HOW HEALTHY IS COMMUNITY-DWELLING ELDERLY POPULATION? RESULTS FROM SOUTHERN ITALY.

Francesca Guerriero¹, Valentina Orlando¹, Daniele Ugo Tari², Annalisa Di Giorgio², Antonio Cittadini³, Gianluca Trifirò⁴, Enrica Menditto¹.
¹ CIRFF, Center of Pharmacoeconomics, Federico II University of Naples, Italy; ² Caserta Local Health Unit, Caserta, Italy; ³ Department of Translational Medical Science, Federico II University of Naples, Italy; ⁴ Department of Clinical and Experimental Medicine, University of Messina, Italy;

Address for Correspondence
Enrica Menditto, PharmD, PhD
CIRFF, Center of Pharmacoeconomics,
University of Naples Federico II, Italy
Via Domenico Montesano 49, 80131 Naples
Tel. +39 081 678660 Fax. +39 081 678658
e-mail: enrica.menditto@unina.it

Abstract - PURPOSE To explore the frequency of polypharmacy, functional and cognitive capacity among the elderly in Southern Italy. METHODS Population-based retrospective cross-sectional study. Information were retrieved from electronic-geriatric-forms matched by record-linkage to outpatient pharmacy-records. The following domains were collected from geriatric forms: BMI, cognitive capacity (SPMSQ), functional status (Barthel-index), mobility, living condition. Polypharmacy status was categorized as non-polypharmacy (0-4), polypharmacy (5-9) and excessive-polypharmacy (≥10). Prevalence of all variables were stratified by age and polypharmacy group. RESULTS 88,878 old people received a geriatric assessment in the years 2013-2014. Mean age was 74.8 (±7.3) years, 56.6% females. Proportion of elderly in excessive-polypharmacy increased with age (18.9% in 65-75 age-group; 27.9% in >85). Referring to cognitive capacity, the proportion of lucid patients decreased with age (from 94.3% to 58.1%), while confused patient increased with age (from 4.7% to 30.9%). Proportion of subjects with a decline in cognitive status, functional status and mobility increased in polypharmacy and excessive polypharmacy group. CONCLUSION Polypharmacy is common in people aged 65 years and older with difficulties in activities of daily living and impaired cognition. Furthermore, its prevalence raises with increasing age. Preventive strategies such as optimization of drug regimen should be performed routinely to reduce risk of adverse-health-events.

Key words: Polypharmacy, elderly, administrative databases, frailty, geriatric assessment.

I. INTRODUCTION

Polypharmacy is one of the most relevant health-related issues in elderly population. Drug treatment may influence both positively and negatively elderly health status. Polypharmacy increases the risk of inappropriate prescribing, drug–drug and drug–disease interactions, and hence the risk of adverse health events including falls, functional impairment, and hospitalization [1-2]. Nowadays, different sets of indicators have been developed in order to provide a measure of prescribing performance and, hence, to assess quality of care in older people [3-4]. However, this may not be sufficient for frail elderly who have several problems related to the functional status, mobility, cognitive status and living condition. In these patients, the most appropriate approach to re-evaluate the drug therapy should combine evidence-based data with information gathered from a multidimensional geriatric assessment. Recently, Multidimensional Assessment Schedule (SVaMA) was developed to effectively explore multiple domains of health, as multidimensional and multidisciplinary tool of choice to determine the prognosis of the functionally compromised and frail elder subject [5]. SVaMa includes information on functional (activities of daily living, ADL, and Instrumental ADL), cognitive status (Short Portable Mental Status Questionnaire, nutrition (Mini Nutritional Assessment), comorbidities (Cumulative Illness Rating Scale), medications and co-habitation status (i.e. living alone or with someone).

In 2012 the European Commission launched an initiative called ‘European Innovation Partnership on Active and Healthy Aging’ (EIP-AHA) with the purpose of stimulating research and innovation in EU and increase understanding around frailty and the prevention, early diagnosis and management of functional decline, both physical and cognitive, in older people [6]. Since 2013 Campania Regional Health-Care System introduced electronic geriatric forms available to general practitioners to perform a multidimensional assessment on community-dwelling older patients. The aim of this population-based retrospective study was to explore the frequency of polypharmacy and the functional status of
older outpatients from Caserta Local Health Unit (LHU), Southern Italy. 

II. METHODS

Study design: we designed a retrospective cross-sectional study.

Setting: electronic geriatric forms from the Local Health Authority (LHU) of Caserta in the Campania Region (Southern Italy), covering a population of about 1,000,000 inhabitants.

Data sources

The data used for this study were obtained from electronic geriatric forms in the SANIARP Portal, a web platform available to general practitioners (GPs) of LHU Caserta, collected from January 1, 2013 to December 31, 2014 (study period). Electronic geriatric card was a short version of SVaMA. The SVaMA is the officially recommended assessment schedule used by the health personnel of the National Health Care System to perform a multidimensional assessment on community-dwelling older persons or nursing home residents to establish accessibility to some health care resources [5]. From the electronic geriatric cards the following information were obtained: Body Mass Index (BMI); cognitive capacity (Short Portable mental Status Questionnaire SPMSQ); functional status (Barthel index); mobility (Barthel index), living condition and senses and communication skills (language understanding, language production, hearing and sight). This data source was matched, by record-linkage analysis to outpatient pharmacy records and the civil registry in order to collect pharmaceutical information (number of drugs) and demographic information (i.e. age, gender, date of death or emigration) of all residents covered by the LHU. All information was linked through a unique and anonymous personal identification code. As 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 [7-8].

Study population

The study population consisted of all subjects of 65 years of age or older who had at least one geriatric assessment form during the study period (January, 1 2013 to December, 31 2014). We considered the latest form for patients with more than one geriatric assessment. Age was calculated at the date of geriatric assessment was carried out.

Variables

Short Portable mental Status Questionnaire SPMSQ is a short questionnaire that is used to screen older adults for dementia signs and other neurologically based deficits and to determine the degree of impairment [9].

Functional status was evaluate by Barthel scale or Barthel Index. This is an ordinal scale used to measure performance in activities of daily living (ADL). Each performance item is rated on this scale with given number of points assigned to each level or ranking [10]. The rating scale autonomy in basic activities of daily living proposal by Katz et al. is one of the tools used in the evaluation of geriatric patient [11]. The tool evaluates accurately basic tasks: to bathe, dressing up, toilet, move, urinary and fecal incontinence, feed themselves. The index measures the different abilities of the patient in taking care of themselves and each is measured in terms of what the patient is functional or not. To each of the items goes given a score dichotomous in which: 0 = dependent; 1 = independent

Mobility was assessed by four tasks: Transfer bed / chair, walk, use of wheelchair, use the stairs. Each performance item is rated on the Barthel index. To each of the items goes given a score dichotomous in which: 1 = moves by self’s; 2= assisted [12].

Living condition was determined on the basis of living condition at the time of examination. Living status was coded for those participants living alone or with someone. (Alone = 1; with someone = 2) [13].

Language (understanding and production) was categorized into 3 groups: Normal, Understand only simple sentences or disorder of language, doesn't understand doesn't speak respectively.

Hearing and Sight was categorized into 4 groups: Normal, Serious deficit, Serious deficit incurable and finally deafness or blindness.

Polypharmacy was defined as a three-class variable: excessive polypharmacy defined as the use of ten or more drugs; polypharmacy as the use of five to nine drugs; non-polypharmacy as the use of four or less drugs concomitantly [14]. Prevalence of all variables were stratified by age-group (65-75 years; 75-84 years; >85 years) and polypharmacy group (non-polypharmacy; polypharmacy; excessive polypharmacy).

Statistical methods

Characteristics of the study population were analysed using descriptive statistics: quantitative variables were described by means and standard deviations while categorical variables were described by counts and percentages. In the case of categorical variables, cross-tabulations with chi-square tests were used for comparing the differences between age group and polypharmacy group. All analyses were performed using SPSS software version 17.1 for Windows (SPSS Inc., Chicago, IL, USA). Statistically significance was set up at p-value < 0.05.
III. RESULTS

A total of about 90,000 elderly were analysed in this study. This amount represents more than 60% of the total elderly population in LHU Caserta. The mean patient age at the index date was 74.8 (±7.3) years with 53.7% of the patients between 65-74 years of age, 34.6% of the patients between 75-84 years of age, 11.7% of patients 85 of age or more. Baseline characteristics of the study population are shown in Table 1. 56.6% of patients were women. The mean BMI of patients was 27.0 (± 4.0). In particular, percentage of overweight elderly decreased from 43.0% in subjects aged 65-74 years to 35.8% in subjects aged 85 or more. Proportion of elderly in polypharmacy increased from 42.7% in subject aged 65-74 years to 45.4% in subject aged 85 or more. More in detail, with regard to excessive polypharmacy, there was a slightly increase from 18.9% in subject aged 65-74 years to 27.9% in subject aged 85 or more. Referring to cognitive capacity, the proportion of confused patients increased from 4.7% in patients aged 65-74 years to 30.9% in patients aged 85 or more. The percentage of very confused patients increased in polypharmacy and excessive polypharmacy group. Referring to SPMSQ score, the percentage of patients dependent in cognitive status, functional status and mobility as shown in Table 2. Proportion of subjects with a decline in cognitive status, functional status and mobility increased in polypharmacy and excessive polypharmacy group. Referring to SPMSQ score, the percentage of confused patients increased from 8.0% in non-polypharmacy group to 15.6% in excessive polypharmacy group. The same trend in proportion occurred for functional status and mobility. In particular, the proportion of elderly dependents increased in all three groups of polytherapy (5.4%; 9.1%; 17.0% respectively). The percentage of elderly assisted increased from 8.3% in non-polypharmacy group to 25.6% in excessive polypharmacy group.

### Table 1. Baseline characteristics of the study population

| Variables               | Age groups, N (%) | Total, N (%) |
|-------------------------|-------------------|--------------|
|                         | 65-74 years       | 75-84 years  | ≥85 years    | p        |
|                         | (53.7)            | (34.6)       | (11.7)       | (100.0)  |
| Gender                  |                   |              |              | <0.001   |
| Female                  | 25,292 (97.1)     | 17,962 (92.9)| 7,057 (87.5)| 50,311   |
| Male                    | 22,449 (97.4)     | 12,815 (91.4)| 3,303 (90.3)| 38,567   |
| BMI                     |                   |              |              | <0.001   |
| Mean (±SD)              | 27.0 (±4.0)       |              |              |          |
| Underweight (BMI <18.49)| 66 (0.1)          | 59 (0.2)     | 43 (0.4)     |          |
| Normal (BMI 18.50 ≤24.99)| 15,385 (9.1)     | 9,998 (8.2)  | 4,097 (8.2)  | 29,480   |
| Overweight (BMI ≥25)| 20,529 (10.3)     | 12,655 (11.6)| 3,714 (11.2)| 36,898   |
| Obese (BMI ≥30)         | 8,610 (0.9)       | 5,957 (1.1)  | 1,873 (3.3)  | 16,440   |
| Number of drugs         |                   |              |              | <0.001   |
| Non-polypharmacy (1-4 drugs) | 18,308 (27.0)   | 7,903 (24.0)| 2,764 (22.0)| 28,975   |
| Polypharmacy (5-9 drugs)| 20,405 (32.2)     | 14,166 (39.5)| 4,702 (36.8)| 39,273   |
| Excessive (≥10 drugs)   | 9,028 (14.8)      | 8,708 (24.0)| 2,894 (22.0)| 20,630   |
| Number of drugs         |                   |              |              | <0.001   |
| Functional status (Barthel index) | 45,041 (27.0) | 25,213 (22.0)| 6,022 (22.0)| 76,276   |
| SPMSQ score             |                   |              |              | <0.001   |
| Lucid                   | 45,041 (27.0)     | 25,213 (22.0)| 6,022 (22.0)| 76,276   |
| Confused (4-8)          | 2,252 (0.1)       | 4,464 (0.3)  | 3,199 (0.4)  | 9,915    |
| Very confused (9-10)    | 448 (0.2)         | 1,100 (0.2)  | 1,139 (0.3)  | 2,687    |
| Functional status       |                   |              |              | <0.001   |
| Independent (0-14)      | 46,373 (27.7)     | 27,271 (19.3)| 6,609 (19.3)| 80,253   |
| Assisted (15-49)        | 2,516 (0.1)       | 5,761 (0.4)  | 5,042 (0.4)  | 13,319   |
| Mobility (Barthel Index)|                   |              |              | <0.001   |
| Moves by itself (0-14)  | 45,225 (25.0)     | 25,016 (16.0)| 5,318 (16.0)| 75,559   |
| Assisted (15-49)        | 2,516 (0.1)       | 5,761 (0.4)  | 5,042 (0.4)  | 13,319   |
| Language (Understanding)|                   |              |              | <0.001   |
| Normal                  | 46,477 (28.1)     | 28,120 (19.1)| 7,946 (17.9)| 82,543   |
| Understand only simple  | 1,000 (0.1)       | 2,055 (0.1)  | 1,819 (0.1)  | 4,874    |
| sentences               |                   |              |              |          |
| Doesn’t understand       | 225 (0.1)         | 815 (0.1)    | 595 (0.1)    | 1,461    |
Language (production)  

| Normal | 46,114 | 27,721 | 7,774 | 81,609 |
|--------|--------|--------|--------|--------|
|        | (96.6) | (90.1) | (75.0) | (91.8) |
| Disorder of language | 1,479 | 2,759 | 2,319 | 6,557 |
|        | (3.1) | (9.9) | (22.4) | (7.4) |
| Doesn't speak | 148 | 297 | 267 | 712 |
|        | (0.3) | (1.0) | (2.6) | (0.8) |

Hearing  

| Normal | 38,731 | 18,528 | 3,443 | 60,702 |
|--------|--------|--------|--------|--------|
|        | (81.1) | (60.2) | (33.2) | (68.3) |
| Serious deficit | 8,513 | 11,338 | 6,042 | 25,893 |
|        | (17.8) | (36.8) | (58.3) | (29.1) |
| Serious deficit incurable | 360 | 726 | 702 | 1,788 |
|        | (0.8) | (2.4) | (6.8) | (2.0) |
| Deafness | 137 | 185 | 173 | 495 |
|        | (0.3) | (0.6) | (1.7) | (0.6) |

Sight  

| Normal | 33,344 | 16,357 | 3,352 | 53,053 |
|--------|--------|--------|--------|--------|
|        | (69.8) | (53.1) | (32.4) | (59.7) |
| Serious deficit | 13,931 | 13,735 | 6,445 | 34,111 |
|        | (29.2) | (44.6) | (62.2) | (38.4) |
| Serious deficit incurable | 384 | 583 | 475 | 1,442 |
|        | (0.8) | (1.9) | (4.6) | (1.6) |
| Blindness | 82 | 102 | 88 | 272 |
|        | (0.2) | (0.3) | (0.8) | (0.3) |

* SPMSQ: Short Portable Mental Status Questionnaire

| Variables | Polypharmacy group, N (%) | Total, N (%) | p |
|-----------|---------------------------|--------------|---|
|           | 0-4 drugs | 5-9 drugs | >10 drugs | 88,878 | 100.0 |
| SPMSQ* score | 28,975 | 39,273 | 20,650 |
| Lucid (0-3) | 26,003 | 33,769 | 16,504 | 76,276 |
|        | (89.7) | (86.0) | (80.0) | (85.8) |
| Confused (4-8) | 2,317 | 4,376 | 3,222 | 9,915 |
|        | (8.0) | (11.1) | (15.6) | (11.2) |
| Very confused (9-10) | 655 | 1,128 | 904,0 | 2,687 |
| Functional status (Barthel Index) | 28 | 42 | (2.3) | (2.9) | (4.4) | (3.0) |
| Independent (0-14) | 27,422 | 35,705 | 17,126 | 80,253 |
|        | (94.6) | (90.9) | (83.0) | (90.3) |
| Dependent (15-49) | 1,553 | 3,568 | 3,504 | 8,625 |
|        | (5.4) | (9.1) | (17.0) | (9.7) |
| Mobility (Barthel Index) | 2,415 | 5,624 | 5,280 | 13,319 |
| Moves by itself (0-14) | 26,560 | 33,649 | 15,350 | 75,559 |
|        | (91.7) | (85.7) | (74.4) | (85.0) |
| Assisted (15-49) | 83 | 143 | 25.6 | (15.0) |

* SPMSQ: Short Portable Mental Status Questionnaire

IV. DISCUSSION

This population-based study investigated the frailty status, assessed through multidimensional evaluation of different domains, in a large population of elderly outpatients by using electronic geriatric forms in the SANIARP portal, a web platform available to GPs of LHU Caserta.

Overall, the study showed that polypharmacy status was very frequent in our population, in detail about 44% of elderly patients received between five and nine drugs and 23.2% took more than ten drugs. While the data regarding polypharmacy (5-9 drugs) are in line with findings from Italian National Agency (AIFA) [15], we found a higher percentage of elderly in excessive polypharmacy 23% vs 11%. This could be due to the different data sources as we analysed not only drugs dispensed by community pharmacies but also drugs dispensed directly by hospital pharmacies. Furthermore underlying population and observation period of the analysis was different. Our findings are clinically relevant insofar as polypharmacy is associated with a higher risk of poor health outcomes such as falls, avoidable hospitalization [16-18]. Furthermore the excessive polypharmacy is associated with decline in nutritional status, functional ability and cognitive capacity in elderly persons aged 75 years and older [19]. Apart from polytherapy we also analysed decline in cognitive status, functional status and mobility. Our findings showed that subjects aged 85 or more 30.9% were confused, 36.2% were dependent, 48.7% were assisted and about 20% had a disorder of language. All these conditions may affect aspects related to therapeutic appropriateness followed by the patient: our findings showed that about 28% of highest age category received more than nine drugs. A recent study conducted by Herr et al. estimated that each additional drug prescribed was associated with an increased risk of being pre-fail or dependent, with adjusted OR 1.12 (95% CI 1.07-1.17), 1.20 (95% CI 1.12-1.128) and 1.26 (95% CI 1.17-1.35), respectively [20].

The study evaluated only polypharmacy status but not wise use of drug therapy so we cannot state whether the 27% of oldest old in polypharmacy is treated appropriately or not. However it must be kept into account that the coexistence of clinical complexity along with the lack of evidence on drug effectiveness from clinical trials in very old persons, does not provide physicians with knowledge on outcomes associated with an aggressive pharmacological treatment.

In view of this evidence, preventive strategies should be devised for old people with regard to physical activity, cognitive status and management of chronic diseases. The optimization of polypharmacy is part of these actions. Different approaches to reduce unnecessary medication use in elderly have been considered, involving pharmacists or geriatricians, using implicit or explicit criteria. Nevertheless, research is still needed to determine the most efficient strategies [21-22].

It is important to outline that there is a lack of consideration of the frail status in therapeutic guidelines although some age-related conditions may have an impact of late-life influencing, such as frailty [23].

Frailty in older people reflects a nonspecific state of vulnerability and a multisystem physiological change with increased risk for adverse health outcomes in older age [24]. In fact, frailty is acknowledged to be a multidimensional concept associated with a greater risk for adverse health-related outcomes such as falls, disability, hospitalization, permanence institutionalization
and death [25]. Our study was limited to describe several domains that can influence frailty status. We did not define a score to assess this aspect. In fact available information are only a part of the complete SvaMa. However we described some of the conditions that should be considered in the evaluation and revision of therapy in elderly patients.

It would be interesting to define frailty scores from our data in order to achieve a better use of patient information. The most recent evidences highlighted how it is possible to calculate, on the basis of validated algorithms, from SVAMA the Multidimensional Prognostic Index (MPI) able to predict the risk of mortality. The clear advantage of this instrument can result in a significant chance to reduce mortality, functional disability and cognitive impairment of older subjects, according to the most recent evidence in clinical geriatric practice [26-27].

The strength of our study is that it was possible to match data coming from different sources (administrative database and electronic geriatric cards in the SANIARP Portal) at single patient level. In this way, we were able to collect information about the functional status, cognitive status and mobility according to drug prescription records, while keeping into account relevant personal details such as sex and age. On the other hand, information about the type of drugs taken by elderly patients and the presence of comorbidities were not investigated as the aim of this study was evaluate level of polypharmacy and excessive polypharmacy according to other domains relevant in the evaluation of drug therapy in the elderly such as functional, cognitive and mobility status. The present initiative is part of the strategy carried out by the EIP-AHA A1 Action Group on adherence and provides preliminary data that might be useful for more focused interventions. Moreover it can represent a point of synergy with EIP-AHA A3 Action Group on frailty as polypharmacy has also great relevance in assessment of vulnerability of elderly patients.

V. CONCLUSION

Our study highlighted that polypharmacy is more frequent in older patients with a decline in cognitive status, functional status and mobility. All these conditions, associated with polypharmacy regimen can influence frailty status and can affect treatment outcomes with a greater risk for adverse health-related outcomes. Our findings emphasize how important are preventive strategies such as optimization of drug regimen for a better and safer management of elderly patients.

ACKNOWLEDGMENT

We thank Salvatore Riegler and Luigi De Luca from CIRFF for assistance with data acquisition and data mining support.

REFERENCES

[1] Bradley MC, Motterlini N, Padmanabhan S, Cahir C, Williams T, Fahe T, Hugheset C, M. Potentially inappropriate prescribing among older people in the United Kingdom. BMC Geriatr 2014; 14: 72.

[2] Wallace E, Sturt E, Vaughan N, Bennett K, Fahey T, Smith SM. Risk prediction models to predict emergency hospital admission in community-dwelling adults: a systematic review. Med Care 2014; 52(8): 751–765.

[3] O’Mahony D, O’Sullivan D, Byrne S, O’Connor MN, Ryan C, Gallagher P. Stop/p Start Criteria For Potentially Inappropriate Prescribing In Older People: Version 2. Age And Ageing 2014; A5145.

[4] Campanelli CM. American Geriatrics Society Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults: The American Geriatrics Society 2012 Beers Criteria Update Expert Panel. Journal of the American Geriatrics Society 2012; 60.4: 616.

[5] Plotto A, Gallina P, Fontana A, Sancarlo D, Bazzano S, Copetti M, Maggi S, Paroni G, Marcato F, Pellegrini F, Donato D, Ferrucci L. Development and validation of a Multidimensional Prognostic Index for mortality based on a standardized multidimensional assessment schedule (MPI-SVaMA) in community-dwelling older subjects. Journal of the American Medical Directors Association 2013; 14(4), 287-292.

[6] Action Plan on Prevention and early diagnosis of frailty and functional decline, both physical and cognitive, in older people. Available at https://ec.europa.eu/research/innovation-union/pdf/active-healthy-ageing/a3_action_plan.pdf Latest access October 2015.

[7] Orlando V, Guerriero F, Putignano D, Monetti VM, Tari DU, Farina G, Illario M, Iaccarino G, Menditto E. Prescription patterns of antidiabetic treatment in the elderly. Results from Southern Italy. Current diabetes reviews 2015; 12, 1-7.

[8] Ferrajolo C, Arcoraci V, Sullo MG, Rafanello C, Sportiello L, Ferrara R, Cannata A, Pagliaro C, Tari MG, Caputi AP, Rossi F, Trifiro G, Capuano A. Pattern of statin use in southern Italian primary care: can prescription databases be used for monitoring long-term adherence to the treatment? 2014; PLoS One 9(7).

[9] Pleifffer E. A Short Portable Mental Status Questionnaire for the Assessment of Organic Brain Deficit in Elderly Patients. Journal of the American Geriatrics Society, 1975; 23.10: 433-441.

[10] Sainsbury A, Seebass G, Bansal A, Young JB. Reliability of the Barthel Index when used with older people. Age and Ageing, 2005; 34.3: 228-232.

[11] Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. The Index of ADL: a standardized measure of biological and psychosocial function. JAMA 1963; 185: 914–919.

[12] Collin C, Wade DT, Davies S, Horne V. The Barthel ADL Index: a reliability study. Int Disabil Stud 1988; 10(2):61–63.

[13] Mulasso A, Roppolo M, Rabaglietti E. The Role Of Individual Characteristics And Physical Frailty On Health
Related Quality Of Life (HRQOL): A Cross Sectional Study Of Italian Community-Dwelling Older Adults. Archives of Gerontology and Geriatrics 2014; 59.3: 542-48.

[14] Hofer-Dückelmann C. Gender and polypharmacotherapy in the elderly: a clinical challenge. Sex and Gender Differences in Pharmacology. Springer Berlin Heidelberg 2012; 169-182.

[15] Onder G, Bonassi S, Abbatecola AM, Folino-Gallo P, Lapi F, Marchionni N, Pani L, Pecorelli S, Sancarlo D, ScuteriA, Trifiro G, Vitale C, Zuccaro SM, Bernabei R, Fint M; on behalf of the Geriatrics Working Group of the Italian Medicines Agency (AIFA). High prevalence of poor quality drug prescribing in older individuals: a nationwide report from the Italian Medicines Agency (AIFA).The Journals of Gerontology Series A: Biological Sciences and Medical Sciences 2014; 69.4: 430-437.

[16] Onder G, Petrovic M, Tangiisuran B., Meinardi MC, Markito-Notenboom WP, Somers A, Rajkumar C, Bernabei R, van der Cammen T JM.. Development and validation of a score to assess risk of adverse drug reactions among in-hospital patients 65 years or older: the GerontoNet ADR risk score. Arch Intern Med 2010; 170:1142–1148.

[17] Tinetti ME, Kumar C. The patient who falls: “It’s always a trade-off”. JAMA 2010; 303:258–266.

[18] Jyrkka J, Enlund H, Korhonen MJ, Sulkava R, Hartikainen S. Polypharmacy status as an indicator of mortality in an elderly population. Drugs Aging 2009; 26:1039–1048.

[19] Jyrkka J, Enlund H, Lavikainen P, Sulkava R, Hartikainen S. Association of polypharmacy with nutritional status, functional ability and cognitive capacity over a three-year period in an elderly population. Pharmacoepidemiol Drug Saf 2011; 20(5): 514–522.

[20] Herr M, Robine JM, Juliette P, Arvieu JJ, Ankri J. Polypharmacy and frailty: prevalence, relationship, and impact on mortality in a French sample of 2350 old people. Pharmacoepidemiology and drug safety 2015; 24:637-646.

[21] Tjia J, Velten SJ, Parsons C, Valluri S, Brienscher BA. Studies to reduce unnecessary medication use in frail older adults: a systematic review. Drugs Aging 2013; 30(5): 285–307.

[22] Patterson SM, Hughes C, Kerse N, Cardwell CR, Bradley MC. Interventions to improve the appropriate use of polypharmacy for older people. Cochrane Database Syst Rev 2012; 5.

[23] Poudel A, Hubbard RE, Nissen L, Mitchell C. Frailty: a key indicator to minimize inappropriate medication in older people. QJM 2013; 106(10): 969–975.

[24] Rodriguez-Mañas, Leocardio, Féart C, Mann G, Viña J, Chatterji S, Chodzko-Zajko W, Gonzalez-Colaço Harmand M, Bergman H, Carcaillon L, Nicholson C, Scuteri A, Sinclair A, Pelaez M, Van der Cammen T, Beland F, Bickenbach J, Delamarche P, Ferrucci L, Fried LP, Gutiérrez-Robledo LM, Rockwood K, Rodriguez Artalejo F, Serviddio G, Vega E. Searching for an operational definition of frailty: a Delphi method based consensus statement. The frailty operative definition-consensus conference project. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences 2013; 68.1: 62-67.

[25] Pilotto A, Sancarlo D, Daragiati J, Panza F. Perspective: the challenge of clinical decision-making for drug treatment in older people. The role of multidimensional assessment and prognosis. Frontiers in medicine 2014; 1.

[26] Sancarlo D, Pilotto A., Panza F, Copetti M., Longo MG, D'Ambrosio P, D’Onofrio G, Ferrucci L, Pilotto A. A Multidimensional Prognostic Index (MPI) based on a comprehensive geriatric assessment predicts short-and long-term all-cause mortality in older hospitalized patients with transient ischemic attack. Journal of neurology 2012; 259(4), 670-678.

[27] Pilotto A, Ferrucci L, Franceschi M, D'Ambrosio LP, Scarcelli C, Cascavilla L, Paris F, Placentinio G, Seripa D, Dallapiccola B, Leandro G. Development and validation of a multidimensional prognostic index for one-year mortality from comprehensive geriatric assessment in hospitalized older patients. Rejuvenation Research 2008; 11(1): 151-161.