



# The Characteristics of the Outpatient Utilisation of Medicines in the Republic of Srpska in the period 2009-2017

Vanda Marković-Peković<sup>1</sup>, Ljubica Bojanić<sup>2</sup>, Svjetlana Stoisavljević-Šatara<sup>3</sup>

## ABSTRACT

**Background:** Monitoring and measuring of the medicine utilisation enables to assess the quality of use of medicines, providing the evidence-based data for the improvement of the prescribing practice and a more rational use of medicines. The aim of this study was to analyse utilisation patterns of medicines and to compare the results with other countries.

**Methods:** A retrospective, observational study to analyse outpatient medicines utilisation in the Republic of Srpska between 2009 and 2017. Data of medicines utilisation were retrieved from the national database in the Public Health Institute of the Republic of Srpska and calculated and analysed by using the Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) methodology. The results were expressed as Defined Daily Doses (DDDs) per 1,000 inhabitants per day.

**Results:** Total medicines utilisation increased, from 448 DDDs in 2009 to 1,036 DDDs in 2017. Cardiovascular medicines (group C) were the most used medicines, and their share in the total utilisation increased from 36.6% in 2009 to 44.4% in 2017. Among them, the most frequently used were angiotensin-converting enzyme inhibitors, plain and in combinations with diuretics, namely enalapril. The share of medicines used in diabetes in the total utilisation increased from 3.9% in 2009 to 5.1% in 2017. Metformin and glimepiride accounted for about 83% of the blood glucose lowering medicines group (A10B). Among the antithrombotic medicines, the most frequently used were platelet aggregation inhibitors (B01AC), mainly acetylsalicylic acid whose use tripled since 2009. Diclofenac was the most frequently used non-steroidal anti-inflammatory and antirheumatic drug (M01).

**Conclusion:** The trend of increased medicines utilisation was observed in this study. This finding is comparable with other countries. Variations between countries in the preferred medicines within a class as well as the extent of medicines use were observed. These differences were probably consistent, but not solely attributable, to differences in local guidelines and reimbursement policies.

**Key words:** utilisation of medicines, ATC/DDD methodology, international comparisons, rational use.

(1) Department of Social Pharmacy and Pharmacy Practice, Faculty of Medicine, University of Banja Luka, Banja Luka, the Republic of Srpska, Bosnia and Herzegovina.

(2) Public Health Institute, Banja Luka, the Republic of Srpska, Bosnia and Herzegovina.

(3) Department of Pharmacology, Toxicology and Clinical Pharmacology, Faculty of Medicine, University of Banja Luka, Banja Luka, the Republic of Srpska, Bosnia and Herzegovina.

## Correspondence:

VANDA MARKOVIĆ-PEKOVIĆ

E: vanda.markovic-pekovic@med.unibl.org

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## INTRODUCTION

Medicines are only one component in the maintenance and restoration of the health of communities and individuals, and are segment in the prevention, diagnosis and treatment of dis-

eases. If used appropriately, medicines have the potential to relieve suffering from disease and to restore health, which is why they are placed amongst the top priorities in every health sys-

tem.<sup>1</sup> With their pharmacological properties, economic impact on health systems and environmental impact, utilisation of medicines exerts important effects on health systems. As in general, consumption of medicines continues to increase,<sup>2-4</sup> the knowledge of the quantitative and qualitative patterns of medicines use is a key element for allocation of health care resources and development of sustainable health policy. In 2016, after inpatient and outpatient care, medicines represented the third largest item of health care spending and accounted for one-sixth of health expenditure in the European Union, thus confirming the vital role that medicines have in the health system.<sup>5</sup>

Systematic use of routinely collected data on medicines can be employed in assessing the value of medicines in use in health care systems, and can give an insight in the efficiency, quality and fairness of health services.<sup>6</sup> Monitoring and measuring of the medicines use enables to assess quality use of medicines, to identify areas of suboptimal medicines use and provide feedback to prescribers, and thus improvement of pharmacotherapy. The volume of prescribed medicines may be affected by a number of factors, such as population size and age, disease prevalence, changes in medical practice, prescriber and patient behaviour, developments in medical practice, new medicines, reimbursement policies, new guidelines that adjust the recommended treatment per patient or which enlarge the population of patients who would benefit from the treatment.<sup>7-8</sup> Our country, like other countries in transition, is characterised by the demographic shift, with an increase in life expectancy and population aging.<sup>9</sup> So, the major burden of diseases is shifted toward the whole range of chronic diseases, and clinical guidelines were developed for the most common non-communicable diseases.<sup>10</sup> At the same time the legislative and organisational system for collecting the data on the medicines utilisation has been established.

Previous studies conducted by our research group have shown the importance of continuous monitoring and analysing of medicines utilisation and expenditure patterns in the population.<sup>4-8</sup> These studies enabled us to assess the influence of multiple measures introduced in our healthcare system in recent years to increase prescribing efficiency, and furthermore

to suggest additional reforms or measures to further enhance the prescribing efficiency. With the aging of our population and the increasing prevalence of multiple medicinal conditions in the elderly, the share of the long-term medicine use has increased proportionally. This points out the public health importance of the utilisation patterns analyses in the elderly population with the aim to optimise drug prescribing for this group. Understanding of current patterns in medicines use is important to support pharmaceutical policy implementation as a part of a sustainable health policy, considering the expected health outcomes and the related impact to the medication expenditure.

In order to continue with the monitoring and evaluation of the utilisation of medicines in our country, the aim of this study was to analyse the utilisation patterns of medicines and to compare the results with the ones in other countries.

## METHODS

This was a retrospective, observational study on outpatient medicines use over the period from 2009 to 2017. Data was retrieved from the national database located in the Public Institute of Health (PHI). Reports on all medicines dispensed to the patients in all retail pharmacies were sent annually to PHI for collation. This period was chosen as PHI has been collecting and processing data since 2009.

Medicines utilisation was calculated using the Anatomical Therapeutic Chemical/Defined Daily Dose (ATC/DDD) methodology,<sup>11</sup> as the internationally accepted methodology for measuring medicines utilisation.<sup>12-16</sup> The ATC system classifies medicines into different groups according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties. Medicines were classified into ATC groups by its international non-proprietary name. The results were expressed as a DDD per thousand inhabitants per day (DDDs). DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults. It is a technical, statistical unit of measurement and does not necessarily reflect the recommended or actual used daily dose. DDD is a tool for national and international compar-

isons between different geographical areas and health facilities.<sup>11</sup> Descriptive analyses on the data were performed. Data were expressed as absolute numbers with or without percentages.

All analyses were undertaken using Microsoft Excel 2010 program. The results were presented in tables.

## RESULTS

Total medicines utilisation increased, from 448 DDDs in 2009, to 1036 DDDs in 2017. The utilisation increased in almost all anatomical groups, and the highest increase was observed in groups C (cardiovascular system), B (blood and blood forming organs) and A (alimentary tract and metabolism). Group C medicines share in the total utilisation of medicines increased from 36.6% in 2009, to 44.4% in 2017 (Table 1).

Medicines acting on the renin-angiotensin system (C09) and calcium channel blockers (C08) had a highest utilisation in the group C. The C09 group share in the total medicine utilisation increased from 15.7% (2009) to 24.6% (2017) (Table 2), and the most prescribed were angiotensin-converting enzyme inhibitors (ACEIs), plain (C09A) and in combinations (C09B) (Table 3). The share of the medicines used in diabetes (A10) in the total medicine utilisation increased from 3.9% (2009) to 5.1% (2017) (Table 2). In total medicines utilisation, the share of psycho-

leptics (N05) ranged from 4.5% (2009) to 3.4% (2017) and of psychoanaleptics (N06) from 1.3% (2009) to 1.9% (2017) (Table 2). Anxiolytics were the most prescribed among psycholeptics (Table 3), namely diazepam followed by alprazolam. Utilisation of antidepressants has grown steadily and has increased 3.5-fold during the observed period (4.7 DDDs in 2009 vs 16.7 DDDs in 2017).

Utilisation of drugs for obstructive pulmonary diseases (R03) has increased 2.5-fold in number of DDDs and the share in the total medicine utilisation increased from 1.4% (2010) to 1.9% (2017) (Table 2).

Among calcium channel blockers (CCBs), selective CCBs with mainly vascular effects (C08C) were prescribed the most, with about seven percent share in total medicines utilisation (Table 3). A continuous increase in the utilisation of drugs for acid-related disorders (A02) was

**Table 1:** Total utilisation of medicines at the level of main anatomical groups (ATC level I), in number of DDDs

ATC code	Anatomical group	2009	2010	2011	2012	2013	2014	2015	2016	2017
C	Cardiovascular system	163.8	242.9	294.4	285.4	300.9	338.7	348.7	422.9	460.2
B	Blood and blood forming organs	52.8	82.7	99.4	94.3	97.1	111.2	127.6	130.2	131.3
A	Alimentary tract and metabolism	60.3	70.8	105.6	105.3	106.7	110.4	108.1	123.1	126.6
N	Nervous system	74.1	93.5	94.0	94.3	99.5	102.4	99.3	84.8	96.0
M	Musculo-skeletal system	17.1	39.6	48.2	47.7	50.4	56.5	55.5	65.6	71.1
R	Respiratory system	24.2	26.5	27.3	23.9	26.3	30.7	34.6	39.5	39.2
G	Genito urinary system and sex hormones	6.7	12.3	13.9	15.4	14.9	16.2	18.3	21.9	24.5
D	Dermatologicals	10.3	15.4	19.9	22.4	23.2	28.0	20.4	24.0	23.6
J	Antinfectives for systemic use	20.7	18.1	18.0	16.0	18.7	15.8	17.7	20.0	23.2
H	Systemic hormonal preparations, excl. sex hormones and insulins	10.0	8.5	11.2	12.2	11.8	14.8	14.8	20.2	21.7
S	Sensory organs	7.3	9.4	10.9	10.6	10.9	12.8	13.3	14.8	15.9
L	Antineoplastic and immunomodulating agents	0.7	2.5	1.9	2.1	2.1	2.2	2.7	2.5	2.9
P	Antiparasitic products, insecticides and repellents	0.7	2.5	1.9	2.1	2.1	2.2	2.7	2.5	2.9
	<b>Total</b>	<b>448.2</b>	<b>622.3</b>	<b>746.5</b>	<b>731.5</b>	<b>764.3</b>	<b>841.7</b>	<b>861.2</b>	<b>969.5</b>	<b>1036.3</b>

**Table 2:** Total medicines utilisation of 20 most prescribed therapeutic groups (ATC level II), in number of DDDs

ATC code	Therapeutic group	2009	2010	2011	2012	2013	2014	2015	2016	2017
C09	Agents acting on the renin-angiotensin system	70.4	106.4	138.7	135.8	148.6	167.8	187.5	229.2	254.8
B01	Antithrombotic agents	30.3	46.8	54.8	55.1	58.9	67.9	86.6	84.9	89.5
C08	Calcium channel blockers	30.5	42.5	50.3	48.4	53.8	64.2	56.6	70.0	72.4
A10	Drugs used in diabetes	17.3	23.2	34.3	33.5	35.5	39.1	41.9	52.3	52.8
M01	Antiinflammatory and antirheumatic products	16.1	25.3	30.4	30.5	31.7	35.4	34.9	40.8	46.1
B03	Antianemic preparations	21.2	34.6	43.7	35.3	34.5	39.8	35.5	44.8	41.4
C07	Beta blocking agents	11.9	16.4	21.3	20.6	22.8	25.5	26.9	34.1	40.2
N05	Psycholeptics	20.0	29.2	33.2	29.3	29.4	31.7	33.7	36.5	35.5
A02	Drugs for acid related disorders	10.9	12.9	19.3	21.7	21.3	23.2	21.9	28.0	30.4
A11	Vitamins	24.0	22.1	38.4	31.7	32.7	30.3	24.9	27.6	29.0
C03	Diuretics	11.4	21.0	20.5	21.7	20.3	22.0	24.4	27.0	28.9
C01	Cardiac therapy	20.9	27.9	33.2	31.5	27.4	28.8	23.1	26.7	27.3
N02	Analgesics	41.0	46.7	39.1	42.3	54.0	44.9	37.9	16.5	25.0
J01	Antibacterials for systemic use	20.2	17.6	17.5	15.7	18.4	15.6	16.8	19.8	23.1
M02	Topical products for joint and muscular pain	0.3	13.2	16.2	15.3	16.5	18.5	18.6	21.7	21.7
N06	Psychoanaleptics	5.7	7.9	11.0	11.9	12.5	14.3	14.4	17.6	20.4
C10	Lipid modifying agents	7.8	12.8	9.1	9.6	10.2	12.3	13.5	18.8	20.0
R03	Drugs for obstructive airway diseases	8.1	8.6	10.4	9.7	10.6	12.3	15.2	19.3	19.6
H03	Thyroid therapy	8.1	8.6	10.4	9.7	10.6	12.3	15.2	19.3	19.6
G04	Urologicals	1.6	2.3	4.6	5.9	6.5	8.2	10.2	12.6	15.0

observed, with the share in the total medicine utilisation of about 3% (Table 2). The most prescribed were drugs for peptic ulcer and gas-

tro-oesophageal reflux disease (A02B) (Table 3), namely proton pump inhibitor pantoprazole and H<sub>2</sub>-receptor antagonist ranitidine (Table 4).

**Table 3:** Total utilisation of ten most prescribed pharmacological groups (ATC level III), in number of DDDs

ATC code	Pharmacological group	2009	2010	2011	2012	2013	2014	2015	2016	2017
C09	Angiotensin-converting-enzyme (ACE) inhibitors, plain	46.7	70.9	93.7	91.6	96.8	109.3	118.7	147.2	154.8
B01A	Antithrombotic agents	46.7	70.9	93.7	91.6	96.8	109.3	118.7	147.2	154.8
C09B	Angiotensin-converting-enzyme (ACE) inhibitors, combinations	30.3	46.8	54.8	55.1	58.9	67.9	86.6	84.9	89.5
C08C	Selective calcium channel blockers with mainly vascular effects	27.8	39.0	46.5	45.1	50.8	61.2	53.7	66.7	69.5
M01A	Antiinflammatory and antirheumatic products, non-steroids	16.1	25.3	30.3	30.5	31.7	35.4	34.9	40.8	48.1
A10B	Blood glucose lowering agents, excl. insulins	12.7	18.0	28.9	28.3	30.4	34.5	35.8	44.9	46.8
C07A	Beta blocking agents	11.9	16.4	21.3	20.6	22.7	25.4	26.7	33.8	37.8
B03B	Vitamin B12 and folic acid	15.3	27.1	35.6	30.0	29.6	33.9	30.9	35.3	32.1
A02B	Drugs for peptic ulcer and gastro-oesophageal reflux disease	10.3	11.9	18.6	21.1	20.8	22.6	21.6	27.6	30.3
N5B	Anxiolytics	17.5	24.9	28.8	25.5	25.2	27.4	28.8	30.4	30.0

Among the antithrombotic medicines (B01A), the most frequently used were platelet aggregation inhibitors excluding heparin (B01AC), namely acetylsalicylic acid whose use tripled since 2009 (Table 4). The most frequently used were blood glucose lowering medicines, excluding insulin

the combination of paracetamol with caffeine, codeine and propyphenazone. The high-ceiling diuretics comprised about 2/3 of diuretics (C03) utilisation and furosemide was the most prescribed (Table 4).

**Table 4:** Twenty most prescribed medicines, in DDDs

ATC code	INN	2009	2010	2011	2012	2013	2014	2015	2016	2017
C09AA02	enalapril	34.3	49.0	63.3	61.7	67.2	74.5	80.3	94.0	96.5
B01AC06	acetylsalicylic acid	45.7	45.5	49.6	50.1	53.6	63.1	81.0	78.2	82.2
C08CA01	amlodipine	32.6	35.5	41.6	40.1	45.0	53.6	45.9	53.8	53.8
C09BA02	enalapril, hydrochlorothiazide	15.5	23.1	28.8	27.6	32.0	33.1	39.1	41.7	52.7
C09AA05	ramipril	3.1	6.1	11.1	12.6	13.0	13.8	17.6	26.3	30.3
A10BA02	metformin	5.1	7.6	11.1	15.9	13.6	16.2	18.0	23.6	26.1
M01AB05	diclofenac	10.3	16.2	19.1	19.5	19.4	20.5	20.7	21.6	25.0
B03BB01	folic acid	0.6	0.7	20.3	21.1	18.5	17.8	18.3	22.4	21.4
N02BE51	codeine, caffeine, paracetamol, propyphenazone	3.4	26.3	19.8	22.1	20.3	19.5	19.0	16.8	20.2
C03CA01	furosemide	5.5	11.1	10.6	12.8	11.3	12.3	13.5	16.8	18.4
N02BE01	paracetamol	3.1	3.4	4.3	5.6	9.2	6.8	7.5	9.6	18.2
C07AB02	metoprolol	5.9	8.6	10.6	10.1	11.2	12.3	12.1	14.2	17.0
A02BC02	pantoprazole	0.6	1.2	2.1	2.8	4.1	7.0	7.3	11.4	14.0
A02BA02	ranitidine	7.2	6.8	11.9	14.2	13.0	12.6	12.0	14.0	13.8
A11GA01	ascorbic acid	16.1	13.3	12.7	10.7	16.0	13.7	12.4	12.8	13.6
H03AA01	levothyroxine	4.0	3.0	5.6	5.6	6.3	8.5	8.1	11.8	13.1
C09AA03	lisinopril	2.2	3.3	5.1	5.6	5.9	6.7	8.1	10.8	12.7
A10BB12	glimepiride	0.5	1.4	2.6	3.8	5.8	8.3	9.0	12.1	12.5
C10AA05	atorvastatin	4.5	7.8	5.5	5.2	5.6	7.6	8.0	11.7	12.4
C07AB07	bisoprolol	0.5	0.1	2.1	2.6	3.8	5.1	6.4	9.8	12.0

INN, International Non-proprietary Name

(A10B) (Table 3), namely metformin and glimepiride who accounted about 83% of A10B group utilisation (Table 4). Non-steroid (M01A) medicines were the most used among anti-inflammatory and antirheumatic medicines (M01) (Table 3), specifically diclofenac (Table 4).

Four out of five most prescribed medicines were cardiovascular medicines. Plain ACEI enalapril was the most frequently used, with the increased share in the total medicines' utilisation from 7.6% (2009) to 9.3% (2017). Amlodipine was the dominantly prescribed selective CCBs. Consumption of non-opioid analgesics (N02B) dominated among analgesics (N02), namely

## DISCUSSION

This study revealed an increasing trend toward the utilisation of medicines, and given the previous studies<sup>17,18</sup> it was not a surprising finding. Similar trend was observed in other studies.<sup>2-4,7</sup> The quantity of medicines tends to increase over time in most therapeutic classes, which may be explained by population ageing, the rise in the prevalence of chronic diseases such as cancer and diabetes, the availability of new medicine treatments or changes in the physicians' prescribing practices,<sup>19</sup> that may have had an influence on our patterns of medicines utilisation, too.

Medicines classes used for treatment of the most common chronic non-communicable diseases were of the highest degree of utilisation,<sup>9, 20</sup> as in other countries.<sup>21-26</sup> Premature mortality related to the major non-communicable diseases can be reduced if appropriate, timely and collective action is taken.<sup>27-29</sup> Among the other activities undertaken towards improvement of health of the population,<sup>30</sup> an update of reimbursable medicines list was carried out precisely to provide better therapeutic choice of medicines, contributing thus to the reduction of morbidity and mortality. Although major non-communicable diseases affect people of all ages, they are often associated with older age groups. Our population is evidently aging as the share of elderly ( $\geq 65$  years) has increased, from 18% (2007) to 22% (2014), and of people aged 50-64 years, from 19% (2010) to 23% (2014). As the trend in ageing of population has significantly increased over the time, it directly influenced the volume of medicines needed for care of elderly people since they have multiple chronic diseases and requires larger number of prescriptions. A recent study among elderly patients has showed an increase of those who use more medicines for longer period of time, with an increased polypharmacy prevalence (use of  $\geq 5$  different medicines).<sup>8</sup>

Cardiovascular (CV) medicines were the most frequently prescribed, like in other countries.<sup>21-26, 31, 32</sup> The trend of steady increase in the CV medicines use has been seen over the last few decades<sup>33</sup> as they are key elements in preventing and treating CV diseases, which are the leading cause of death and disability worldwide.<sup>34-36</sup> It has also been a leading cause of our population's mortality for the last 20 years.<sup>9, 37</sup> The health policy planners therefore focused their attention on a national CV programme, implementation of the national and European guidelines<sup>38-42</sup> and selection of the reimbursed medicines. A decrease in CV mortality, from 53.6% in 2002 to 48.7% in 2016<sup>9, 17</sup> might be attributable to improved CV care, including pharmacotherapy, as the association between the increase in CV medicines use and a decrease in CV mortality was confirmed.<sup>43,44</sup> Despite the significant increase in CV medicines use, the mortality rate was rather high and CV diseases has remained a leading cause of morbidity and mortality.<sup>44</sup>

The highest utilisation of antihypertensive medicines, such as ACEIs, CCBs and beta blockers,

and the increased utilisation of diuretics, are in accordance with clinical guidelines for hypertension. These medicines, with ARBs, are major classes for the treatment of hypertension, used either as monotherapy or in combination with other drugs (mainly diuretics). Over the past 20 years a constant increase in utilisation of these classes was noticed.<sup>45</sup> Enalapril as a monotherapy and in combination with hydrochlorothiazide was the most used ACEI, followed with ramipril (monotherapy) and lisinopril (combination). As a monotherapy, the ACEIs were also frequently prescribed in Serbia,<sup>21,23</sup> Finland<sup>46</sup> and Norway.<sup>31</sup> High use of ACEIs in combination with diuretics was not surprising, because treatment of hypertension should be preferentially based on combinations of ACEIs or ARBs with a CCB and/or a thiazide diuretic as the most effective evidence-based treatment strategy to improve blood pressure.<sup>42</sup> These combinations are available on our market in a single pill and in a range of doses, enabling simplification of treatment, flexible prescribing and better patient adherence. Country differences were noticed in the preferred ACEIs<sup>23, 24, 26, 31, 32, 47</sup> and ARBs.<sup>23, 24, 31, 46</sup> They may be influenced by the recommendation to assess the clinical effects, which are proven to be divergent today, of each medicine and their indications in light of the comorbidities.<sup>48</sup>

Although amlodipine was the most preferred CCB, an increase in lercanidipine utilisation was notable (rising from 0.5 DDDs in 2011 to 11 DDDs in 2017). This trend was noticed in other countries<sup>23-25, 31</sup>, and could be explained by more favourable tolerability profile.<sup>49</sup> It is a medicine of a higher cost within the class,<sup>50, 51</sup> and value for money is also an important consideration when choosing a preferred medicine. Patients should be provided with a medication appropriate to their clinical needs and at the lowest cost to them and health system. Acetylsalicylic acid was the most frequently used among the anti-thrombotic medicines, as generally considered effective for the secondary prevention of cardiovascular disease and one of the most frequently used drugs worldwide.<sup>52</sup>

Among statins, atorvastatin was the most prescribed, with the growth in rosuvastatin use (0.7 DDDs in 2011; 5.6 DDDs in 2017). The cross-country variations in the statin use was also noticed by other authors.<sup>53</sup> Atorvastatin reference prices were higher than those of simvastatin, while rosuvastatin was the most expensive

statin. Therapeutic switch from rosuvastatin to atorvastatin was not associated with any differences in safety or lipid control, but resulted in significant drug cost savings.<sup>54</sup> Some studies suggest a continued suboptimal prescribing of lipid lowering medicines in CV population along with the expansion of its use, a shift in use towards asymptomatic and older populations, and overtreatment of people who are unlikely to benefit from this therapy.<sup>33</sup> Further studies of statin use are needed for deeper analysis.

Diabetes was the fifth leading cause of death in women and the seventh in men in 2016.<sup>9</sup> Endocrine, nutritional and metabolic diseases (ICD E00-E90) accounted for about 3% in the total morbidity since 2010.<sup>9, 55</sup> This chronic disease requires continuous medical care, including expenditure in pharmaceutical supplies. Therefore, besides biguanides and sulphonylureas (SUs), during this follow-up period new oral antidiabetic medicine classes became reimbursed, as dipeptidyl peptidase 4 (DPP-4) inhibitors, glucagon-like peptide-1 (GLP-1) analogues and sodium-glucose co-transporter 2 (SGLT2) inhibitors. An increasing trend in the utilisation of metformin and glimepiride may be influenced by the guidelines that suggest metformin as a first choice<sup>56-58</sup> and SUs as an initial drug treatment if metformin is contraindicated or not tolerated, or as a dual therapy with metformin if initial treatment with metformin has not reached the patient's individual goals.<sup>57</sup> International comparisons showed an increasing trend in metformin use, and at the same time by decrease in SUs use.<sup>46, 59-61</sup> We have also noticed a decrease in the use of other available SUs, except for glimepiride. Pharmaceutical marketing might have had some influence on prescribing the first choice among the SUs, as pointed out by Pavlov in Croatia.<sup>62</sup> This possible influence should be clarified in future research. DPP-4 and GLP-1 were less frequently used but an increase in their use was also observed.

Utilisation of proton pump inhibitors (PPIs) and especially of pantoprazole has steadily grown, as elsewhere.<sup>24, 25, 31, 46</sup> Several PPIs, including pantoprazole, were reimbursed, and pantoprazole is the only one also available on the market as a non-prescription medicine (20 mg dose). Ranitidine utilisation was high compared to the other countries.<sup>24, 25, 31, 46</sup> At low doses (75 mg) it is available on our market as an over-the-counter (OTC) medicine. The reason for its still wide use,

despite the availability of the more effective acid-suppressant PPIs, is to be further explored. A decreasing trend in the use of diclofenac was expected regarding the new scientific evidences about its safety profile, i.e. cardiovascular side effects, as informed by the Agency of Medicines and Medical Devices of Bosnia and Herzegovina at the beginning of 2014. Moreover, this is a sole prescription medicine for oral use. In other countries ibuprofen is preferred due to a better safety profile and more OTC medicines available in pharmacies because of which diclofenac exhibits a declining trend.<sup>24, 25, 31, 46</sup> Ibuprofen utilisation has grown over the period.

The strength of this study is a nine-year follow-up period, a timeline that is long enough to allow for the determination of the existing trends. The medicines utilisation data came from the official national source, thus providing robustness. Data built on the medicines dispensed to patients were considered as a strength, although there was awareness that it does not necessarily ensure that the medicine was taken by the patient. The nature of the data in this administrative database that allowed only determination of trends may be considered as a limitation. More in depth analysis could be performed with available data on the age, gender, diagnosis, clinical information, changes in medicines use, therapy intensification, medication duration etc. Beyond the limitations, these results can serve as a starting point for further studies about the use of medicines and its rationality.

## CONCLUSION

The utilisation of medicines showed an increasing trend, which is similar to other countries. In addition to the similarities, certain differences in the use of medicines were also observed among the countries, as variations in the preferred medicines within a class and the extent of medicines use. These differences were probably consistent, but not solely attributable, to differences in local guidelines and reimbursement policies. Value for money, for health system and patients who pay for their own medicines, is an important consideration when choosing a preferred medicine according to scientific evidence and the patient's needs.

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None.

## CONFLICT OF INTEREST

None.

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