

# The Evaluation of Antibiotics DDD Consumption in Septic Surgical Department in Republic of Moldova

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## Abstract

Antibiotics consumption evaluation in Moldova's hospitals is in the embryonic phase of study and implementation of consumption surveillance programmes would be a solution to the problem. The study used 2009 - 2014 data of consumption of anti-infectives for systemic use, from septic surgical department that shows the dynamics consumption indicating nature and value indexes.

In septic surgical department DDD/1000 OBD decreased from 680 in 2009 to 349 in 2014 or by 48.7%, when per institution, from 662.4 to 464.1 DDD/1000 OBD or by 30% respectively. A decrease from 610 in 2009 to 265 DDD/1000 in 2014 or by 56.56% for parenteral forms and vice versa for the ones with enteral use forms increased consumption from 70 to 89 DDD/1000 or by 27.14%. The DDD/1000 OBD cost registered 8314 at the beginning and 5559 leis at the end of the evaluated period or a decline of 33.14%, and conversely, the cost of one medium DDD increased from 12.33 in 2009 to 16.44 leis in 2014 or by 33.3%. The decreased DDD/1000 OBD characterized the measures taken for improving rational use of antibiotics from one side; and some inadequacies in organizing the current supply from the other side. The increase of cost of one DDD clearly shows the increase of antibiotic medical remedies price for the evaluated period.

**Key words:** Antibiotics, defined daily dose, consumption, rational use, hospitals

## INTRODUCTION

The World Health Organisation "European strategic action plan on antibiotic resistance 2011–2016" mentioned that, "Antimicrobial resistance is not a new phenomenon, but increasing and new resistant strains continue to emerge". The main aims of plan include the following measures: raise awareness of the emergence and spread of antibiotic resistance; promote prudent use of antibiotics; address antibiotic use in human and animals and other measures as a result of reduction of morbidity, mortality and related costs [1, 2]. Of all 20-50% antibiotics prescribed only in United States of America acute care hospitals are either unnecessary or inappropriate [3, 4]. Taking in consideration this situation in 2014 Centers for Disease Control and Prevention recommended that all acute care hospitals implement Antibiotic Stewardship Programs [5]. Hospital based programs dedicated to improving antibiotic use, demonstrates that growing body of evidence can optimize the treatment of infections as all to reduce adverse events associated with antibiotic use [6, 7]. An early switch from parenteral to oral antibiotics is highly desirable especially in resource limited setting to decrease cost of therapy and should be actively implemented [8]. We have to recognize that in Moldova drugs consumption analysis in defined daily doses, as an important indicator for optimisation of drug remedies' rational use in society and hospitals, particularly are not addressed enough and highlighted by scientific research literature.

The primary aim of the study was to evaluate institutional representative data on antibiotics utilization according to World Health Organization (WHO) requirements in septic surgical institutional department, projected to determine DDD/1000 value [9, 10]. Based on obtained data, it aimed to make conclusions on the use of anti-infectives for systemic use in surgical department and to propose recommendations for ensuring their optimization.

Emergency Medicine Institute of Moldova (EMI) was founded in 1959 and consists from 9 clinical services with 600 beds overall including surgery for 140 beds, municipal center with 8 seats hemodialysis and 9 beds. There are 4 outpatient departments of traumatology and orthopedics as well [11].

## MATERIAL AND METHODS

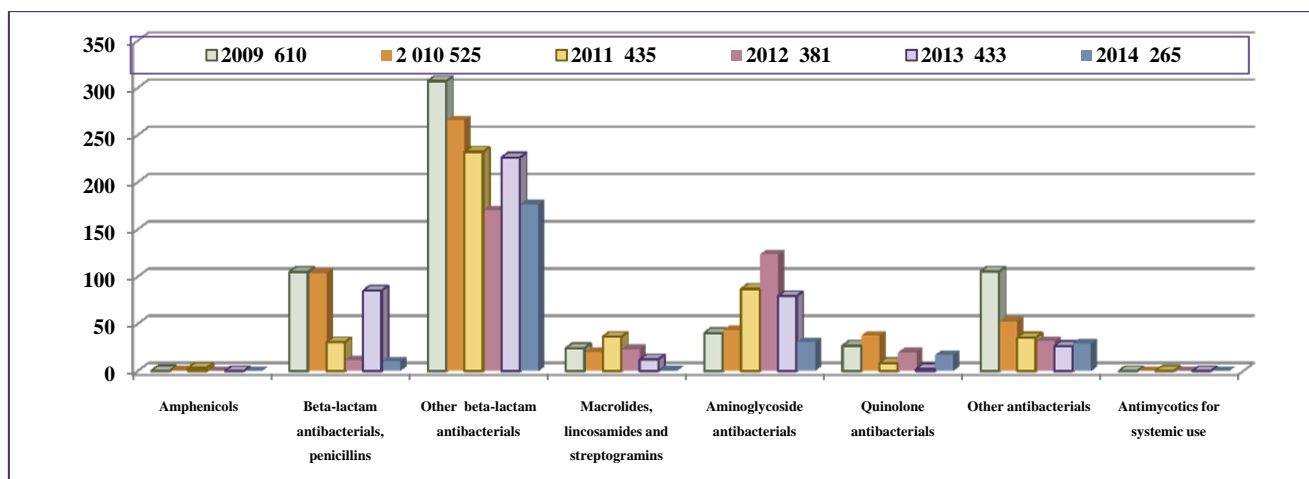
For this study were used data on six-year (2009-2014) period, in septic surgical department of EMI for 40 beds, which show the dynamics of consumption of medicinal remedies pharmacotherapeutic group J–Anti-infectives for systemic use, as classified Anatomical Therapeutic Chemical, classification system of World Health Organization (ATC) indicating the nature and value indexes. Statistical, analytical, mathematical, comparisons, logical and descriptive were used as the methods of study.

## THE RESULTS OF THE INVESTIGATION

To evaluate the consumption of anti-infectives for systemic use drugs in DDD/1000 in EMI we followed 10 steps of study [12] and compare for the period of 2009-2014 the statistics data concerning the number of treated patients (for only patients with health insurance and other free treated by the state categories of citizens), the number of bed/days (2009 = 14030; 2010 = 14212; 2011 = 12875; 2012 = 12372; 2013 = 12464; 2014 = 12104) and data about total annual consumption of antibiotics were used.

All in all 50 antimicrobial remedies (both for parenteral and enteral use) treating assistance of hospitalized patients in the evaluated period were used, from which with only enteral form 22 names, with only parenteral form 28 names and with both forms 10 names, which represents 39 active antimicrobial substances.

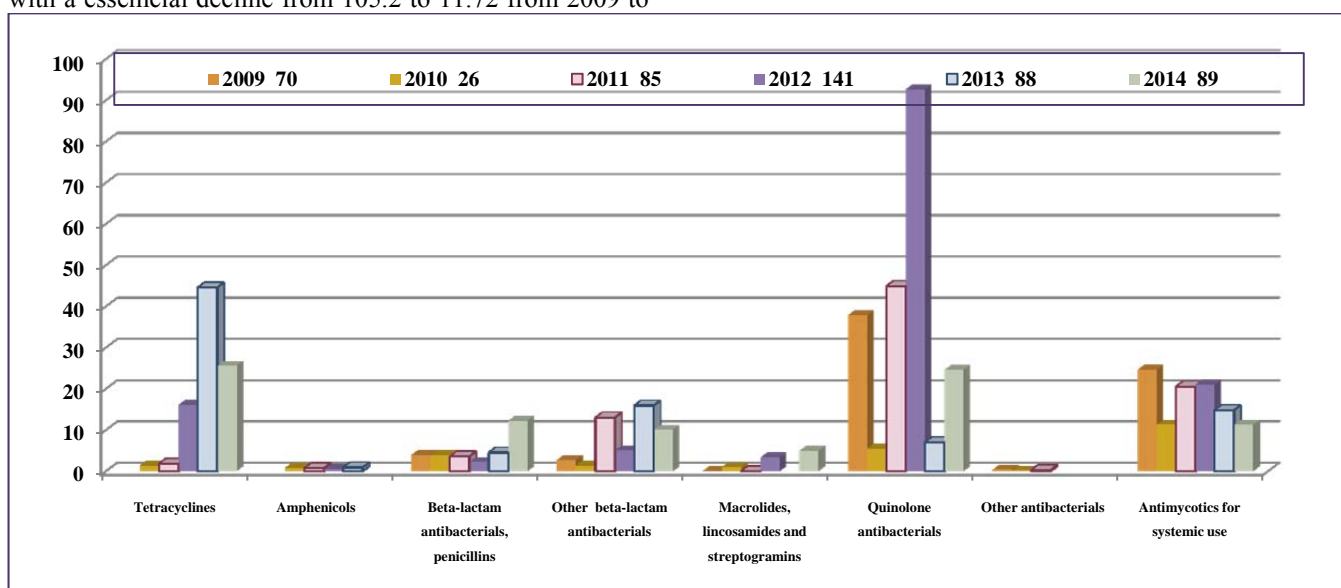
Consumption rate of parenteral forms of medical remedies antibiotics subgroups evaluated in DDD/1000 during 2009-2014 in figure 1 is shown.



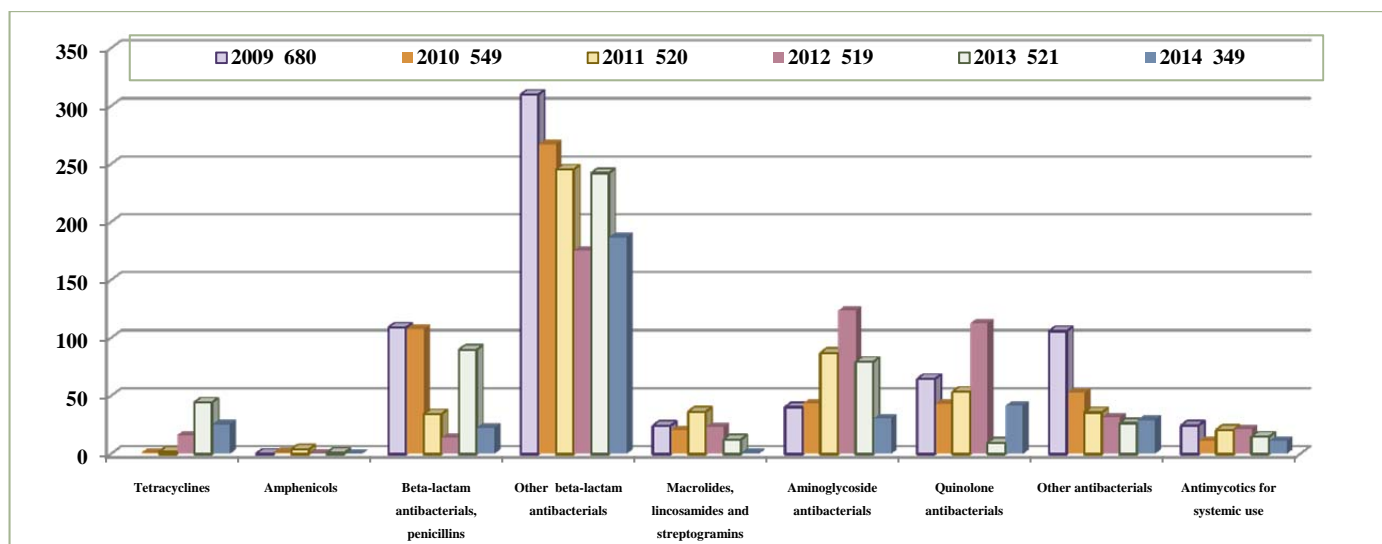
**Fig. 1. Parenteral forms consumption of antibacterials for systemic use in DDD/1000**

Figure 1 states that for the evaluated period the average consumption annual rate of all antibiotic subgroups registered a decline from 610 in 2009 to 265 DDD/1000 in 2014 or by 56.56%, with an exception in 2013, when was recorded an increase by 52 DDD/1000 comparatly to 2012. The folowing changes of consumption for pharmacoterapeutic subgroups with theirs representative medical remedies and defined daily doses in grams were recorded. The highest consumption with a decrease from 310 in 2009 to 187 DDD/1000 in 2014 was registered for other beta-lactam antibacterials (Cefazolinum 3.0, Cefuroximium 3.0, Cefotaximum 4.0, Ceftazidimum 4.0, Ceftriaxonum 2.0, Cefoperazonum 4.0, Cefepimum 2.0) folowed by other antibacterials (Vancomycinum 2.0 and Metronidazolium 1.5) with an essencial decrease from 105.56 in 2009 to 29.33 DDD/1000 in 2014. The mean consumprion of DDD/1000 were recorded several subgroups. Beta-lactam antibacterials, penicillins (Ampicillinum 2.0, Amoxycillinum 2.0, Amoxicillinum + Acidum clavulanicum 3.0, Ticarcillinum + Acidum clavulanicum 15.0) substitutes an unstable consumption with a essemcial decline from 105.2 to 11.72 from 2009 to

2012 and from 85.37 in 2013 to 10.41 DDD/1000 in 2014. Macrolides, lincosamides and streptogramins (Clarithromycinum 0.5, Azithromycinum 0.5, Lincomycinum 1.8) recorded an increase of consumption from 24.45 in 2009 to 36.5 in 2011 and an abrupt decrease to 0.83 DDD/1000 in 2014. Aminoglycoside antibacterials (Streptomycinum 1.0, Gentamycinum 0.2, Kanamycinum 1.0, Amikacinum 1.0) recorded an considerable increase of consumption from 40.45 in 2009 to 123.6 in 2012 and an sharp decrease to 30.56 DDD/1000 in 2014 and quinolone antibacterials (Gatifloxacinum 0.4, Acidum pipemidicum 0.8) registered a moderate decrease in the evaluated period from 26.94 to 16.94 DDD/1000. The lowest consumption was recorded by amphenicols (Chloramphenicolium 3.0) with a consumption only during 2009 and 2011, that constituted respectively 0.36 and 3.34 DDD/1000, folowed by antimycotics for systemic use (Fluconazolium 0.2) with a consumption only during 2011 and 2013, that constituted respectively 0.31 and 0.08 DDD/1000. In figure 2 consumptionrate of enteral forms of antibacterials for systemic use subgroups in DDD/1000 during 2009-2014 is showed.



**Fig. 2. Enteral forms consumption of antibacterials for systemic use in DDD/1000**



**Fig. 3. The total consumption of antibacterials for systemic use in DDD/1000**

Figure 2 demonstrates that the average consumption annual rate of antibiotics for oral usage increased from 70 in 2009 to 89 DDD/1000 OBD in 2014 or by 27.14%. The following changes in consumption were recorded. The highest consumption with the bit of 92.7 in 2012 and with a decrease from 37.85 in 2009 to 24.62 DDD/1000 in 2014 was registered for quinolone antibacterials (Gatifloxacinum 0.4, Acidum pipemidicum 0.8), folowed by antimycotics for systemic use from with a moderate decrease from 24.66 to 11.32 DDD/1000 (Ketoconazolom 0.2 and Fluconazolom 0.2) in the mentioned period. The mean with the increasing of consumption of DDD/1000 were recorded by the following subgroups: tetracyclines (Doxycyclinum 0.1) from 1.41 in 2009 to 25.61 DDD/1000 in 2014, folowed by beta-lactam antibacterials, penicillins (Ampicillinum 2.0, Amoxycillinum 1.0, Amoxicillinum + Acidum clavulanicum 1.0) from 3.99 to 12.31, other beta-lactam antibacterials (Cefalexinum 2.0, Cefuroximom 0.5, Cefaclorum 1.0gram and Cefixim 0.4) from 2.75 to 10.08 and macrolides, lincosamides and streptogramins (Erytromycin 1.0, Midecamycinum 1.0, Clarithromycinum 0.5 and Azithromycinum 0.3) from 0 to 4.96 DDD/1000. The lowest consumption were registered for amphenicols (Chloramphenicolum 3.0) with a consumption only during 2010 and 2013, that constituted respectively 0.91 and 0.96 DDD/1000 and other antibacterials (Furazidinum 0.2, Nitrofurantoinum 1.5 and Nitroxolinum 1.0) only during 2009 and 2011, that constituted respectively 0.43 and 0.31 DDD/1000.

In figure 3 the total (parenteraland enteral forms) antibiotic groups used rates is demonstrated.

The average aggregated annual rate for total antibiotics in the evaluated period as shown in figure 3 decreased from 680 in 2009 to 349 DDD/1000 in 2014 or by 48.68%.

The highest yearly consumption was registered for other beta-lactam antibacterials from 310.05 DDD/1000 or 45.60% of the total in 2009 to 187 DDD/1000 or 53.60% of the toatal in 2014 respectively and with a decrease of 39.69% for mentioned period. To the mean positon were

placed five subgroups. Beta-lactam antibacterials, penicillins with almost identical DDD/1000 higher consumption recorded of 109.19; 107.77 and 89.94 in 2009; 2010 and 2013 or 16.06%; 19.62% and 17.26% from the total as all as almost lower DDD/1000 consumption of 34.33; 13.98 and 22.72 or 6.60%; 2.69% and 6.51% from the total in 2011; 2012 and 2014 respectively. The next mean record was registered by aminoglycoside antibacterials with an increase from 40.45 in 2009 to 123.6 in 2012 and a decrease to 30,56 DDD/1000 in 2014. Quinolone antibacterials in the evaluated period maintained a decrease of consumption from 64.79 in 2009 to 41.56 DDD/1000 with an exeption of 112.7 DDD/1000 in 2012. Other antibacterials recodred a dicline of consumption from 105,99 DDD/1000 in 2009 or 15.59% from the total to 29,33 or 8.41% from the total in 2014 respectively and a decrease of 3.61 times for mentioned period. To the last positions with a median yearly consumption between 1 and 20 DDD/1000 were placed tetracyclines, amphenicols, macrolides, lincosamides and streptogramins and antimycotics for systemic use.

In table 1 the ratio DDD/1000 of parenteral to enteral use forms and share from the total is shown.

In table 1 the ratio between antibiotics DDD/1000 parenteral to enteral use forms and percentage from the total are presented. This ratio decreased from 8.7 to 3.0 times and the percentage from 89.71% in 2009 to 74.86% in 2014 and vice versa enteral use forms increased consumption from 10.29% to 25.14% respectively. Recent analyses of antibiotic consumption shows that similar data for whole institution during 2009 – 2012 varied from 85.9 to 84.2% for parenteral forms of use and 14.1 to 15.2% for enteral forms of use respectively [13].

The comparison of total antibiotics consumption data evaluated in DDD between 1547 International hospitals and surgery departments of 405 International hospitals with the similar data from Emergency Medicine Institute and surgery department in figure 2 is presented.

**Table 1: The ratio of antibiotics DDD/1000 for parenteral to enteral use forms and percentage from the total**

The ratio DDD/1000 of parenteral to enteral use and percentage from the total							
Years	2009	2 010	2011	2012	2013	2014	
Parenteral	610	525	435	381	433	265	
Enteral	70	26	85	141	88	89	
The ratio of parenteral to enteral	8.7:1	20.2:1	5.1:1	2.7:1	4.9:1	3.0:1	
Total	680	551	520	522	521	354	
Percentage forms from total	parenteral	89.71%	95.28%	83.65%	72.99%	83.11%	74.86%
	enteral	10.29%	4.72%	16.35%	27.01%	16.89%	25.14%

**Table 2: Surveillance studies of antibiotic use in International hospitals in comparison with the similar data from Emergency Medicine Institute (EMI) and surgical departments**

Setting	Surveillance time-period	Data source Pharmacy dispensing	Frequency of data collection	Use of antibiotics in DDD/1000 bed-days over the study period
Emergency Medicine Institute	6 years (2009–2014)	records (PDR)	Annual	662.4, hospital-wide in 2009; 464.1, hospital-wide in 2014
Septic surgery department of EMI	6 years (2009–2014)	(PDR)	Annual	680, department-wide in 2009; 349, department-wide in 2014.
1115 hospitals in France [14]	3 years (2008–2010)	(PDR)	Annual	370.0, hospital-wide in 2008; 393.0, hospital-wide in 2010.
34 public public hospitals and 43 private hospitals located in south-western France [15]	2005	(PDR)	Annual	395, hospital-wide; 422, hospital-wide.
49-59 hospitals in The Netherlands [16] medium 54 hospitals	5 years (1997–2001)	(PDR)	Annual	472.0 hospital-wide in 1997; 547.0 hospital-wide in 2001.
55 public hospitals in Denmark [17]	5 years (1997–2001)	Danish Medicines Agency	Annual	380.0 hospital-wide in 1997; 448.0 hospital-wide in 2001.
1 university hospital in Switzerland [18]	5 years (1996–2000)	(PDR)	Not specified	400.0 hospital-wide.
Military Medical Academy, Sofia, Bulgaria [19]	1 year (2011)	(PDR)	Annual	403.0 hospital-wide.
1 general hospital in Spain [20]	5 years (1996–2000)	(PDR)	Annual	595.0 hospital-wide.
8 university hospitals in Germany [21]	3 years (1998–2000)	(PDR)	Annual	601.0 medical wards; 793.0 surgical wards.
40 non-university regional acute care general hospitals in southwestern Germany, 2001-2002 [22]	2 years (2001–2002)	(PDR)	Annual	499.0 with a mean in internal medicine; 434.0 surgery 4with a mean in surgery.
530 French hospitals in 2007 from wich195 in general and 357 for hospitals detailed clinical surgery activity [23]	1 years (2007)	(PDR)	Annual	557.0 in medicine; 553.0 in surgery.

Table 2 states that the average annual rate for total-hospital antibiotics utilization period in EMI decreased from 662.4 in 2009 to 464.1 DDD/1000 in 2014 or by 30%.

The results of 464.1 DDD/1000 recorded in EMI in 2014 was higher with 67.61 DDD/1000 or 14.57% than the medium consumption of 396.49 DDD/1000 registered in case of 1249 International hospitals [(1115x393 + 34x395 + 43x422 + 55x448 + 1x400 + 1x403) : 1249] and lower with 84.59 DDD/1000 or with 18.23% in case of 298 International hospitals where the mentioned medium was 548.69 DDD/1000 [(8x601 + 54x547 + 1x595 + 40x499 + 195x583) : 298] respectively.

The overall medium consumption in 1547 (1249+298) International hospitals constituting 425.81 DDD/1000 was less than consumption of 464.1 DDD/1000 in EMI in 2014 with 38.29 DDD/1000 or with 8.25%.

That decrease in septic surgery department of EMI was from 680 in 2009 to 349 DDD/1000 in 2014 or by 48.68%.

In case of 405 International hospitals medium consumption in clinical surgery activity was (8x793 + 40x434 + 357x553) : 405 = 545.99 DDD/1000, that was with 196.99 DDD/1000 more than results recorded in surgery department of EMI in 2014 or by 56.44%.

In figure 4 the total consumption of other beta-lactam antibacterials for parenteral and enteral use in DDD/1000 is demonstrated.

The chart 4 demonstrates the total consumption for the evaluated period of parenteral and enteral forms of cephalosporin's G-I (Cefalexin and Cefazolinum) has decreased form 181.3 to 67.66 or with 62.68%. The cephalosporin's G-II (Cefuroximum, Cefaclorum) and G-III (Cefotaximum, Ceftazidimum, Ceftriaxonum, Cefixim, Cefoperazonum, Cefoperazonum + Sulbactamum) as well decreased the consumption form 127.69 (25.69 + 102) in 2009 to 119.01 DDD/1000 (33.67 + 85.34) or by 6.80%. The cephalosporin's G-IV (Cefepimium) had some consumption only in 2010-2011, and carbapemens (Meropenemum, Imipenemum + Cilastatinum) had decreased from 1.07 to 0.25 DDD/1000. The total consumption of the group encounters a decrease from 310 to 187 DDD/1000 or with 39.68%.

The value cost of DDD/1000 in lei for parenteral forms of antibacterials for systemic use during 2009-2014 in figure 5 is shown.

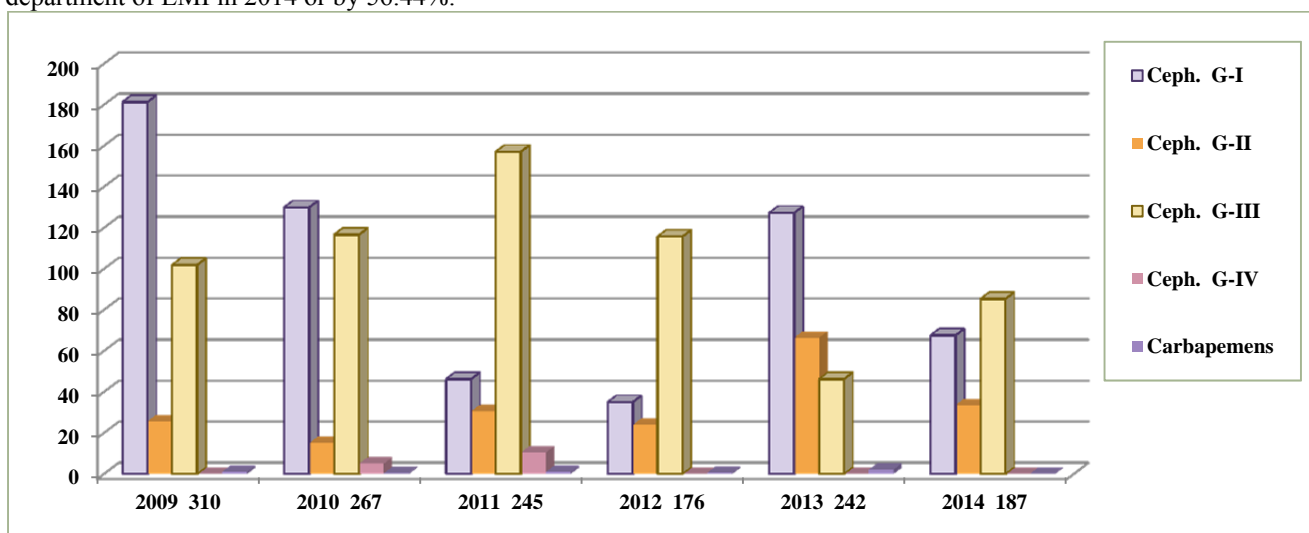


Fig. 4. Total consumption of other beta-lactam antibacterials for parenteral and enteral use in DDD/1000

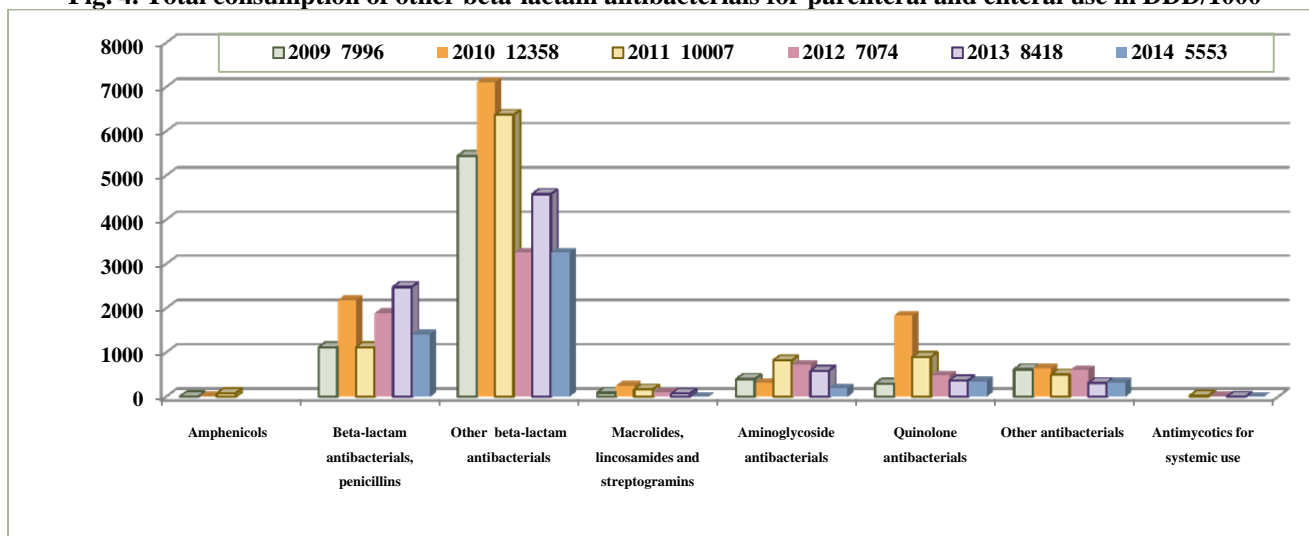


Fig. 5. Value cost of parenteral forms of antibacterials for systemic use per DDD/1000 in lei

Figure 5 states that for the evaluated period, the average consumption annual rate in value indexes (lei) of all antibiotic subgroups recorded a decline from 7996 in 2009 to 5553 lei per DDD/1000 in 2014 or by 30.55%. The consumption more than 1000 lei per DDD/1000 were registered for other beta-lactam antibacterials form 5448.64 to 3258.1 lei and beta-lactam antibacterials from 1124.43 to 1413.7 lei respectively.

The consumption rate of DDD/1000 in value indexes (lei) for antibiotic subgroups of enteral forms remedies evaluated during 2009-2014 in figure 6 is shown.

From figure 6 can be derived that for the evaluated period the average consumption annual rate in value indexes (lei) of all antibiotic subgroups recorded a decline from 318 in 2009 to 177 lei per DDD/1000 in 2014 or by 44.34%. The

consumption more than 100 lei per DDD/1000 was registered for antimycotics for systemic use from 183.54 lei in 2009 to 175.87 lei in 2012.

The total institutional antibiotic consumption in value indexis varied from 1562575 lei in 2009 to 1500888 lei in 2014 that represents respectively 17% and 14% from whole amount of drugs [24, 25]. The same data for septic surgery department were 116707 lei in 2009 and 69457 lei in 2014 or 23.50% and 19.85% from whole amount of drugs, and 7.47% and 4.63% from the total institutional antibiotics consumption respectively.

The consumption share in value indexes (lei) of parenteral and enteral forms of antibiotics subgroups in DDD/1000 during 2009-2014 is shown in figure 7.

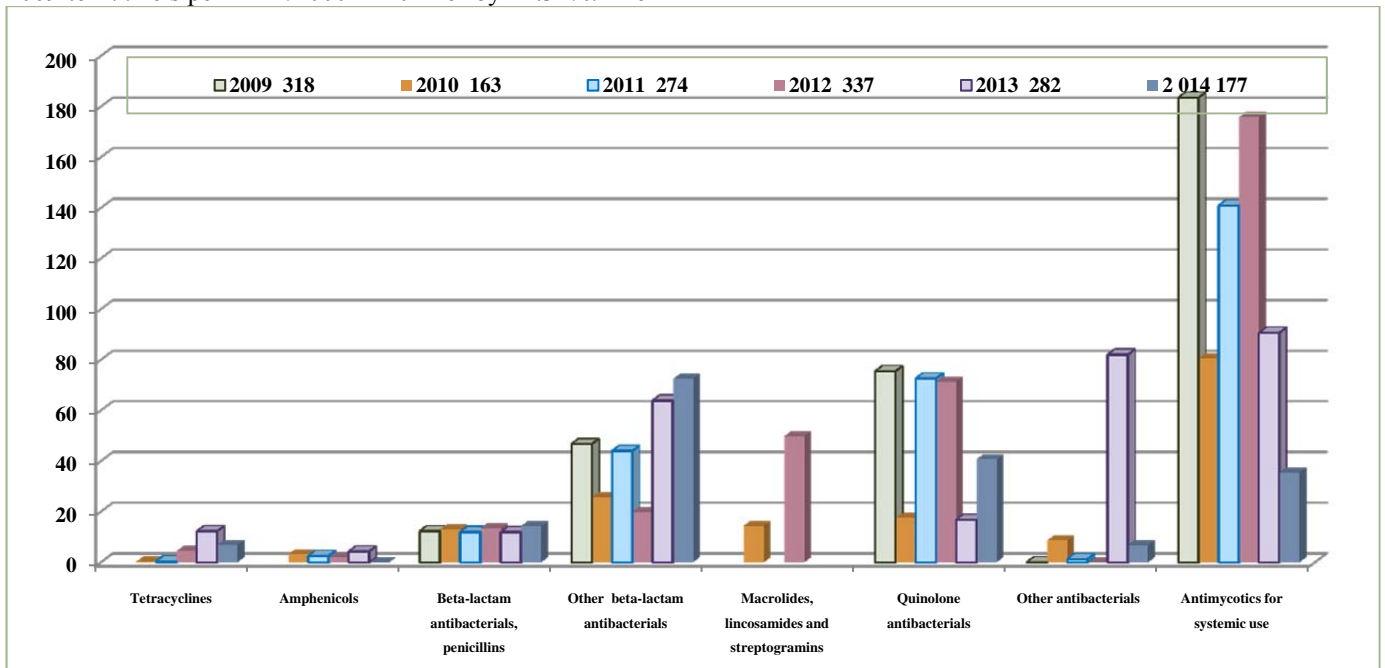


Fig. 6. Value cost for enteral forms of antibacterials for systemic use per DDD/1000 in lei

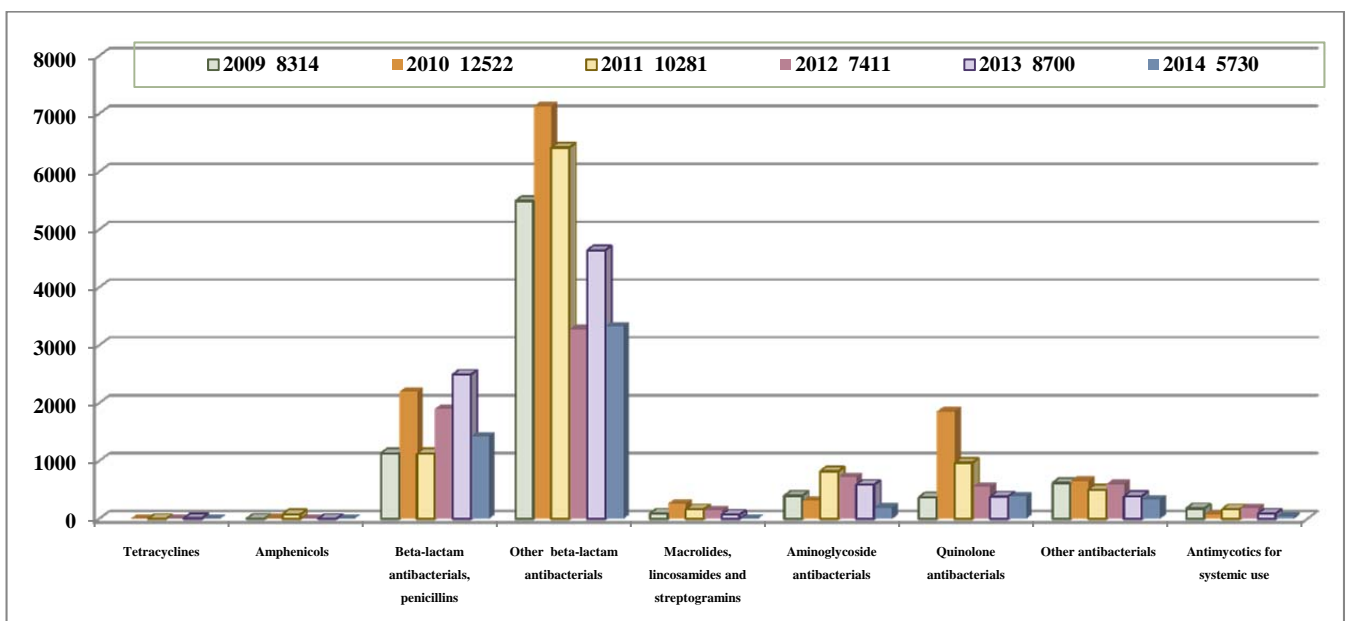


Fig. 7. Total value cost of antibacterials for systemic use per DDD/1000 in lei

Cost of one medium DDD antibacterial for systemic use of parenteral, enteral forms and total in leis Table 3

Surgical septic department						
Data for determining and cost	2009	2010	2011	2012	2013	2014
Parenteral cost lei DDD/1000	7996	12358	10007	7074	8418	5553
Enteral cost lei DDD/1000	318	164	274	337	282	177
Parenteral and enteral cost lei DDD/1000	8314	12524	11028	7411	8700	5730
Parenteral DDD/1000	610	524	435	378	433	260
Enteral DDD/1000	70	26	85	141	88	89
Parenteral and enteral DDD/1000	680	549	519	521	521	349
Parenteral cost lei 1 (one) DDD	13.1	23.61	23.02	18.73	19.44	21.36
Enteral cost lei 1 (one) DDD	4.57	6.35	3.22	2.39	3.2	1.99
Total cost lei 1 (one) DDD	12.23	22.81	19.81	14.22	16.7	16.44

Cost of one medium DDD other beta-lactam antibacterials in leis for parenteral and enteral forms and total Table 4

Septic surgical department						
Data for determining and cost of one DDD in leis	2009	2010	2011	2012	2013	2014
Parenteral cost lei DDD/1000	5449	7109	6375	3260	4581	3258
Enteral cost lei DDD/1000	47	26	44	20	64	73
Parenteral and enteral cost lei DDD/1000	5495	7134	6419	3280	4645	3331
Parenteral DDD/1000	610	525	435	381	433	265
Enteral DDD/1000	70	26	85	141	88	89
Parenteral and enteral DDD/1000	680	550	520	522	522	354
Parenteral cost lei one DDD	8.08	12.97	12.35	6.28	8.91	9.41
Enteral cost lei one DDD	0.67	1.00	0.52	0.14	0.73	0.81
Total (Parenteral and enteral) cost lei one DDD	8.93	13.55	14.67	8.56	10.58	12.30

In chart 7 the presented data demonstrates that for the evaluated period the average consumption annual rate in value indexes of all antibiotic subgroups recorded a decline from 8314 in 2009 to 5730 leis per DDD/1000 in 2014 or by 31.08%. The cost of DDD/1000 more than 1000 leis were registered for 2 subgroups. First, with the highest in different years of the evaluated period, the cost of DDD/1000 varied from 7134.2 leis to 3279.76 leis for other beta-lactam antibacterials. The second record was ranked by beta-lactam antibacterials, penicillins from 249.45 leis to 1134.81 leis for the same period.

To determine the cost of one medium DDD for systemic use antibacterials and for other beta-lactam antibacterials, separately for parenteral and enteral pharmaceutical forms were divided the value cost of DDD/1000 to the DDD/1000 respectively. The obtained results in table 3 and 4 in leis is shown.

Table 3 demonstrates the total cost of one medium DDD that increased from 12.23 leis in 2009 to 16.44 leis in 2014 or by 34.42%, for parenteral from 13.1 to 21.36 or by 63.05% and for enteral use this cost registered a decrease from 4.57 to 1.99 or by 2.30 times.

The ratio between cost of one medium DDD of parenteral and enteral forms were respectively 2.87:1; 3.72:1; 7.15:1; 7.84:1; 6.08:1 and 10.73:1 for the evaluated years.

The calculation of one medium DDD cost in leis for parenteral and enteral forms as well as the total for other beta-lactam antibacterials in table 4 is shown. The total cost of one medium DDD has increased from 8.93 in 2009 to 12.30 leis in 2014 or by 37.74%. For parenteral forms, from 8.08 to 9.41 leis or by 16.46% and for enteral forms 0.67 to 0.81 leis or by 20.90%.

The ratio between cost of one medium DDD of parenteral and enteral forms were respectively 12.06:1; 12.97:1;

23.75:1; 44.86:1; 12.21:1; and 11.62:1 for the evaluated years.

#### CONCLUSIONS:

1. The average annual institutional rate for the total antibiotics consumption for the stated period in EMI, had decreased from 662.4 in 2009 to 464.1 DDD/1000 OBD in 2014 or by 30%. The overall medium consumption in 1547 International hospitals constituting 425.81 DDD/1000 was less than 38.29 DDD/1000 or with 8.25% than the consumption in 2014 in EMI.
2. A considerable decrease in the evaluated period was registered in EMI septic surgery department from 680 in 2009 to 349 DDD/1000 in 2014 respectively or by 48.68%. In case of 405 International hospitals the medium consumption in clinical surgery activity (data from 1996, 1997, 1998, 2000, 2001, 2002, 2007, 2008 and 2010) were 545.99 DDD/1000, or with 134 less than the same data from 2009 and with more than 196.99 DDD/1000 results recorded in septic surgery department in 2014.
3. A departmental decrease from 610 in 2009 to 265 DDD/1000 in 2014 or by 56.56% for antibiotics with parenteral forms and vice versa for the ones with enteral use forms increased consumption from 70 to 89 DDD/1000 or by 27.14%.
4. There were evaluated 50 antimicrobial remedies (for parenteral and enteral use) treating the assistance of hospitalized patients in the evaluated period were used, from which with only enteral form 22 names, with only parenteral form 28 names and with both forms 10 names, which represents 39 active antimicrobial substances.

5. Total institutional antibiotic consumption in value index varied from 1562575 leis in 2009 to 1500888 leis in 2014 that represents 17% and 14% from whole amount of drugs [18, 19]. The same data for septic surgery department were 116707 leis in 2009 and 69457 leis in 2014 or 23.50% and 19.85% from whole amount of drugs, and 7.47% and 4.63% from the total institutional antibiotics consumption respectively.
6. The cost of DDD/1000 registered 8314 leis at the beginning and 5559 leis at the end of the evaluated period or a decline with 33.1%, and vice versa the cost of 1 (one medium DDD) increased from 12.33 leis in 2009 to 16.44 leis in 2014 or with 33.3%.
7. The ratio between parenteral and enteral forms cost of 1 (one) medium DDD antibacterials for systemic use were 2.87:1; 3.72:1; 7.15:1; 7.84:1; 6.08:1 and 10.73:1 for the evaluated years. For other beta-lactam antibacterials this ratio was 12.06:1; 12.97:1; 23.75:1; 44.86:1; 12.21:1; and 11.62:1 respectively.

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