

ANALYSIS OF RISK FACTORS FOR INAPPROPRIATE PRESCRIBING OF PSYCHOTROPIC DRUGS IN PRIMARY HEALTH CARE IN ELDERLY PATIENTS

Filip Mihajlovic¹, Filip Milutinovic², Djordje Djordjevic², Sara Mijailovic³, Sanja Vukojicic⁶ and Dragan Milovanovic^{4,5}

¹ University of Kragujevac, Faculty of Medical Sciences, Department of Pharmacy, Kragujevac, Serbia

² University Clinical Center Kragujevac, Clinic of Urology, Kragujevac, Serbia

³ Faculty of Medical Sciences Kragujevac, Department of Medical Statistics and Informatics, Kragujevac, Serbia

⁴ Faculty of Medical Sciences Kragujevac, Department of Pharmacology and Toxicology, Kragujevac, Serbia

⁵ University Clinical Center Kragujevac, Department of Clinical Pharmacology, Kragujevac, Serbia

⁶ Kragujevac Primary Health Care Center, Kragujevac, Serbia

Received: 31.03.2022.

Accepted: 17.04.2022.

Corresponding author:

Filip Mihajlovic

Faculty of Medical Sciences, 34 000 Kragujevac,
Svetozara Markovica Street 69

E-mail: f.mihajlovic@yahoo.com

Phone: +381693857063

ABBREVIATIONS

STOPP - Screening Tool of Older Person's potentially inappropriate Prescriptions

START - Screening Tool to Alert doctors to the Right Treatment

WHO - World Health Organization;

PIM - Potentially Inappropriate Medicines;

PPO - Potential Prescription Omissions;

CNS - Central Nervous System;

IPD - irrational prescribing of drugs;

IPPD - inappropriate prescribing of psychotropic drugs;

RSD - Serbian dinar;

SSRI - selective serotonin reuptake inhibitors;

SNRI - selective serotonin and norepinephrine reuptake inhibitors;

sGP (*general practitioner*) - selected general practitioner;

PSR (*pharmaceutical sales representative*) - expert associate of a pharmaceutical company.

ABSTRACT

Older people are at risk of inappropriate drug prescribing because pharmacodynamics and pharmacokinetics, and consequently the efficacy and safety of drugs, change after patient's age. The aim of study is to identify major significant risk factors for Potentially Inappropriate Medicines (PIM) of psychotropic drugs and Potential Prescription Omissions (PPO) of psychotropic drugs in population of patients over 65 years of age with associated pathological conditions according to Screening Tool of Older Person's potentially inappropriate Prescriptions/Screening Tool to Alert doctors to the Right Treatment (STOPP/START) criteria. The study was designed as a cross-sectional study involving 492 patients and 9 selected general practitioners. It was conducted in period from May 2020 to December 2021, after receiving decision from Ethics Committee of HC Kragujevac. 492 patients, mean age 71.77 ± 5.95 , with 62.2% women, participated in the study. 164 PIMs were identified in 139 patients (28.2%). The most common were: use of benzodiazepines over 4 weeks (43.9%) with simultaneous use of different groups of antidepressants (20.3%). Patients with more than two psychotropic drugs have a higher risk for PIM [adjusted OR 2.83, 95% CI (1.98 - 4.140), $p < 0.001$]. 439 PPOs were also identified in 270 patients (54.8%). Risk factors for PPO are: age, number of illnesses, total number of medications, number patients, depression presence, patient's place of residence, cigarettes usage and monthly income level. STOPP/START criteria can have a major impact in recognizing inadequate prescribing of psychotropic drugs at patients over 65 years of age. Patients who use benzodiazepines more than four weeks and / or antidepressants may be at increased risk of PIM psychotropic drugs. The total number of drugs and presence of symptoms of depression bring higher risk of PPO psychotropic drugs.

Keywords: STOPP/START, psychotropic drugs, older population.



UDK: 615.214.24-053.9

Eabr 2025; 26(2):137-144

DOI: 10.2478/sjecr-2022-0020

INTRODUCTION

Age of population is an important health factor that is of great importance for analysis of the biological structure of population and is determined by ratio of older population in the total population in a given territory. The age of 65 years and older is considered as social age limit in modern living conditions^{1,2}. Due to the intensive aging of the population nowadays, older population is emerging as biggest drug users, primarily due to the significantly higher frequency of various diseases at that age. Often, these patients suffer from several associated illnesses, which imposes need for simultaneous usage of bigger number of drugs at same time, whether it is causal or symptomatic treatment. Older people are often treated in several different health care institutions, which belong to different levels of health care, from primary to tertiary. Every visit to another health institution creates an additional risk for irrational use of drugs, due to lack of information related to history of disease coming from different sources and/or unsatisfactory communication between health care professionals and between health professionals and patients³.

Aging leads to a decrease in neurons density of central nervous system (CNS). It is estimated that people over the age of 80 lose about 30% of brain mass, primarily gray mass, which is contributed by atherosclerosis, which leads to impaired brain function. Production of important neurotransmitters, including catecholamine, serotonin and acetylcholine, is reduced, which is associated with changes in mood, memory and motor functions⁴. The older population is particularly sensitive to substances that have an effect on the CNS. Therefore, they need to adjust doses of psychotropic drugs (benzodiazepines, barbiturates, antidepressants). Even drugs that do not have side effects on CNS, these effects are more noticeable at people over 65 years of age⁵.

The significance of IPD problem older population is reflected in its high prevalence ranging from about 15% to almost 80% depending on study site (country, region, primary, secondary or tertiary level of health care) and overall methodological approach. In the examination (especially the type of instrument by which the IPD was identified)^{6,7}.

The aim of this research is to determine significant risk factors for potentially inappropriate prescribing of psychotropic drugs in a population of patients over 65 years of age with associated pathological conditions who are on an outpatient treatment regimen, using explicit STOPP START criteria⁸ from 2015.

MATERIAL AND METHOD

Study population

The research was conducted on a sample of 492 consecutively selected, chronically ill patients aged ≥ 65 years, both sexes, with different sociodemographic and

clinical characteristics, who receive health services at the expense of the compulsory health insurance fund.

Research was conducted in five out of nine general practice institutions that operate within the General Medicine Service of the Primary Health Care Center Kragujevac, in the period May 2020 - December 2021. It was conducted after the approval by the Ethics Committee of the Kragujevac Health Center. The research was conducted in compliance with the principles of the Declaration of Helsinki and in accordance with the principles of Good Clinical Practice. In order to collect the highest quality data, an unstructured questionnaire was prepared for patients or their caregivers and their Selected physicians (sGP). The research included nine selected general practitioners.

Study design

The design of the study is a cross-sectional study, in which they are with the help of STOPP and START criteria and sociodemographic questionnaire identified risk factors for Potentially Inappropriate Medicines (PIM) of psychotropic drugs and Potential Prescription Omissions (PPO) psychotropic drugs in patients over 65 years of age.

Inclusion and exclusion criteria

In order to collect as many patients as possible who have inappropriately prescribed psychotropic drugs in their therapy, following criteria for inclusion in the study will be respected when selecting study participants:

- patients on outpatient treatment are in primary health care;
- have at least two chronic diseases that require daily use of drugs, to use at least two prescription drugs every day;
- they have been prescribed the same prescription drugs in the last three months, and that they have received dated and signed informed consent for participation and testing.

Excluding criteria:

- patients under 65 years of age,
- patients who have not seen a doctor in the last 6 months,
- patients who died during the recruitment period,
- terminally or seriously ill patients who receive health care through the home treatment service,
- patients hospitalized during the research period, patients with malignant diseases who underwent chemotherapy and / or radiotherapy,
- patients with incomplete documentation,
- patients who are already involved in another study and patients who are treated on their own initiative in private health care institutions.

Calculation of the sample size

The required sample size was calculated using G* Power software⁹ calculation of the sample size is based on the expected difference between subjects who have IPPD, ie those who do not have risk, in the prevalence of exposure to main risk factors for PIP and PMP recorded in previous studies.¹⁰ Taking into account recently conducted studies in this field in the region of the world, 492 respondents were needed to conduct the research in terms of the minimum number of participants for this cross-sectional study.

Procession of the statistical data

The IBM SPSS Statistics 23 software package was used for statistical data processing. Frequencies and percentages are shown for category variables. Mean values and standard deviation are shown for continuous variables that follow the normal distribution, and the median and IQR are shown for continuous variables that do not follow the normal distribution. Continuous variables were compared between groups by the Mann-Whitney-U test, while for the categorical ones the chi-square or Fisher's exact test was used. Univariate and multivariate logistic regression analysis was performed to identify significant predictors for the presence of START and STOPP criteria. Raw as well as adjusted odds ratio (OR) values are shown along with a 95% confidence interval.

RESULTS

Sociodemographic characteristics

Out of 515 respondents, 492 respondents agreed to participate in the study (96%). Socio-demographic characteristics of the respondents are shown in Table 1. The average age of the respondents was 71.77 ± 5.95 , with 62.2% of women participating in the study. The number of diagnoses established in the study was 914. At least two psychotropic drugs were used in 240 patients (48.8%). The average number of prescribed drugs per patient was 4.37 ± 2.234 .

Potentially Inappropriate Medicines PIM psychotropic drugs

According to the STOPP criteria, 164 PIM of psychotropic drugs were identified in 139 patients (28.2%). Nine out of 14 STOPP criteria were identified as inappropriate prescribing in this study. The most common use of benzodiazepines over 4 weeks (43.9%) and concurrent use of different groups of antidepressants (20.3%). 69.5% of PIM of psychotropic drugs were associated with four diagnoses: anxiety, depression, heart failure, and arterial hypertension. Using multivariate logistic regression, we identified independent risk factors for PIM of psychotropic drugs in our study (Table 2). Patients with more than 5 prescribed medications are at higher risk for PIM of psychotropic medications. A statistically significant higher risk for PIM was identified in patients diagnosed with depression [adjusted OR 18.13, 95% CI (3.36-97.70)],

$p=0.001$. The total number of diseases shows a statistically significant risk for PIM of psychotropic drugs [adjusted OR 8.80, 95% CI (1.91-7.57)], $p=0.001$. Patients number of sGP may be a potential risk factor for PIM of psychotropic drugs [adjusted OR 1.03, 95% SI (1.00-1.05)], $p=0.027$. Patient's place of residence [adjusted OR 2.73, 95% SI (1.05-7.078)], $p=0.038$ and bad life habits [adjusted OR 0.098, 95% SI (0.017-0.560)], $p=0.009$ such as cigarettes usage more than one pack per day, may be risk factors for PIM of psychotropic drugs. Visits number of PSR may be a risk factor for PIM of psychotropic drugs, [adjusted OR 0.069, 95% CI (0.020-0.232)], $p=0.001$.

The influence of several risk factors on the probability that PIM of psychotropic drugs occurred in the study is explained by the values of coefficient between 59.6% (Cox and Snell) and 79.5% (Nagelkerke), which confirm the IPPD.

Potential Prescription Omissions (PPO) psychotropic drugs

According to the START criteria, 439 psychotropic PPO were identified in 270 patients (54.8%). Four out of 6 START criteria were identified as a potential failure of prescribing psychotropic drugs. The most common omissions in prescribing psychotropic drugs were related to the use of antipsychotics [adjusted OR 4.04, 95% CI (1.73-9.47)], $p=0.001$ and anxiolytics [adjusted OR 0.303, 95% CI (0.140-0.657)], $p=0.002$. Using multivariate logistic regression, we identified independent risk factors for PPO of psychotropic drugs in our study (Table 3). The number of diagnostic procedures performed in the last year may be a risk factor for PPO of psychotropic drugs [adjusted OR 1,262, 95% CI (1,036-1,537)], $p = 0.002$. Place of residence [rural life adjusted OR 11.33, 95% CI (2,838-45,273)], $p=0.001$, and single life [adjusted OR 0.27, 95% CI (0.14-0.51)], $p=0.001$, can be potential risk factors for PPO of psychotropic drugs.

The influence of several risk factors on the probability that PPO psychotropic drugs occurred in the research is explained by the values of coefficient between 41.6% (Cox and Snell) and 56.5% (Nagelkerke), which confirm the IPPD.

DISCUSSION

The emergence of inappropriate prescribing of drugs is present today at all levels of health care in countries with different levels of socio-economic development, and the factors that affect it are monitored and examined over the years. According to results of literature search so far, this is one of the first researches that deals with the inappropriate prescribing of psychotropic drugs.

The results of the research indicate a high rate of IPPD. Excessive use of benzodiazepines for more than four weeks in patients over 65 years of age is present in Switzerland¹¹, United Kingdom¹² and Australia¹³. The reason for frequent use may be the problem that benzodiazepines do not have a restrictive diagnosis when prescribing, but also availability in pharmacies. In our study, the place of getting the therapy in

terms of private or public pharmacies, did not show statistical significance ($p > 0.005$). Concurrent use of antidepressants and benzodiazepines coincident with use in Asian countries¹⁴. Simultaneous application is most often due to overlapping reports at the primary and tertiary levels health care. According to STOPP criteria, antidepressants are contraindicated in patients with heart disease and dementia^{15,16}. The use of antidepressants of different groups (SSRI/SNRI) can lead to worsening of the symptoms of the underlying diseases (dementia, heart failure). A statistically significant higher risk for PIM in patients diagnosed with depression [adjusted OR 18,13, 95% SI (3.36 - 97.70)], $p = 0.001$, indicates that sGP should pay more attention to this phenomenon. The number of patients of sGP, place of residence of patients proved to be risk factors for PIM outcomes of psychotropic drugs. The obtained results coincide with the results from Serbia¹⁷, which indicate that the avoidance of large poly-pharmaceuticals and the application of non - pharmacological measures can reduce the risk of PIM. Reducing the exposure of sGP to promotion material of PSR can also reduce the risk of PIM^{18,19}.

With this research, the potential prescribing failure of psychotropic drugs is reflected in the omission of antipsychotic and anxiolytic therapy. This phenomenon can be partly explained by the abuse of benzodiazepines²⁰ so the symptoms of these psychotic disorders are often masked by the use of benzodiazepines. A study in Serbia from 2018 showed that benzodiazepines from the group of anxiolytics are used in a high percentage in our population, which coincides with the results of our research. On the other hand, benzodiazepines, as effective and almost irreplaceable drugs in some indication areas, are exposed to a negative campaign by the pharmaceutical industry for pharmacoeconomic reasons²¹, which is also confirmed by this study.

The shortcomings of this research relate to the limitations of "face to face" survey due to the current COVID-19 pandemic in our country, which has affected population of patients over 65 years old the most. Prescribing therapy with sGP was done in person, but also by phone. Often, the data from the socio-demographic questionnaire regarding patient were obtained from family members/guardians who came to the outpatient clinics of the Kragujevac Medical Center mainly to extend the therapy or to receive instructions for emergency specialist-consultative services.

Table 1. Sociodemographic characteristics of the study population

Characteristics of the study population	Total (n=492) n (%); mean±SD; median (IQR)
Age	71.77±5.954; 70.0; (6.0)
Sex (female)	306 (62.2%); 186; (37.8)
Total number of prescribed medications	4.37±2.234; 4.0; (3.0)
Most common diagnoses	
arterial hypertension	254 (51.6%); 238; (48.4)
cardiac insufficiency	218 (44.3%); 274; (55.7)
depression	106 (21.5%); 386; (78.5)
type 1 diabetes mellitus	80 (16.3%); 412; (83.7)
benign prostatic hyperplasia	70 (14.2%); 422; (85.8)
asthma	26 (5.3%); 466; (94.7)
epilepsy	18 (3.7%); 474; (96.3)

Table 2. Risk factors associated with potentially inappropriate prescribing of psychotropic drugs according to STOPP/START criteria

STOPP criteria	Raw OR 95% (CI)		Adjusted OR 95% (CI)	
Risk factors				
Arterial hypertension	2.451 (1.705-3.522)	0.000	0.419 (0.141-1.245)	0.118
Cardiac insufficiency	0.604 (0.422-0.864)	0.006	1.296 (0.470-3.575)	0.617
Asthma	2.431 (1.036-5.701)	0.041	1.329 (0.231-7.644)	0.750
Depression	93.449 (22.711-384.515)	0.000	18.138 (3.367-97.704)	0.001
Number of diseases	2.332 (1.858-2.927)	0.000	3.805 (1.911-7.578)	0.001
Total number of drugs	1.391 (1.265-1.530)	0.000	1.031 (0.812-1.310)	0.801
Problems with the use of psychotropic drugs	24.554 (5.863-102.834)	0.000	43.517 (5.453-347.267)	0.001
Number of OTC sales	2.029 (1.536-2.680)	0.000	1.625 (0.892-2.959)	0.113
Number of dietary supplements	1.538 (1.218-1.942)	0.002	1.262 (0.689-2.309)	0.451

STOPP criteria	Raw OR 95% (CI)		Adjusted OR 95% (CI)	
Use of antidepressants	84.389 (20.501-347.370)	0.000	52.810 (6.217-448.561)	0.000
PSR visits				
once a week	Ref.			
two/more times a week	0.203 (0.120-0.343)	0.000	0.069 (0.020-0.232)	0.001
once every two weeks	0.063 (0.037-0.109)	0.000	0.508 (0.196-1.316)	0.163
Number of patient examinations in the last 12 months	1.388 (1.255-1.535)	0.000	1.307 (1.005-1.699)	0.046
Number of hospitalizations in the last 12 months	1.540 (1.248-1.900)	0.000	1.089 (0.736-1.612)	0.669
Number of performed diagnostic procedures	1.233 (1.111-1.369)	0.000	1.196 (0.930-1.539)	0.163
Years of service of the eGP	1.138 (1.104-1.173)	0.000	1.017 (0.926-1.116)	0.728
Number of patients of the sGP	1.004 (1.003-1.006)	0.000	1.003 (1.000-1.005)	0.027
Number of adverse reactions to psychotropic drugs	6.411 (2.222-18.500)	0.001	0.572 (0.029-11.313)	0.714
Age	1.031 (1.001-1.063)	0.045	0.920 (0.861-0.982)	0.012
Place of residence				
city	Ref.			
suburb	3.362 (2.241-5.044)	0.000	2.738 (1.059-7.078)	0.038
rural life	6.562 (3.299-13.054)	0.000	2.979 (0.577-15.377)	0.192
Education				
uneducated	Ref.			
primary school	0.541 (0.316-0.929)	0.026	0.823 (0.240-2.823)	0.756
High School	0.847 (0.489-1.467)	0.554	0.484 (0.096-2.443)	0.379
college	0.286 (0.082-0.998)	0.050	0.023 (0.000-2646.848)	0.525
Cigarette consumption				
non smoker	Ref.			
one pack a day	2.231 (1.537-2.504)	0.000	1.612 (0.493-5.266)	0.429
more than one pack	1.468 (0.916-2.353)	0.111	0.098 (0.017-0.560)	0.009
Alcohol consumption				
does not consume	Ref.			
one cup per day	2.530 (1.634-3.917)	0.000	2.824 (0.917-8.699)	0.071
more than one cup	3.053 (1.947-4.788)	0.000	2.870 (0.600-13.716)	0.187
Physical activity				
inactive	Ref.			
daily	0.976 (0.622-1.531)	0.914	4.809 (1.370-16.882)	0.014
once a week	1.174 (0.738-1.869)	0.498	2.167 (0.546-8.595)	0.271
several times a week	4.583 (2.254-9.318)	0.000	7.203 (1.562-33.210)	0.011
Diet				
less than three meals	Ref.			
three meals	0.447 (0.301-0.663)	0.000	0.491 (0.172-1.400)	0.183
three meals and two snacks	0.527 (0.313-0.888)	0.016	1.461 (0.330-6.470)	0.617
Monthly income				
5,000 - 10,000	Ref.			
11,000 -15,000	0.626 (0.396-0.991)	0.046	0.372 (0.140-0.992)	0.048
16,000 - 20,000	0.147 (0.086-0.253)	0.000	0.065 (0.016-0.270)	0.000
over 20,000 RSD	0.293 (0.100-0.861)	0.026	1.050 (0.158-6.993)	0.960

*p-statistical significance

Table 3. Risk factors associated with potential failure to prescribe psychotropic drugs according to STOPP / START criteria

START criteria	Raw OR 95% (CI)		Adjusted OR 95% (CI)	
Risk factors				
Arrhythmia	0.478 (0.303-0.752)	0.001	0.756 (0.331-1.724)	0.505
COPD	0.242 (0.075-0.782)	0.018	0.033 (0.005-0.207)	0.001
Depression	3.929 (2.278-6.779)	0.000	1.507 (0.499-4.552)	0.467
Number of diseases	1.277 (1.060-1.537)	0.010	1.198 (0.787-1.826)	0.400
Total number of drugs	1.227 (1.120-1.344)	0.000	1.458 (1.172-1.815)	0.001
Number of OTC sales	1.757 (1.321-2.338)	0.000	1.514 (0.943-2.433)	0.086
Number of dietary supplements	1.445 (1.136-1.838)	0.003	1.328 (0.867-2.036)	0.192
Antipsychotics	1.866 (1.167-2.982)	0.009	4.049 (1.730-9.476)	0.001
Anxiolytics	0.578 (0.349-0.849)	0.005	0.303 (0.140-0.657)	0.002
PSR visits				
once a week	Ref.			
two/more times a week	0.238 (0.146-0.387)	0.000	1.689 (0.596-4.784)	0.324
once every two weeks	0.632 (0.390-1.026)	0.064	0.342 (0.132-0.886)	0.027
Number of patient examinations in the last 12 months	1.110 (1.016-1.214)	0.021	0.968 (0.766-1.225)	0.788
Number of hospitalizations in the last 12 months	1.355 (1.090-1.685)	0.006	1.104 (0.820-1.486)	0.514
Number of performed diagnostic procedures	1.174 (1.056-1.305)	0.003	1.262 (1.036-1.537)	0.021
Degree of professional development of the sGP				
general practitioner	Ref.			
specialist in general medicine	3.919 (2.211-6.945)	0.000	0.953 (0.205-4.440)	0.952
Number of patients of the sGP	1.003 (1.002-1.004)	0.000	1.002 (1.000-1.004)	0.091
Place of residence				
city	Ref.			
suburb	1.308 (0.878-1.947)	0.186	2.065 (1.021-4.177)	0.05
rural life	3.385 (1.636-7.000)	0.001	11.334 (2.838-45.273)	0.001
Community living				
marriage	Ref.			
alone	0.404 (0.275-0.593)	0.000	0.276 (0.148-0.516)	0.001
with friends	1.327 (0.263-6.698)	0.732	4.437 (0.043-452.717)	0.528
with relatives	0.442 (0.108-1.807)	0.256	0.070 (0.002-2.256)	0.148
Cigarette consumption				
non smoker	Ref.			
one pack a day	1.984 (1.301-3.025)	0.001	1.242 (0.535-2.883)	0.614
more than one pack	2.104 (1.277-3.466)	0.004	1.862 (0.663-5.233)	0.238
Alcohol consumption				
does not consume	Ref.			
one cup per day	2.824 (1.804-4.422)	0.000	2.094 (0.884-4.956)	0.093
more than one cup	2.527 (1.607-3.974)	0.000	1.478 (0.556-3.931)	0.433
Diet				
less than three meals	Ref.			
three meals	0.640 (0.431-0.951)	0.027	1.399 (0.663-2.953)	0.379
three meals and two snacks	1.219 (0.700-2.121)	0.484	4.376 (1.540-12.430)	0.006
Monthly income				
5,000 - 10,000	Ref.			
11,000 -15,000	0.603 (0.381-0.953)	0.030	0.774 (0.345-1.737)	0.535
16,000 - 20,000	0.977 (0.586-1.629)	0.928	2.900 (1.203-6.993)	0.018
over 20,000 RSD	0.488 (0.171-1.392)	0.180	1.426 (0.310-6.550)	0.648

START criteria	Raw OR 95% (CI)		Adjusted OR 95% (CI)	
Social activities	Ref.			
parties	1.476 (0.789-2.784)	0.229	1.903 (0.702-5.158)	0.206
travel adventures	0.278 (0.085-0.905)	0.034	0.253 (0.044-1.457)	0.124
theatrical performances	1.997 (1.085-3.678)	0.026	0.709 (0.282-4.841)	0.464
sport matches	1.216 (0.633-2.336)	0.558	1.492 (0.460-4.841)	0.505
political activities				

*p- statistical significance

CONCLUSION

28.2% of patients with PIM and 54.8% of patients with PPO indicate a high rate of IPPD, which suggests that STOPP/START criteria may be useful in identifying inappropriate prescribing, improving current prescribing and dispensing of psychotropic drugs. The implementation of STOPP/START criteria in everyday practice would greatly improve the current regulatory policy. Pharmacists should also focus more on patients with over four drugs that suffer from anxiety, depression, heart failure and arterial hypertension, as these patients may be at higher risk for PIM. In addition, more frequent diagnostic procedures, adequate therapy for depression and anxiety disorders can reduce the risk of PPO psychotropic drugs. All of the above, requires greater synchronization of health care in the relationship medical specialist – sGP - pharmacist.

CONFLICTS OF INTEREST

There is no conflict of interest among the signed authors.

REFERENCES

- Spasic B. Why Serbs are disappearing?. 9. edition. Kragujevac: Printing house Skver. 2009. pp 39-41.
- Institute of Public Health of Serbia "dr Milan Jovanovic Batut". Health statistical yearbook of Republic of Serbia for 2010. year. Belegarde: Available at <http://www.batut.org.rs/download/aktuelno>, Last visited: 10.04.2020.
- Marengoni A, Angleman S, Melis R, Mangialasche F, Karp A, Garmen A, et al. Aging with multimorbidity: A systematic review of the literature. *Ageing Res Rev* 2011. 10(4):430-439.
- Nezić L. Clinical pharmacology in geriatrics. Medical Faculty of Banja Luka. 2018. pp: 20-1
- Janković MS. Pharmacology and Toxicology. Medical Faculty Kragujevac, 2011. pp: 59-60.
- Louis-Simonet M, Kossovsky MP, Sarasin FP, Chopard P, Gabriel V, Perneger TV, et al. Effects of a structured patient-centered discharge interview on patients' knowledge about their medications. *Am J Med* 2004; 117(8):563-568
- Galvin R, Moriarty F, Cousins G, Cahir C, Motterlini N, Bradley M, et al. Prevalence of potentially inappropriate prescribing and prescribing omissions in older Irish adults: findings from The Irish Longitudinal Study on Ageing study (TILDA). *Eur J Clin Pharmacol* 2014; 70(5):599-606.
- Oxford academic. Age and Ageing. STOPP and START criteria 2015. Available at: <https://www.farmaka.be/frontend/files/publications/files/liste-stoppp-start-version-2.pdf>? Last visited: 19. 12. 2020.
- Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Beh Res Methods* 2007; 39(2):175-191.
- Kovačević VS., Simišić M., Stojkov RS., et al. Potentially Inappropriate Prescribing in Older Primary Care Patients. 2014. 9: 4 (e95536).
- Xhylljeta Luta, Christophe Bagnoud, Mark Lambiris et al. Patterns of benzodiazepine prescription among older adults in Switzerland: a cross-sectional analysis of claims data. *BMJ Open*. 2020. 10(1): e031156.
- Donovan T. Maust, Frederic C. Blow, Ilse R. Wiechers, Helen C. Kales, Steven C. Marcus. National trends in antidepressant, benzodiazepine, and other sedative-hypnotic treatment of older adults in psychiatric and primary care. *J Clin Psychiatry*. 2017. 78(4): e363-e371.
- Leo A Coleman, Jonathan Brett, Benjamin J Daniels, Michael O Falster. Medicine reviews: do they reduce benzodiazepine use in older Australians? 2021. 8;31(3):30452015.
- Xiao-Mei Zhong, Fei Wang, Qing Zhang et al. Concurrent benzodiazepine use in older adults treated with antidepressants in Asia. 2019. 31(5):685-691.
- Rebecca Hedrick, Samuel Korouri, Emile Tadros et al. The impact of antidepressants on depressive symptom severity, quality of life, morbidity, and mortality in heart failure. *Drugs in Context* 2020. 9: 2020-5-4.
- Bianca Kollhorst, Kathrin Jobski, Jutta Krappweis, Tania Schink, Edeltraut Garbe, Niklas Schmedt. Antidepressants and the risk of death in older patients with depression: A population-based cohort study. 2019. *PLoS ONE* 14(4): e0215289.
- Projovic I., Vukadinovic D., Milovanovic O., et al. Risk factors for potentially inappropriate prescribing to older patients in primary care. *Eur J Clin Pharmacol*. 2016. 72(1):93-107.
- Spurling GK, Mansfield PR, Montgomery BD, Lexchin J, Doust J, Othman N, Vitry A. Information from pharmaceutical companies and the quality, quantity, and cost of physicians' prescribing: a systematic review. *PLoS Med* 2010. 7(10):e1000352.

19. Iria Fernández-Álvarez, Maruxa Zapata-Cachafeiro, Juan Vázquez-Lago et al. Pharmaceutical companies information and antibiotic prescription patterns: A follow-up study in Spanish primary care. PLoS One. 2019. 22;14(8):e0221326.
20. Samardžić J., Zeković J., Stevanović A., Jančić j., Dimitrijević I. Benzodiazepine (ab)use and addictive potential: Analyses of consumption in Serbia for the period 2014–2016. Engrami. 2018.40: (2).
21. Balon R., Chouinard G., Cosci F., et al. International Task Force on Benzodiazepines. Psychother Psychosom 2018. 87(4):193-94.