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Prescription Patterns of Antidiabetic Treatment in the Elderly. Results from Southern Italy

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Abstract: The treatment of diabetes in the elderly is a major challenge both in terms of clinical management and of public health. Evidence about prescribing patterns in the elderly diabetic population is limited. The aim was to describe trends in antidiabetic drug (AD) utilization patterns in the elderly in Southern Italy with a focus on drugs for cardiovascular prevention and pharmaceutical costs. The data used for this study were obtained from pharmacy records of Caserta Local Health Authority, a province in Southern Italy with 1 million of inhabitants, comprising urban and rural areas. Subjects above 65 years who received at least one dispensing of antidiabetic between January 2010 and December 2014 were selected. Prevalence and incidence rates (%) of AD use were calculated for each calendar year and stratified by class therapy and age group. Sub-analyses by cardiovascular co-medication therapy and pharmaceutical cost analysis were performed. The prevalence rate decreases from 22.0% in 2010 to 17.5% in 2014 ($p<0.001$). Proportion of subjects treated with monotherapy increases over the study period (33.9% in 2010; 38.6% in 2014; $p<0.001$). In particular, increases the proportion of users of metformin (18.2% in 2010; 23.7% in 2014; $p<0.001$), while the proportion of users of sulfonylureas dropped (11.0% in 2010; 7.2% in 2014; $p< 0.001$). About 90% of elderly diabetic patients are treated with drugs for cardiovascular prevention. The per/patient/yearly drug costs were 2,349 €: 28.5% for AD therapy and 71.5% for other treatments. Trend in drug utilization patterns showed a tendency towards treatment recommendations in older adults.

Keywords: Drug utilization, antidiabetic drugs, elderly, administrative databases, prescription patterns, cardiovascular prevention.

1. INTRODUCTION

The increasingly aging population comes with a higher burden of chronic conditions, both alone or in combination with other conditions. Among them is diabetes, whose increasing prevalence is becoming an epidemic among the elderly population. Indeed, more than 25% of the worldwide population aged 65 years is affected by diabetes [1]. According to the World Health Organization in 2014 the global prevalence of diabetes was estimated to be 9% among adults and in 2012, it was the direct cause of 1.5 million deaths [2]. On a national scale, in Italy about 20% of adults aged $\geq$ 65 years suffer from diabetes [3]. The overall goals of diabetes management in the elderly are similar to those in younger adults and include management of both hyperglycemia and risk factors. Indeed, diabetes related morbidity is also due to the increased risk cardiovascular diseases and for this reason, patients affected by diabetes are often in polytherapy to reduce the cardiovascular risk. Multiple therapy is per se a concern of even greater proportions in frail older patients [4, 5]. Indeed, in this population, hypoglycemia, and hypotension due to drug interactions often occurs. Another concern for the diabetic elderly is the impact of the disease on the functional status, with a higher risk of institutionalization and death [6, 7]. For these reasons, the treatment of diabetes in the elderly is a major challenge both in terms of clinical management and of public health.

Over the last decade several new antidiabetic drugs (ADs) have been introduced in the market enabling physicians to tailor therapy for each individual patient. Trends in consumption of ADs and related costs are increasing worldwide [8]. Tracking and monitoring of drug use in chronic diseases such as diabetes are essential in public health policies. Administrative databases can be useful tools to evaluate appropriateness of therapy [9, 10]. Several studies have analyzed in different countries the use of patients of drugs in chronic conditions [11-15]. Nevertheless, to date we are missing information on the prescribing patterns and therapy costs in the elderly diabetic population. Aim of the present study is to describe trends in ADs drug utilization patterns in a cohort of elderly Italian patients from Southern Italy during

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2010-2014 with a focus on drugs for cardiovascular prevention and pharmaceutical costs.

2. MATERIALS AND METHOD

We conducted a retrospective cross-sectional study using healthcare administrative data from the Local Health Authority (LHU) of Caserta in the Campania Region (Southern Italy), covering a population of about 1,000,000 inhabitants, comprising urban and rural areas.

2.1. Data Sources

In Italy, all diabetes care expenditure is fully covered by the National Health Service (NHS).

The data used for this study were obtained from outpatient drug dispensed records collected from January 1, 2010 to December 31, 2014 (study period). Outpatient pharmacy records include: all information about drugs dispensed by local pharmacies and reimbursed by the NHS; drugs dispensed directly by local health authorities; drugs dispensed through local pharmacies on behalf of local health authorities. Dispensing data records contain information regarding the patient identification code, drug code, dose, formulation, number of packages, date of prescription, date of dispensation, drug price. Drugs are classified according to the Anatomical Therapeutic Chemical (ATC) classification system [16].

This data source was matched by record-linkage analysis to the civil registry in order to collect demographic information (i.e. age, gender, date of death or emigration) of all residents covered by the NHS. All information was linked through a unique and anonymous personal identification code. Because this automated system is anonymous, neither ethical committee approval nor informed consent was required. Furthermore the anonymous data file is routinely used by the local health authority for epidemiological and administrative purposes. Permission to use it for the present study was granted by the responsible authority. The reliability of this strategy to produce pharmacoepidemiological information has been previously documented [17].

2.2. Study Population

The study population consisted of all subjects of 65 years of age or older receiving at least one prescription for any ADs (ATC: A10*) during the study period (January, 1 2010 to December, 31 2014). Age was calculated at the date of first prescription. Subjects were included if they were alive and if they were registered in the civil register of the LHU.

According to their first prescription, subjects were stratified in two main categories:

- monotherapy AD: including Metformin (A10BA), Sulfonylureas (A10BB), Acarbose (A10BF) Thiazolidinediones (A10BG) DPP-4 inhibitors & GLP1-R (A10BH, A10BX) Repaglinide (A10BX02), Insulin (A10AB);
- polytherapy AD: including Fixed combination (A10BD), No-fixed combination (Dual oral therapy, Oral ADs plus insulin)

No-fixed combinations were calculated on the basis of co-prescription of more than one ADs (ATC IV code).

Subjects were characterized on the basis of gender, age (65-75; 75-84; ≥85), co-prescription of drugs for cardiovascular prevention included agents acting on the renin-angiotensin system (RAS – acting agents) (ATC: C09*), lipid-lowering drugs (ATC: C10*) and antiplatet drugs (ATC: B01AC*).

2.3. Data Analysis

Prevalent users were calculated as subject 65 years of age or older receiving at least one prescription of AD. Prevalence of AD use was evaluated per calendar year and it was calculated as the number of prevalent users divided by the number of all resident subjects alive in the same year. Prevalence rates were expressed as percentage. Prevalence rates were stratified by year and age group (65-74; 75-84; >85). Patterns of use of drug class for cardiovascular prevention were calculated and stratified by age group and calendar year.

Characteristics of the study population were analyzed using descriptive statistics: quantitative variables were described by means and standard deviations while categorical variables were described by counts and percentages. Chi square test for trend was used to assess the statistical significance among patients exposed and not exposed to ADs for patients' characteristics (age, gender, pattern prescription) and years. All analyses were performed using SPSS software version 17.1 for Windows (SPSS Inc, Chicago, IL, USA).

2.4. Cost Analysis

The yearly cost of drug use was calculated multiplying the boxes prescribed during the year by the unit cost at the time of prescription. Drug cost was expressed in Euro as mean cost per patient per year. Drug cost was calculated for all drugs prescribed to the elderly diabetic patients and was stratified in cost for ADs treatment, cost for cardiovascular prevention drugs and other treatments.

3. RESULTS

3.1. Cohort Characteristics

The prevalence rate decreases from 22.0% in 2010 to 17.5% in 2014 ($p<0.001$). Prevalence stratified by year and age group is shown in (Fig. **1**). The percentage of males and females remains unchanged over the study period. Proportion of prevalent ADs users decreased over the study period (from 31,210 in 2010 to 27,772 in 2014; $p<0.001$). The mean age (SD) of the study population was 74.5 (6.6) in 2010 and 73.3 (6.1) in 2014.

The main demographic characteristics and pattern prescription of patients treated with ADs are shown in Table **1**. A proportion of ADs users were classified in mutually exclusive categories.

Proportion of elderly diabetic patients treated with monotherapy increases over the study period (from 33.9% in 2010 to 38.6% in 2014; $p <0.001$). In particular, there was a significant increase in the proportion of patients treated with metformin (from 18.2% in 2010 to 23.7% in 2014; p value<

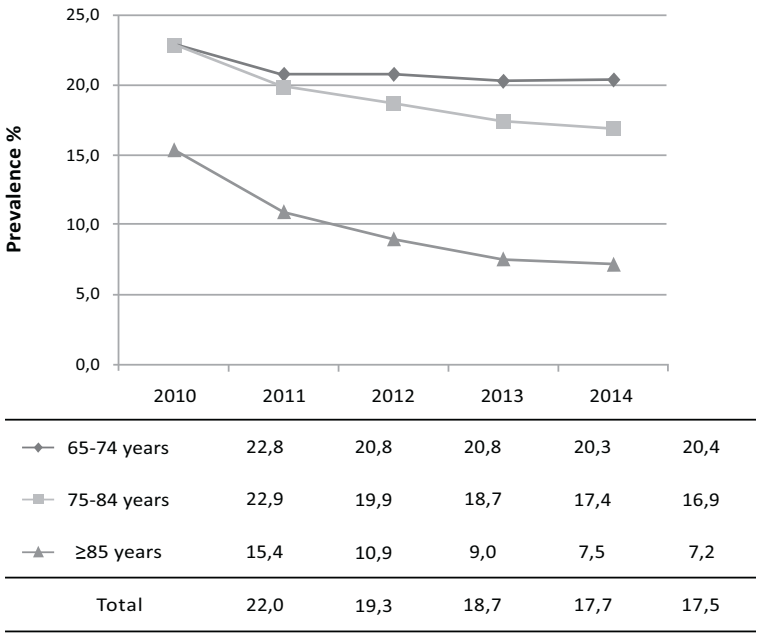

Fig. (1). Prevalence (%) stratified by calendar year and age group.

Table 1. Characteristics of elderly patients in treatment with antidiabetic drugs.

	2010	**2011**	**2012**	**2013**	**2014**
	(n=31,210)	*(n=28,622)*	*(n=28,271)*	*(n=27,430)*	*(n=27,772)*
Mean age (±)	74.5 (6.6)	74.0 (6.3)	73.7 (6.2)	73.4 (6.1)	73.3 (6.1)
Gender (%)					
Male	12,841 (41.1)	11,778 (41.2)	11,734 (41.5)	11,504 (41.9)	11,686 (42.1)
Female	18,369 (58.9)	16,844 (58.8)	16,537 (58.5)	15,926 (58.1)	16,086 (57.9)
Monotherapy ADs (%)	**10,591 (33.9)**	**9,452 (33.0)**	**10,203 (36.1)**	**10,397 (37.9)**	**10,709 (38.6)**
Metformin	5,669 (18.2)	5,225 (18.3)	5,816 (20.6)	6,142 (22.4)	6,576 (23.7)
Sulfonylureas	3,425 (11.0)	2,462 (8.6)	2,373 (8.4)	2,096 (7.6)	1,996 (7.2)
Acarbose	188 (0.6)	389 (1.4)	382 (1.4)	455 (1.7)	541 (1.9)
Thiazolidinediones	34 (0.1)	53 (0.2)	34 (0.1)	36 (0.1)	22 (0.1)
GLP-1 analogues and DPP-4 inhibitors	14 (<0.1)	105 (0.4)	221 (0.8)	226 (0.8)	165 (0.6)
Glinides	1,209 (3.9)	1,078 (3.8)	1,319 (4.7)	1,377 (5.0)	1,320 (4.8)
Monotherapy Insulin (%)	**4,474 (14.3)**	**4,395 (15.4)**	**4,848 (17.1)**	**4,581 (16.7)**	**4,357 (15.7)**
Polytherapy (%)	**16,145 (51.7)**	**14,775 (51.6)**	**13,220 (46.8)**	**12,452 (45.4)**	**12,706 (45.8)**
Fixed combination	10,774 (34.5)	9,260 (32.4)	8,358 (29.6)	7,587 (27.7)	7,143 (25.7)
No-fixed combination	5,371 (17.2)	5,515 (19.3)	4,862 (17.2)	4,865 (17.7)	5,563 (20.0)
Dual oral therapy	3,094 (9.9)	3,027 (10.6)	2,587 (9.2)	2,569 (9.4)	2,979 (10.7)
Oral ADs plus insulin	2,281 (7.3)	2,495 (8.7)	2,281 (8.1)	2,303 (8.4)	2,592 (9.3)

0.001), while the proportion of patients treated with sulfonylurea dropped (from 11.0% in 2010 to 7.2% in 2014; p< 0.001). The proportion of patients treated with thiazolidinediones remains unchanged over the study period and slightly increased the proportion of users of GLP1 analogues and DPP-4 inhibitors (from <0.1 in 2010 to 0.6% in 2014; p value< 0.001).

An increase in the proportion of patients exposed to therapy with insulin alone was also observed over the years (from 14.3% in 2010 to 15.7% in 2014; p<0.001). AD pat-

Table 2. Utilization of drug class for cardiovascular prevention in diabetic subjects stratified by age group and calendar year.

	2010	**2011**	**2012**	**2013**	**2014**
	(n=31,210)	(n=28,622)	(n=28,271)	(n=27,430)	(n=27,772)
Drug class for cardiovascular prevention (%)	**27,276 (87.4)**	**25,332 (88.5)**	**24,406 (86.3)**	**24,007 (87.5)**	**24,944 (89.8)**
65-74 years	**14,952 (54.8)**	**14,456 (57.1)**	**14,517 (59.5)**	**14,712 (61.3)**	**15,492 (62.1)**
Antiplatelet drugs	823 (3.0)	610 (2.4)	656 (2.7)	647 (2.7)	581 (2.3)
RAS – acting agents	2,696 (9.9)	2,831 (11.2)	2,975 (12.2)	2,894 (12.0)	2,573 (10.3)
Lipid modifying agents	699 (2.6)	769 (3.0)	898 (3.7)	895 (3.7)	865 (3.5)
More than one	10,734 (39.3)	10,246 (40.4)	9,988 (40.9)	10,276 (42.8)	11,473 (46.0)
75-84 years	**10,188 (37.3)**	**9,210 (36.4)**	**8,522 (34.9)**	**8,100 (33.7)**	**8,204 (32.9)**
Antiplatelet drugs	774 (2.8)	598 (2.4)	593 (2.4)	523 (2.2)	490 (2.0)
RAS – acting agents	1,681 (6.2)	1,783 (7.0)	1,827 (7.5)	1,683 (7.0)	1,497 (6.0)
Lipid modifying agents	261 (1.0)	292 (1.1)	342 (1.4)	354 (1.5)	319 (1.3)
More than one	7,472 (27.4)	6,537 (25.8)	5,760 (23.6)	5,540 (23.1)	5,898 (23.6)
≥85 years	**2,136 (7.8)**	**1,666 (6.6)**	**1,367 (5.6)**	**1,195 (5.0)**	**1,248 (5.0)**
Antiplatelet drugs	230 (0.8)	175 (0.7)	168 (0.7)	164 (0.7)	153 (0.6)
RAS – acting agents	460 (1.7)	396 (1.6)	354 (1.4)	313 (1.3)	297 (1.2)
Lipid modifying agents	37 (0.1)	43 (0.2)	45 (0.2)	48 (0.2)	53 (0.2)
More than one	1,409 (5.2)	1,052 (4.1)	800 (3.3)	670 (2.8)	745 (3.0)

tern stratified by drug class, age group and calendar year are reported in electronic supplementary material Table **S1**.

Referring to Polytherapy, the proportion of the elderly diabetic patients decreases (from 51.7 in 2010 to 45.8 in 2014; $p<0.001$). Among patients on combination therapy the percentage treated with a fixed combination of ADs dropped steadily (from 34.5% in 2010 to 25.7% in 2014; $p<0.001$) while there was an increase in the proportion of patients using no-fixed combination (from 17.2 % in 2010 to 20.0% in 2014; $p< 0.001$). The proportion of patients treated with dual oral therapy and oral ADs plus insulin increases (from 9.9% in 2010 to 10.7% in 2014; $p<0.001$) (from 7.3 in 2010 to 9.3 in 2014; $p<0.001$) respectively.

Overall about 90% of elderly diabetic patients are treated with drugs for cardiovascular prevention. In particular, the proportion of elderly diabetic patients received drugs for cardiovascular prevention was 87.4 in 2010 and 89.8 in 2014 (Table **2**). Among these 62.1% belong to 65-74 age group. The largest increase during the study period occurred in subjects aged 65-74 years (54.8% in 2010 vs 62.1% in 2014). On the other hand, the trend was downward both in the 75-84 and in ≥85 age groups (37.3/ in 2010 vs 32.9% in 2014 and 7.8% in 2010 vs 5.0% in 2014 respectively). Overall more than 60% of subjects are treated with more than one drug class for cardiovascular prevention, the percentage decrease with age group (46.0%; 23.6%; 3.0% respectively).

3.2. Cost Analysis

The per patient yearly drug costs were 2,349 €: 670.2€ (28.5%) for ADs therapy and 1,679.4€ (71.5%) for other treatments. Detailed drug costs are shown in (Fig. **2**).

Referring to ADs therapy, the insulin costs was 412€, hypoglycemic drugs cost was 139.4€ and fixed association cost was 118.1 €.

Referring to other treatments, 375.3€ (15.9%) were for cardiovascular prevention drugs while 1,304.2€ (55.5%) was for all other drugs.

4. DISCUSSION

This retrospective, population-based drug utilization study generates information on the recent trend of ADs prescription behavior in the elderly over the last five years providing up-to-date data. A decrease in the prevalence of ADs use in older adults was observed from 2010 to 2014 (22.0% in 2010; 17.5% in 2014). These results are in line with the trend observed in the same population for the years 2009-2012 [18]. Our analysis points out that this decrease was primarily due to a reduction in prevalent ADs use in the 75 year and older age groups. Prevalence is related to duration of the disease and the incidence of new users. The observed decrease in prevalence could be related to a concurrent decline in incidence rates. This trend has been observed in our study in contrast with national and international forecasting for increases in incidence of new users of ADs. This issue

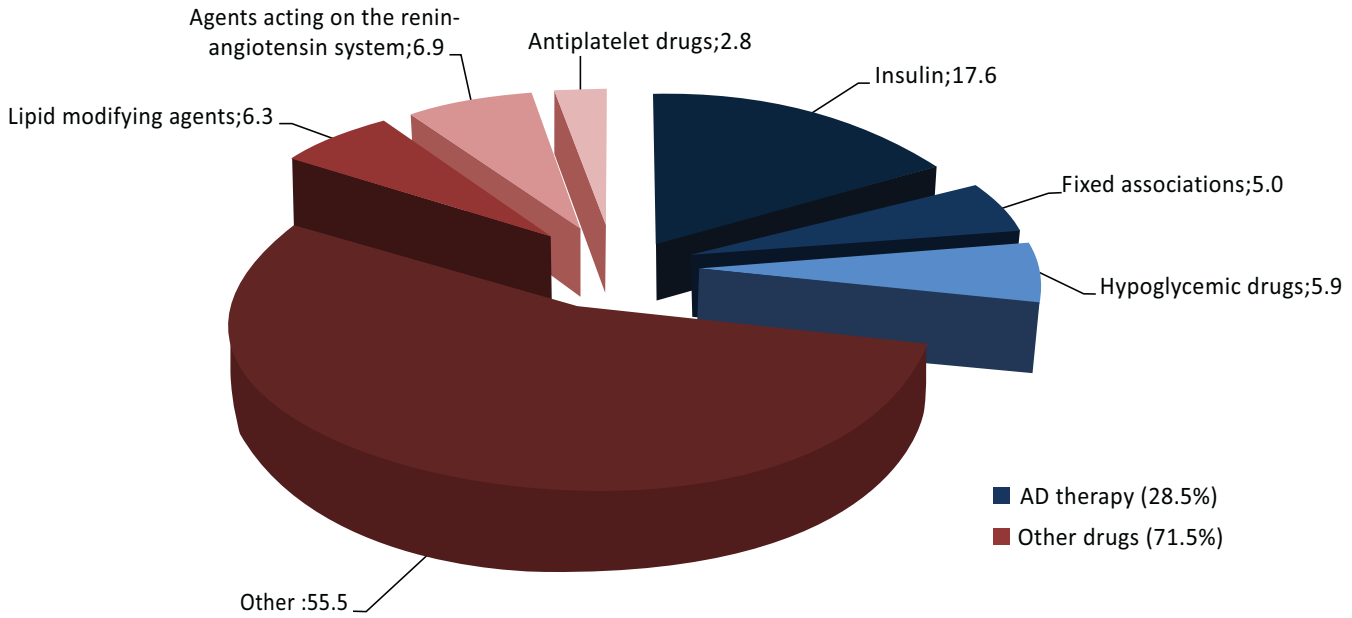

Fig. (2). Costs for AD therapy and cost for other treatment.

has already been discussed in the study conducted by Rafaniello *et al.* that highlighted the hypothesis that, due to the low-cost of off-patent ADs (*i.e.* metformin, sulfonylureas), part of the subjects is paying out-of-pocket, thus escaping the databases [18]. For instance, we analyzed data from the IMS Health regional system to evaluate differences between sell-in and sell-out figures in the retail channel as a proxy of drugs dispensed by pharmacies but not reimbursed by NHS. For metformin and sulfonylureas, less than 10% of total DDDs (Defined Daily Doses) of the retail channel were paid directly by patients. While this is an issue to be considered, it is likely to be of little influence on observed time trends. Other possible drivers for this trend could be institutionalization of patients as well as switch to an exclusively lifestyle treatment. A similar trend in incidence of ADs use in patients aged 70 years and older was observed in a nationwide prescription database study carried out in Norway over 2006-2011 [19].

The most used glucose lowering drug was found to be metformin. This is in line with international guidelines considering metformin as the first-line therapy in type-2 diabetes [20]. Its low risk for hypoglycemia may be beneficial in older adults and its low cost may make it an efficient choice in older adults who are functional [4]. An increased use of this drug in monotherapy was observed over the years (from 18.2% in 2010 to 23.7% in 2014). Analyzing use of metformin by age group we found that the major of users belong to 65-74 age group. This could be explained with the recent concerns about use metformin in frail patients, especially those with impaired renal function [4]. On the other hand we detected a drop in the proportion of subjects treated with sulfonylureas (from 11.0% in 2010 to 7.2% in 2014) this is in line with recommendation to avoid the use of these drugs in the elderly for the greater risk of hypoglycemic episodes. This trend is in line with studies conducted in Italy and other European countries [14, 18, 19] on the overall population and in Northern Italy on the elderly [11] even if on a different time frame.

Since 2008 incretin-based therapies have being available on the Italian market. Regarding this newer ADs, although DPP-4 inhibitors appear to impart little risk of hypoglycemia, less than 1% of the elderly diabetic patients in our population study were treated with these drugs. The observed underutilization may be due to lack of information of long-term safety in real-life of these agents and the higher cost. In Italy incretins reimbursement from NHS was subject to enrollment of patients into a web-based system to monitor the appropriateness of use, safety profile, and effectiveness (Italian Medicine Agency Monitoring Registry). A recent study conducted by Nicolucci *et al.* reporting the results of the first 30-months monitoring, showed that in the real world Italian setting, prescriptions of incretins have been made in many cases outside the regulatory limits. Nevertheless, when appropriately utilized, incretins may grant results at least in line with pivotal trials [21].

As expected, treatment with insulin alone regards a significant percentage of elderly patients and increases over the years. Furthermore percentage of patients treated with insulin alone increases in older age groups.

The present study also assessed prescription behavior of cardiovascular prevention drugs in the elderly diabetic patients. As expected, in line with recommended guidelines, about 90% of the elderly diabetic population is in treatment with cardiovascular prevention drugs with an upward trend (87.4 in 2010; 89.8 in 2014). These results confirm the trend showed by Baviera *et al.* over the years 2000-2010 reporting that the proportion of elderly diabetic subjects taking recommended drugs for cardiovascular prevention increased over the years [11].

Our analysis showed that a higher proportion of subject treated with more than one drug for cardiovascular preven-

tion was observed in subjects aged 65-74 years compared to those in the ≥85 age group. This could be explained by lower functional status, polypharmacy and higher risk of drug interactions in these patients. In particular we observed a less propensity to prescribe statins in diabetic patients aged ≥85 years. This is in line with recent consensus document suggesting to limit statin prescriptions in older diabetic patients only when life expectancy is at least equal to the timeframe of primary or secondary prevention trials [4].

We also estimated pharmaceutical cost in elderly diabetic patients. Our data showed that 28.5% of drug costs regard ADs therapy while about 70% is related to other drugs. From an economic perspective this could be explained by the large amount of drugs required by diabetic comorbidities and complications. Our data showed that the yearly per patient cost in 2014 was 2,349 €. These figures are higher than those reported in other studies [22, 23]. This could be partly explained by the fact that we analyzed exclusively elderly patients. It is well known that elderly people are more subject to multimorbidity. This is especially true in diabetic patients.

The analysis of pharmacy records, although being a powerful tool, might lead to some underestimations: as previously reported we are unable to detect drug use in nursing homes and we couldn't capture patients who decided to buy directly low-cost drugs. Furthermore we are unable to estimate possible switch to non-pharmaceutical approaches. Other limitations of our study are the lack of information regarding biochemical parameters even if this is a common limitation of drug utilization studies carried out by administrative databases.

CONCLUSION

Our study highlighted a decrease in prevalence and incidence of ADs use over 2010-2014 in Southern Italy. Specific trend in drug utilization patterns showed an increased attention towards treatment recommendations in older adults. Safety concerns in the elderly regarding polypharmacy such as presence of multimorbidity and hypoglycemic episodes could also have contributed to such a trend. Our study provides up-to-date information about ADs use patterns in the elderly population that is of particular interest in an historical moment in which demographical trends indicate constant increase in the numbers of elderly population.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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SUPPLEMENTARY MATERIAL

Supplementary material is available on the publishers Web site along with the published article.

REFERENCES

[1] International Diabetes Federation, 2013. Available from: http: //www.idf.org/diabetesatlas. [cited: 2nd March 2015]

[2] Global status report on non communicable diseases 2014. Geneva, World Health Organization, 2012.

[3] ISTAT, The National Institute of Statistics. Annuario statistico italiano 2013. Available from: http: //www.istat.it/it/files/2013/12/ASI_2013.pdf. [cited: 2nd March 2015]

[4] Kirkman S, Briscoe VJ, Clark N, *et al*. Diabetes in older adults: a consensus report. J Am Geriatr Soc 2012; 60(12): 2342-2356.

[5] Ligthelm RJ, Kaiser M, Vora J, *et al*. Insulin use in elderly adults: risk of hypoglycemia and strategies for care. J Am Geriatr Soc 2012; 60: 1564.

[6] Sinclair A, Morley JE, Rodriguez-Manas L, *et al*. Diabetes mellitus in older people: position statement on behalf of the International Association of Gerontology and Geriatrics (IAGG), the European Diabetes Working Party for Older People (EDWPOP), and the International Task Force of Experts in Diabetes. J Am Med Dir Assoc 2012; 13: 497-502.

[7] Inzucchi SE, Bergenstal RM, Buse JB, *et al*. Management of hyperglycaemia in type 2 diabetes: a patient-centered approach. Position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) Diabetologia 2012; 55: 1577-1596.

[8] Kanavos P, van den Aardweg S, Schurer W Diabetes expenditure, burden of disease and management in 5 EU countries. LSE Health and Social Care 2012. Available from: http: //www.lse.ac.uk/LSE HealthAndSocialCare/research/LSEHealth/MTRG/LSEDiabetes Report26Jan2012.pdf. [cited: 2nd March 2015]

[9] Ayanian JZ. Using administrative data to assess health care outcomes. Eur Heart J 1999, 20.23: 1689-1691.

[10] Schneeweiss S, Avorn J A review of uses of healthcare utilization databases for epidemiologic research on therapeutics. J Clin Epidemiol 2005; 58: 323-37.

[11] Baviera M, Cortesi L, Tettamanti M, *et al*. Changes in prescribing patterns and clinical outcomes in elderly diabetic patients in 2000 and 2010: analysis of a large Italian population-based study. Eur J Clin Pharmacol 2014; 70: 965-974.

[12] Baviera M, Monesi L, Marzona, I, *et al*. Trends in drug prescriptions to diabetic patients from 2000 to 2008 in Italy's Lombardy Region: a large population-based study. Diabetes Research and Clinical Practice 2011; 93(1), 123-130.

[13] Boyc KS, Yurgin N, Lage MJ. Trends in the prescription of antidiabetic medications in France: evidence from primary care physicians. Advances in Therapy 2007; 24(4), 803-813.

[14] Filion KB, Joseph L, Boivin JF, *et al*. Trends in the prescription of anti-diabetic medications in the United Kingdom: a population-based analysis. Pharmacoepidemiology and Drug Safety 2009; 18(10), 973-976.

[15] Wong HK, Ong KL, Cheung CL, *et al*. Utilization of glucose, blood pressure, and lipid lowering medications among people with type II diabetes in the United States, 1999–2010. Annals Epidemiol 2014; 24(7), 516-521.

[16] World Health Organization Collaborating Centre for Drug Statistics Methodology. Available from: http: //www.whocc.no/atc_ddd_index/.Updated December 19, 2014. [cited: 2nd March 2015]

[17] De Berardis G, D'Ettorre A, Graziano G, *et al*. The burden of hospitalization related to diabetes mellitus: a population-based study. Nutr Metab Cardiovasc Dis 2012; 22, 605-612.

[18] Rafaniello C, Arcoraci V, Ferrajolo C, *et al*. Trends in the prescription of antidiabetic medications from 2009 to 2012 in a general practice of Southern Italy: A population-based study. Diabetes Res Clin Pract 2015 Feb 3. Epub ahead of print

[19] Strøm H, Selmer R, Birkeland KI, *et al*. No increase in new users of blood glucose-lowering drugs in Norway 2006-2011: a nationwide prescription database study. BMC Public Health 2014; 14(1), 520.

[20] American Diabetes Association Standard of medical care in diabetes-2014. Diabetes Care 2014; 37(Suppl1): S14-80.

[21] Montilla S, Marchesini G, Sammarco A, *et al*. Drug utilization, safety, and effectiveness of exenatide, sitagliptin, and vildagliptin for type 2 diabetes in the real world: Data from the Italian AIFA

Anti-diabetics Monitoring Registry. Nutr Metab Cardiovasc Dis 2014; 24(12), 1346-1353.

[22] Marchesini G, Forlani G, Rossi E, Berti, *et al*. The direct economic cost of pharmacologically-treated diabetes in Italy-2006. The ARNO observatory. Nutr Metab Cardiovasc Dis 2011; 21(5), 339-346.

[23] Colombo GL, Rossi E, De Rosa M, *et al*. Antidiabetic therapy in real practice: indicators for adherence and treatment cost. Patient Prefer Adherence 2012; 6: 653-61.

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