of the study population were prescribed a single drug during the study period, 32.4% were prescribed two different drugs, and 15.3% were prescribed three or more. In Aragon, the corresponding percentages were 64.2%, 27.1%, and 8.7%.

Overall consumption of antihypertensive drugs was 310.1 DID in Campania and 256.8 DID in Aragon. Sex-related differences were observed in both Campania (305.9 and 315.0 DID in men and women, respectively) and Aragon (258.4 and 254.7 DID in men and women, respectively), as well as a significant increase in drug use with increasing age. For example, consumption in the ≥60 years population was >700 DID in Aragon and >900 DID in Campania.

Analyses of the different therapeutic subgroups of drugs prescribed in the two study regions revealed significant overall (Figure 2) and sex- and age-linked (Figures 3 and 4) differences. In Aragon, particularly among women, the DID for diuretics (13.7) was significantly higher than that recorded in Campania (1.4). These differences were particularly marked among elderly users, with 55.3 (Aragon) and 6.3 (Campania) DID for diuretics in the ≥80 years age-group. Conversely, in Campania the number of DID for beta-blocking agents was much higher than in Aragon for all age groups, and especially among women, for whom DID in Campania was more than twice that in Aragon. Similarly, the number of DID for calcium channel blockers and agents affecting the renin-angiotensin system was higher in the Italian population. Thus, for all three drug types (beta-blocking agents, calcium channel blockers, and drugs affecting the renin-angiotensin system), the volume prescribed was higher in Campania than Aragon for both men and women, and these differences were maintained for all age groups.

Tables 2 and 3 show the most prescribed antihypertensive drugs in Campania and Aragon, as determined using the DU90% method. A total of 17 and 19 chemical subgroups were prescribed, respectively, 7 and 8 of which accounted for 90% of the total DID. The subgroups accounting for the greatest prescribed volume were ACE inhibitors and angiotensin II antagonists (25.4% and 17.2% of the total DID in Campania and 23.8% and 22.8% in Aragon). Furthermore, angiotensin II antagonists in combination with diuretics and dihydropyridine derivatives (mainly amlodipine) accounted for >10% of the total DID in both regions. In Campania, the subgroup of beta-blocking agents accounted for 11.1% of total DID.

4. Discussion

The present study reveals striking differences in the use of antihypertensive drugs in two southern European populations. The proportion of the study population that was prescribed antihypertensive drugs (all age groups and both sexes) and the total volume consumed were higher in Campania (Italy) than Aragon (Spain). Differences in the antihypertensive drug subtypes prescribed were also observed. Below, we discuss some of the factors that may contribute to the observed differences.

First, it is important to consider certain aspects of the healthcare systems of the study populations that significantly influence prescribing habits. Although both the Spanish and Italian National Health Services automatically extend coverage to all citizens, regional inequalities in health system performance have been described in Italy, where access to healthcare varies largely by region and income group [10]. For example, healthcare spending in Campania, like most of southern Italy, is below the national average. This gives rise to variation in available resources and perceived quality of care and in the prevalence of certain chronic conditions. Conversely, the region of Aragon scores around average for most healthcare quality indicators calculated for all Spanish Autonomous Communities [10]. Consequently, the comprehensive healthcare provided to chronic patients in Campania may suffer from certain limitations [16] compared with that of Aragon, thereby affecting the decision to treat and/or the choice of antihypertensive drug.

The observed discrepancies may also be explained by unequal distribution of hypertension in the two populations. According to previous studies, the prevalence of hypertension in Spanish and Italian adult populations does not appear to differ markedly, at around 50% in men and slightly less than 40% in women in both countries [17,18]. Moreover, the level of awareness of hypertension in both populations is relatively low [9,19]. However, it could be possible that the results obtained in Aragon and Campania were not exactly comparable to the overall numbers in Spain and Italy, respectively. The lack of clinical information represents, thus, a limitation in the interpretation of differences observed in drug prescribing.

Differences in the prevalence of other CV risk factors or diseases in both populations may also have influenced the respective prescribing patterns of antihypertensive drugs. The latest Country Health Profile reports [10], completed by the Organisation for Economic Co-operation and Development (OECD) and the European Observatory on Health Systems and Policies, report comparable prevalence of diabetes, smoking, and obesity in Italy and Spain. Both are developed southern European regions and the corresponding populations are traditionally considered at low risk of CV diseases. Furthermore, given that the respective national recommendations are based on the same European guidelines [14], the definition of hypertension, treatment goals in the elderly, and choice of hypertensive drug should not differ greatly. These similarities, together with policies established in recent years in both countries to create a healthy environment, raise awareness of the disease and promote healthy behaviors in the population [14].

Both study populations are ageing and include a large proportion of elderly individuals (in 2016, individuals aged ≥65 years accounted for 21% and 18% of the populations of Aragon and Campania, respectively, while those ≥80 years accounted for 8% and 5%, respectively). In the present study, stratification of antihypertensive

users by age revealed that individuals aged ≥80 years represented a larger proportion of the study population in Aragon (26.8%) than Campania (14.8%), while those aged <60 years accounted for a much lower proportion in Aragon (23.7%) than Campania (34.5%). Contrary to expectations, these demographic discrepancies did not influence antihypertensive prescribing rates, and unadjusted and age-adjusted rates were higher in Campania than Aragon.

Significant differences in total consumption were observed (310.1 DID in Campania versus 256.7 DID in Aragon).

Two previous studies of hypertension control in the general populations of Italy [9] and Spain [19] revealed marked differences between the two populations in the percentage of treated hypertensive patients with controlled blood pressure (57.6% in Italy [2013-14] versus 42.9% in Spain [2008-2010]). A priori, this better disease control in Campania could be considered a consequence of the greater intensity of antihypertensive drug use observed in our study. However, differences in the period analyzed, the data sources used, and the general methodology applied in the Spanish and the Italian studies make the results not comparable. On the other hand, a greater intensity of drug use does not always correlate with improved disease control in the population. Drug effectiveness is significantly influenced by patient adherence and persistence [20]. Previous studies conducted in both populations [11,21] have revealed suboptimal patient persistence for drugs other than antihypertensives, suggesting that persistence with antihypertensive drugs may also be suboptimal.

Differences in consumption were found, with much higher DID values recorded for calcium-channels blockers, beta-blocking agents, and drugs affecting the renin-angiotensin system in Campania. European guidelines do not recommend a specific initial therapy for hypertension, while others such as the National Institute for Health and Care Excellence (NICE) guidelines for hypertension in adults [22] recommend initiating treatment with drugs that target the renin-angiotensin system (mainly ACE inhibitors). Given the risk of possible adverse effects, beta-blocking agents are not recommended as an initial therapy for hypertension by either the NICE or the Spanish Society of Family and Community Practice [23]. However, the former recognizes that their use should be considered in younger patients and those with certain comorbidities, particularly those for whom agents acting on the renin-angiotensin-system are contraindicated, women of child-bearing age, and those with evidence of increased sympathetic drive [22]. In this context, the significant differences in the consumption of beta-blocking agents observed between our study populations are difficult to explain. Given that the characteristics of the two populations appear to differ little, the increased consumption in the Italian population may be the result of traditional prescribing habits. For diuretics, the number of DID was greater in Aragon than Campania. Until

recently, diuretics were considered the first choice of drug for initiation of antihypertensive treatment [14]. However, current guidelines mainly focus on their use in combination with other antihypertensives. The use of diuretics in Campania has decreased markedly over the last few years, while in Spain the number of DID for diuretics has remained unchanged [24]. The high rate of prescription of these drugs in Aragon therefore appears to be related to prescribing habits.

Despite the observed differences in drug consumption by subgroup, the DU90% method revealed that each of the four chemical subgroups studied accounted for similar percentages of the total DID in both populations. Similarly, ACE inhibitors alone and angiotensin receptor blockers alone were the two most consumed subgroups in each region.

Current European guidelines also make no recommendations as to whether patients should begin treatment with monotherapy or a drug combination [14]. An obvious advantage of monotherapy is that effectiveness and adverse effects can be ascribed to a single agent. However, in cases of ineffective or poorly tolerated monotherapy it can be difficult to find an alternative and patient adherence can be negatively affected. Combination therapy is associated with earlier and more effective blood pressure reduction and a reduced incidence of adverse effects, and is therefore potentially more beneficial in high-risk and less adherent patients [6]. The choice between these two approaches will depend on the patient's clinical status and other diagnoses, information not recorded in the data sources used in the present study. Moreover, local guidelines for treatment of hypertension may differ slightly from European guidelines, thereby influencing patterns of drug use. It is also possible that some drugs classified in the present study as a single active principle could correspond to combinations of several drugs (e.g., the ATC code C09BA02 corresponds to the combination of enalapril + diuretics). The appropriateness of the drug types prescribed in each region was not assessed in the present study, but warrants further research.

4.1. Strengths and limitations of the study

To our knowledge, this is the first study to compare the prescribing patterns of antihypertensive drugs in primary care settings in two European countries. Up to now, it was difficult to perform such an analysis because comparable sources of information were either unavailable or inaccessible. Our study was conducted using two administrative pharmacy claim databases of recognized validity and high quality of registration. These databases constitute invaluable sources of information for drug-utilization research and analyses of the effects of drugs in large populations [25]. Despite these strengths, several considerations or limitations of our study should be noted. First, only outpatient consumption that was covered by the public health services was analyzed.

Therefore, no data relating to consumption funded by other administrative/funding entities (e.g., prescriptions provided by private healthcare providers) or to drugs acquired without prescription were included in the analysis. However, these categories do not appear to account for a large proportion of prescriptions: for the majority of residents in Spain and Italy purchases of prescription drugs, especially those for chronic conditions, are covered by the respective public health systems. Second, although the terms "consumption" and "prescribing" are used throughout this paper, in reality the data analyzed pertain to drugs that are both prescribed and filled. Third, no clinical information was recorded in the data sources used for our analysis. The availability of such data would allow, for instance, exclusion of drugs prescribed for indications other than hypertension (e.g., beta blockers prescribed for ischemic heart disease or cardiac arrhythmia). However, given that pharmacological subgroups with a main indication other than arterial hypertension were excluded from our analysis, it is unlikely that this category accounts for a large proportion of the prescriptions analyzed. Furthermore, the availability of information on clinical status, comorbidities, and other CV risk factors for the study populations could allow analysis of the appropriateness of prescribing based on current recommendations. Finally, owing to the cross-sectional design of the study it was not possible to distinguish between incident and prevalent cases of hypertension. Assessment of the intensity of use as well as the type of substance used by stratifying patients according to the treatment start date could facilitate interpretation of the differences and similarities observed between study populations.

4.2. Clinical implications

The intensity of antihypertensive drug use observed in the two study populations is remarkable considering that both Spain and Italy are traditionally considered to have a low risk of CV disease. The marked variability in prescribing patterns between Campania and Aragon may be attributable to the unequal distribution of certain healthcare resources, differences in the prevalence of behavioral risk factors for CV disease, price differences for the same drugs, and prescribing habits, all of which play important roles in determining the choice of antihypertensive therapy. Another important factor is the marketing policies used by the pharmaceutical industry, primarily to target GPs. Indeed, up to several years ago pharmaceutical companies were one of the main sources of information for GPs in both countries [26,27].

Our findings underscore the importance of promoting safe and effective practices when managing hypertensive patients. Prescribing decisions should be made in accordance with evidence-based recommendations, considering the patient's situation and preferences. To this end, effective disease management could be achieved by adopting a multidisciplinary approach, whereby a range of healthcare providers, as well as the patients

themselves, collaborate in the process of CV disease prevention, treatment, and control. Distribution of resources according to the needs of the population is essential, as this helps to increase accountability and improve quality of care and patient health status, thereby reducing health inequalities [10].

5. Conclusions

There exist differences in the pattern of use of antihypertensive drugs in the two Southern European populations studied. They affect not only to the intensity of use but also to the type of substances utilized.

The variability found with regards to the pattern of use may be attributed to modifiable behaviors or actions, since they both are regions traditionally classified as low-risk for CV diseases. Urgent measures should be taken based on evidence-based recommendations, such as those contained in current clinical guidelines, consider the patient's perspective, and always be focused on a multidisciplinary approach.

Key issues

- Both the proportion of subjects treated, in all age groups and both sexes, and the total volume of antihypertensives consumed are higher in Campania (Italy) compared with Aragon (Spain).
- Calcium channel blockers, agents acting on the renin-angiotensin system and, especially, beta-blocking agents, were more consumed in Campania. On the contrary, users in Aragon, especially women and the elderly, consumed diuretics to a larger extent, compared with the Italian region.
- Pharmacy claims databases allow the performance of cross-national comparisons which may represent a stimulus to improve the quality of drug utilization
- Understanding the reasons of the variability found is needed. Meanwhile, the process of prevention-treatment-control of CV disease should be addressed from a multidisciplinary approach that involves a variety of figures, including the patient him/herself.

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Declaration of Interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes

employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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Author contributions

SM, MJR and EM were involved in the conception and design, analysis and interpretation of the data; SM was involved in drafting of the paper; MJR, VO, GL, CF, IA, MJL, VR y EM revised it critically for intellectual content; all authors gave the final approval of the version to be published; and all authors agree to be accountable for all aspects of the work.

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Table legends

Table 1. Sex and age distribution of the two study populations: individuals treated with antihypertensive drugs in 2016.

Table 2. Ranking of antihypertensive drugs accounting for 90% of total Defined Daily Doses (DDDs) prescribed in Campania in 2016.

ATC: Anatomical Therapeutic Chemical; DID: DDD/1,000 inhabitants/day; ACE: angiotensin-converting-enzyme.

Table 3. Ranking of antihypertensive drugs accounting for 90% of total Defined Daily Doses (DDDs) prescribed in Aragon in 2016.

ATC: Anatomical Therapeutic Chemical; DID: DDD/1,000 inhabitants/day; ACE: angiotensin-converting-enzyme.

Figure captions

Figure 1. Prescribing rates (number of individuals who received one or more prescriptions per 1000 inhabitants) for antihypertensive drugs in Campania and Aragon in 2016, stratified by sex and age group.

Figure 2. Comparison of the number of Defined Daily Doses/ 1,000 Inhabitants/Day (DID) for the different therapeutic subgroups, 2016.

Figure 3. Antihypertensive drug consumption in Campania and Aragon. Data are expressed as the number of Defined Daily Doses/ 1,000 Inhabitants/Day (DID) in 2016 for each therapeutic subgroup, stratified by age group. Note that the scale in the x-axis differs for each age subgroup.

Figure 4. Antihypertensive drug consumption in 2016 in Campania and Aragon, stratified by sex. Data are expressed as the number of Defined Daily Doses/ 1,000 Inhabitants/Day (DID).

Table 1. Sex and age distribution of the two study populations: individuals treated with antihypertensive drugs in 2016.

	Campania	**Aragon**
Total number of antihypertensive drug users	848,581	263,958
Sex		
Women, n (%)	456,117 (53.8%)	136,820 (51.8%)
Men, n (%)	392,464 (46.2%)	127,138 (48.2%)
Age		
<40 years old	26,130 (3.1%)	4,924 (1.9%)
40-59 years old	266,817 (31.4%)	57,535 (21.8%)
60-79 years old	430,455 (50.7%)	130,635 (49.5%)
≥80 years old	125,179 (14.8%)	70,864 (26.8%)

Table 2. Ranking of antihypertensive drugs accounting for 90% of total DDDs prescribed in Campania in 2016.

Rank	ATC code	Chemical subgroup	DID	DID %	Cumulative %
1	C09AA	ACE inhibitors, alone	78.8	25.4	25.4
2	C09CA	Angiotensin II antagonists, alone	53.3	17.2	42.6
3	C08CA	Dihydropyridine derivatives	44.3	14.3	56.9
4	C09DA	Angiotensin II antagonists + diuretics	40.2	13.0	69.9
5	C07AB	Beta blocking agents, selective	34.4	11.1	80.9
6	C09BA	ACE inhibitors + diuretics	22.6	7.3	88.2
7	C09BB	ACE inhibitors + calcium channel blockers	10.4	3.4	91.6
8-17		Others	26.0	8.4	100.0
		Total	310.1	100.0	

ATC: Anatomical Therapeutic Chemical; DID: DDD/1,000 inhabitants/day; ACE: angiotensin-converting-enzyme.

Table 3. Ranking of antihypertensive drugs accounting for 90% of total DDDs prescribed in Aragon in 2016.

Rank	ATC code	Chemical subgroup	DID	DID %	Cumulative %
1	C09AA	ACE inhibitors, alone	61.1	23.8	23.8
2	C09CA	Angiotensin II antagonists, alone	58.6	22.8	46.7
3	C09DA	Angiotensin II antagonists + diuretics	33.9	13.2	60.0
4	C08CA	Dihydropyridine derivatives	32.2	12.6	72.4
5	C07AB	Beta blocking agents, selective	15.9	6.2	78.6
6	C09BA	ACE inhibitors + diuretics	15.0	5.8	84.4
7	C03BA	Sulfonamides, alone	8.3	3.2	87.7
8	C09DX	Angiotensin II antagonists, other combinations	6.7	2.6	90.3
9-19		Others	24.9	9.7	100.0
		Total	256.7	100.0	

ATC: Anatomical Therapeutic Chemical; DID: DDD/1,000 inhabitants/day; ACE: angiotensin-converting-enzyme.

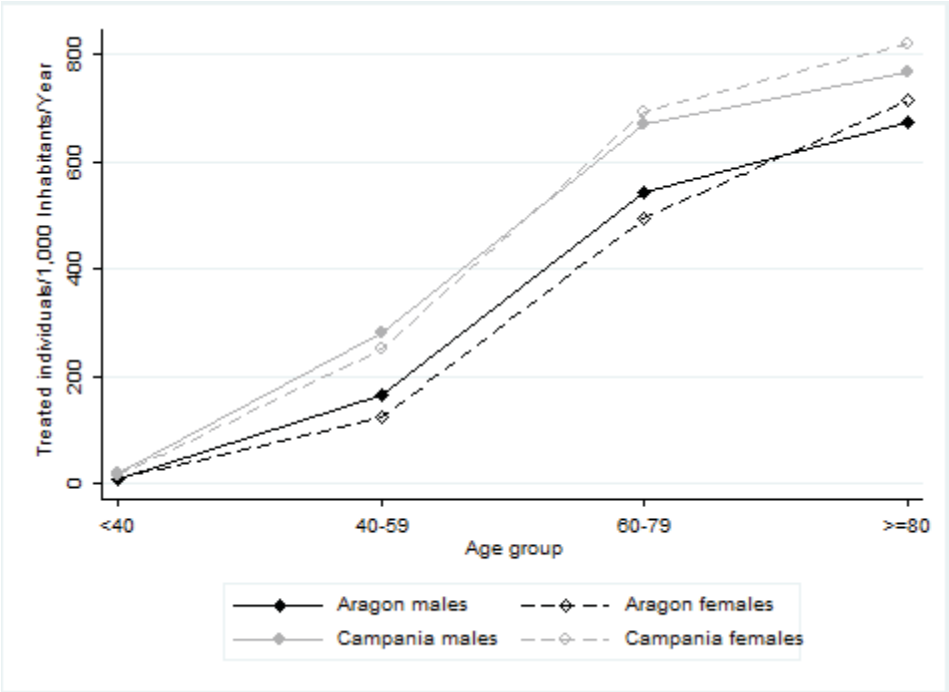

Figure 1

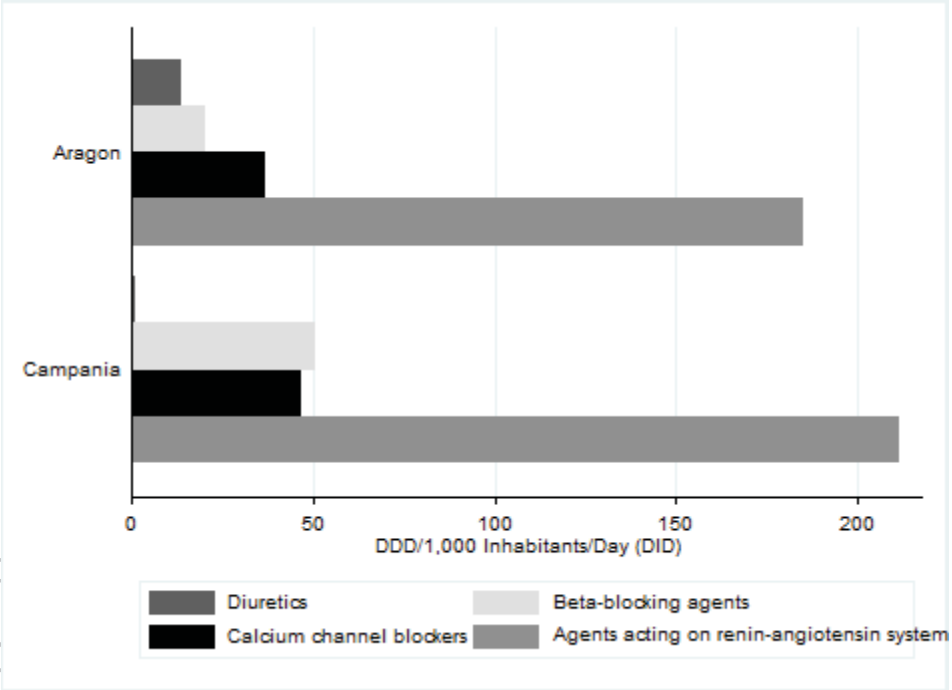

Figure 2

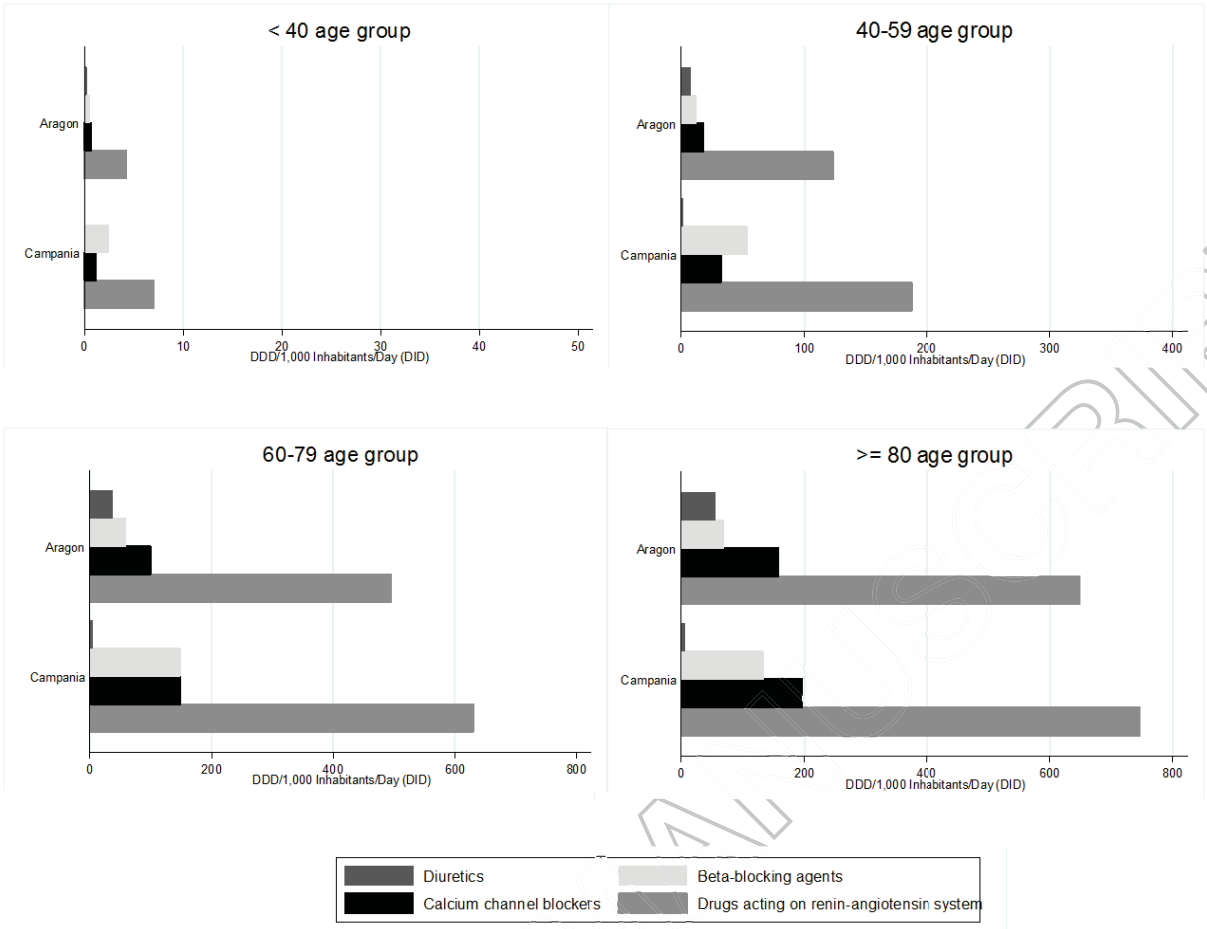

Figure 3

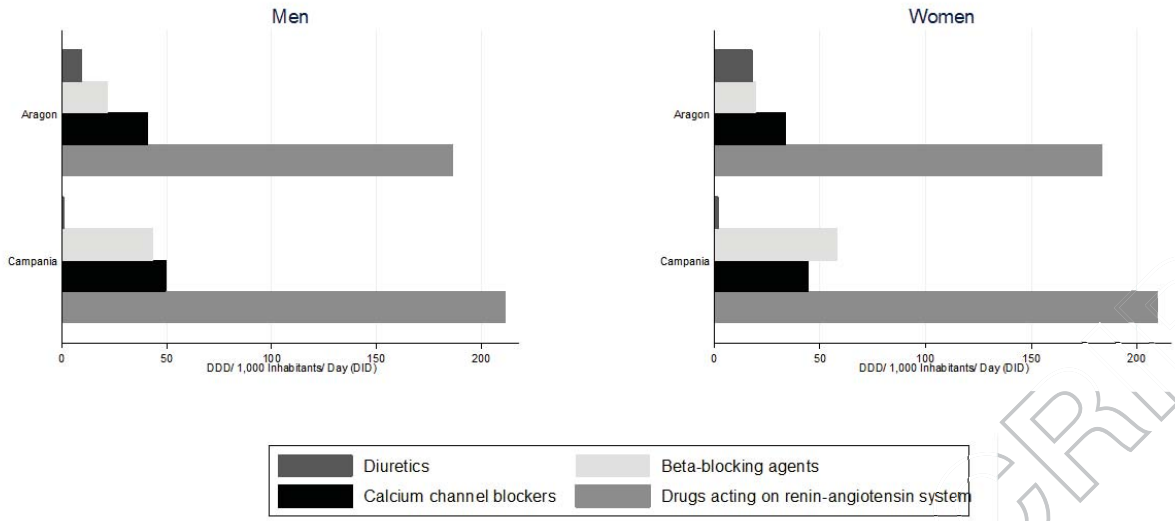

Figure 4