

AKADEMIJA MEDICINSKIH ZNANOSTI HRVATSKE  
KOLEGIJ JAVNOG ZDRAVSTVA, ODBOR ZA PRAĆENJE REZISTENCIJE  
BAKTERIJA NA ANTIBIOTIKE U REPUBLICI HRVATSKOJ  
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## **Potrošnja antibiotika u Hrvatskoj Antibiotic consumption in Croatia**

### **European Surveillance of Antibiotic Consumption (ESAC)**

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## Potrošnja antibiotika u Hrvatskoj

Sistematsko praćenje potrošnje antibiotika u Hrvatskoj, izraženo u definiranim dnevnim dozama na tisuću stanovnika dnevno, započelo je u okviru European Surveillance of Antibiotic Consumption (ESAC) projekta kojeg je pokrenula Europska zajednica 2001.g. Do tada dostupni podatci o potrošnji antibiotika u Hrvatskoj bili su izražavani u količini potrošenih financijskih sredstava što je ovisilo i o skupoći lijeka, a ne samo o količini prodanog lijeka te se nije moglo uspoređivati s razinom rezistencije bakterija na antibiotike u Hrvatskoj. Podatci o potrošnji antibiotika u ovom izvješću dobiveni su na osnovi podataka veleprodaje i izraženi prema preporukama ESAC-a tj. kao broj definiranih dnevnih doza (DDD) na tisuću stanovnika dnevno. Odvojeno su prikazani podatci za izvanbolničku (tablica 1) i za bolničku (tablica 2) potrošnju. DDD su određene prema normama Svjetske zdravstvene organizacije (WHO ATC/DDD klasifikacija).

Tijekom zadnjih šest godina, od kako su dostupni podatci o potrošnji antibiotika u Hrvatskoj, izvanbolnička potrošnja antibiotika raste (slika 1) uz najveći skok potrošnje zabilježen 2002.g., što je, međutim, prvenstveno bio odraz uvođenja novog preparata ko-amoksiklava s povećanim udjelom amoksicilina u dnevnoj dozi, a ne povećanog broja prodanih paketića. U 2005.g. je ponovno došlo do porasta izvanbolničke potrošnje antibiotika. Među beta-laktamskim antibioticima došlo je do porasta antibiotika širokog spektra (beta-laktama s inhibitorima beta-laktamaza, cefalosporina II i III generacije) te pada potrošnje penicilina uskog spektra što predstavlja negativan trend u propisivanju antibiotika. Porasla je i potrošnja drugih grupa antibiotika, prvenstveno makrolida, ali i tetraciklina i kinolona što je rezultiralo porastom ukupne izvanbolničke potrošnje antibiotika na 23.57 DDD/TID.

U okviru ESAC projekta potrošnja antibiotika u bolnicama prikazuje se u vrlo grubim podacima (izražena na 1000 stanovnika dnevno) zbog teškog usklađivanja denominatora među različitim državama. Podatci o bolničkoj potrošnji za cijelu Hrvatsku dobiveni su preko podataka veleprodaje i prikazani su u tablici 2. Ovi podatci omogućuju komparaciju bolničke potrošnje u Hrvatskoj s potrošnjom u ostalim zemljama Europe, no ne pružaju dovoljno kvalitetne podatke za analizu bolničke potrošnje antibiotika u Hrvatskoj. Odbor je, stoga, 2004.g. pokrenuo individualno praćenje potrošnje antibiotika u bolnicama uz mogućnost odvojenog prikazivanja potrošnje u jedinicama intenzivne medicine te uz prikaz broja primitaka i broja bolničkih dana kao denominatora, što je prikazano kao posebna studija.

### *Potrošnja antibiotika u bolnicama*

U okviru Odbora za praćenje rezistencije bakterija na antibiotike u Republici Hrvatskoj i APUA Croatia tijekom 2005. godine prikupljeni su podatci o bolničkoj potrošnji antimikrobnih lijekova (grupa J01 po ATC klasifikaciji SZO) za 2004.godinu. U istraživanju je sudjelovalo 11 bolnica, od kojih su četiri bile kliničke, a sedam županijskih.

Podaci o potrošnji antimikrobnih lijekova dobiveni su iz bolničkih ljekarni i upisani u ABC kalkulator, verzija 3.0 (2005). Odvojeno je prikazana potrošnja antimikrobnih lijekova za cijelu bolnicu te potrošnja u jedinicama intenzivnog liječenja (JIL) i prema vrstama JIL-a (kirurški, internistički, opći, pedijatrijski). Potrošnja antimikrobnih lijekova izražena je u definiranim dnevnim dozama (DDD), a kao denominatori su uzeti bolnički dani (BOD) i broj primitaka.

U većini bolnica potrošnja antibiotika se kreće između 40 i 50 DDD/100 BOD. Samo u dvije bolnice ona iznosi ispod 40 DDD/100 BOD, odnosno u dvije iznad 50 DDD/100BOD. Između kliničkih bolnica potrošnja je iznimno raznolika, što ovisi o vrsti, odnosno specijalističkom profilu bolnice. Očekivano, najviša potrošnja antibiotika na broj bolničkih dana zabilježena je u Klinici za infektivne bolesti, a najviša ukupna potrošnja antibiotika u KBC Zagreb.

Potrošnja  $\beta$  laktamskih antibiotika (J01C; J01D) čini više od 50% ukupne antibiotičke potrošnje unutar svake bolnice. Kod penicilinske skupine najveća je potrošnja kombinacije (J01 CR); tj. amoksicilina i klavulanske kiseline. Kod cefalosporinske skupine (J01D) uočavaju se velike razlike u propisivanju. U većini bolnica najveća je potrošnja cefalosporina 2. generacije (J01 DC). Potrošnja karbapenema u svim županijskim bolnicama je ispod 1 DDD/100 BOD, dok se u kliničkim bolnicama kreće u rasponu od 1-3 DDD/100 BOD.

Kinoloni su skupina s najvećom varijabilnošću u potrošnji među praćenim bolnicama (slika 2).

Potrošnja antibiotika u JIL-u uočljivo varira, što ovisi o tipu bolnice i vrsti JIL-a. U županijskim bolnicama ta potrošnja se kreće iznad 100 DDD/ 100 BOD (osim u bolnici V).

Ovim praćenjem, po prvi puta su prikupljeni i obrađeni podatci o potrošnji antimikrobnih lijekova dobiveni iz bolničkih ljekarni 11 bolnica u Hrvatskoj. Iako je time obuhvaćen samo dio bolničke potrošnje, uočavaju se određene specifičnosti u upotrebi antibiotika ovisno o bolnici, što govori o određenim navikama u propisivanju antibiotika u lokalnoj sredini . Ovi podatci su tek početak kontinuiranog praćenja bolničke potrošnje antimikrobnih lijekova, koji će u slijedećem vremenskom razdoblju omogućit povezivanje potrošnje antibiotika i nastanka rezistencije u određenim sredinama. Cilj je optimalna i racionalna antibiotska terapija te obuzdavanje rezistencije bakterija na antibiotike.

## **Antibiotic consumption in Croatia**

Continuous surveillance of antibiotic consumption expressed in defined daily doses per thousand inhabitants daily (DDD/TID) was first introduced in Croatia through the European Surveillance of Antibiotic Consumption (ESAC) project that was initiated by the European Union in 2001. Before 2001 antibiotic consumption data available in Croatia were expressed in terms of financial means spent which depended not only on the amount of a drug spent but also on the price of the drug and thus was not suitable for correlation with antibiotic resistance rates in Croatia. In this report antibiotic consumption results are based on the wholesales data for the whole Croatia and are expressed as DDD/TID. Ambulatory (table 1) and hospital (table 2) consumption data are reported separately. DDDs are determined by the World health organization (WHO ATC/DDD classification).

During the last six years since the antibiotic consumption data are available there is a constant increase in ambulatory antibiotic consumption (figure 1) and the biggest increase was recorded in 2002 which was mostly due to the introduction of the new co-amoxiclav bid formula with the increased amoxicillin content in a daily dose without a parallel increase in the number of packages. In 2005 antibiotic consumption is still increasing. Among beta-lactam antibiotics consumption of broad spectrum antibiotics (beta-lactams with beta-lactamase inhibitors, II and III generation cephalosporins) is increasing and consumption of narrow spectrum penicillins is decreasing which is a negative trend in antibiotic prescribing. There is also an increase in consumption of other antibiotic classes, particularly macrolides, but also tetracyclines and quinolones, resulting in the increase of the total ambulatory consumption that reaches 23.57 DDD/TID.

In the ESAC project hospital antibiotic consumption is presented with very rough data (expressed in DDD per thousand inhabitants daily) because it was difficult to harmonize denominators among different countries.

U okviru ESAC projekta potrošnja antibiotika u bolnici prikazuje se u vrlo grubim podacima (izražena na 1000 stanovnika dnevno) zbog teškog usklađivanja denominatora među različitim državama. Hospital antibiotic consumption data for the whole Croatia were obtained through wholesales data and are presented in table 2. These data enable the comparison of hospital consumption in Croatia with consumption in other European countries but do not provide a possibility for a detailed analysis of hospital consumption in Croatia. In 2004 the Committee has, therefore, started antibiotic consumption surveillance in individual hospitals which provides opportunity to analyse antibiotic consumption in intensive care units separately, and with linking consumption data to the number of admissions and the number of bed days. These data are presented separately.

### *Hospital antibiotic consumption*

In 2005 the Committee for antibiotic resistance surveillance and the APUA Croatia Chapter started collecting hospital antibiotic consumption data. Consumption data for antibiotics (J01 group according to the WHO ATC classification) were collected retrospectively for 2004. Altogether 11 hospitals, four university and seven county hospitals, took part in the study.

Antibiotic consumption data were provided by the hospital pharmacy and entered in the ABC calculator, version 3.0 (2005). Antibiotic consumption in intensive care units (ICU), characterized as medical, surgical and paediatric ICU are presented separately from the data for the whole hospital. Antibiotic consumption is expressed in defined daily doses (DDD) and hospital admissions and hospital bed days (BD) are used as denominators.

In the majority of hospitals antibiotic consumption was between 40 and 50 DDD/100 BD. Antibiotic consumption was below 40 DDD/100 BD in two hospitals only, and above 50 DDD/100BD in another two hospitals. There is a great variation in antibiotic consumption among the hospitals depending on the type and specific profile of the hospital. Not surprisingly the highest antibiotic consumption per 100 BD was recorded in the University hospital for Infectious diseases, whereas the highest total antibiotic consumption was recorded in the Clinical hospital center Zagreb.

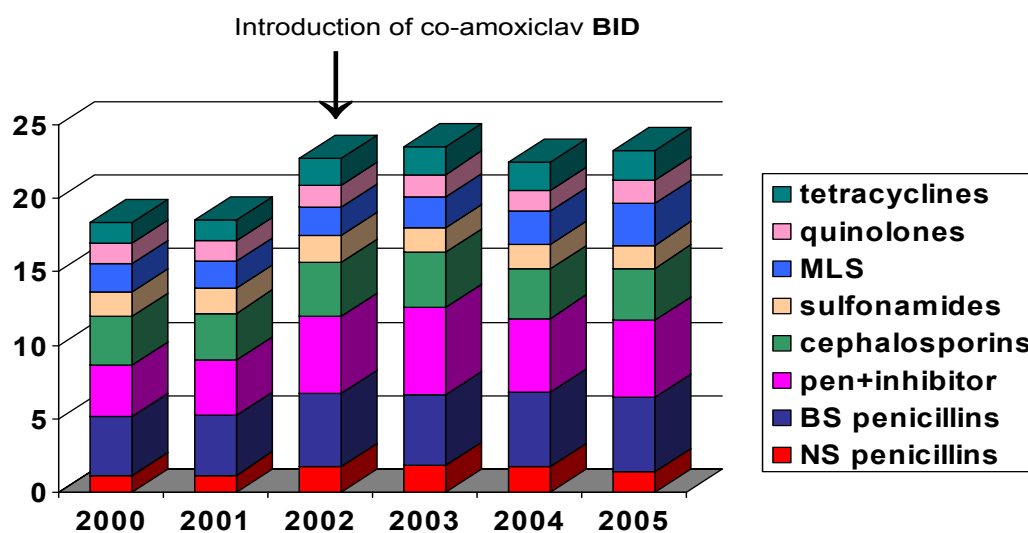
$\beta$ -lactam antibiotics (J01C; J01D) comprise over 50% of total antibiotic consumption in each of the participating hospitals. Among penicillins, combinations of amoxicillin and beta-lactamase inhibitors (J01 CR) are used most. There is a great variation in prescribing cephalosporins (J01D) among hospitals. In most hospitals II generation cephalosporins (J01 DC) are predominant cephalosporins used. Carbapenem consumption in all county hospitals is below 1 DDD/100 BD, whereas in the university hospitals it is between 1 and 3 DDD/100 BD.

Fluoroquinolones are used with great diversity among hospitals (figure 2).

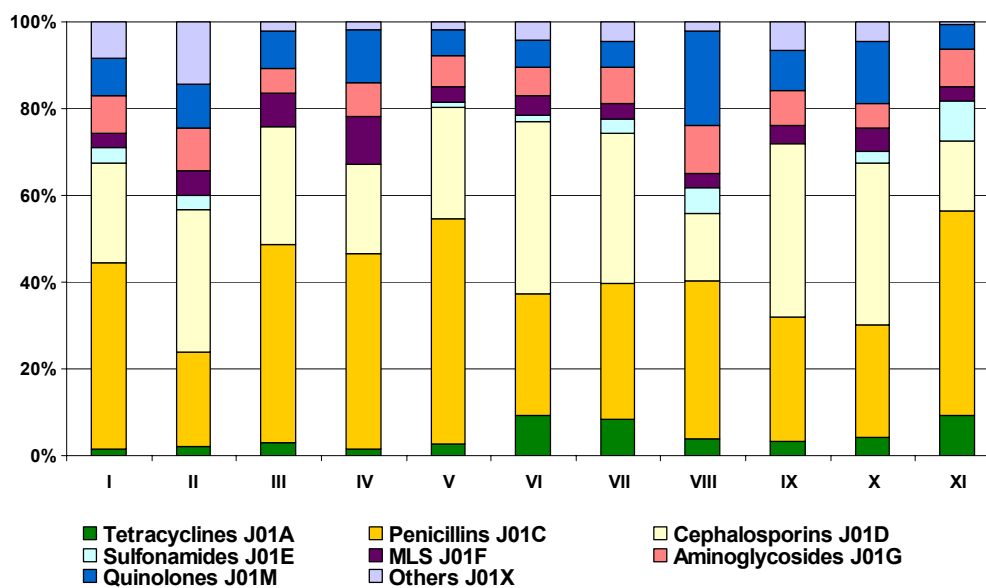
Antibiotic consumption in ICU varies greatly depending on the type of hospital and type of the ICU (figure 4). In county hospitals it is above 100 DDD/ 100 BD (except in the hospital V).

This is the first Croatian study based on the antibiotic consumption data obtained from the 11 hospitals. Although the total hospital consumption in Croatia was not covered certain trends in individual hospitals could be demonstrated. These data are only the beginning of a hopefully continuous antibiotic consumption surveillance which will enable better understanding of antibiotic prescribing habits and its influence on antibiotic resistance rates in individual hospitals. The aim of this study is rationalization in antibiotic prescribing and control of antibiotic resistance spread.

**Slika 1 Figure 1**  
**Izvanbolnička potrošnja antibiotika 2000 - 2005**  
**Ambulatory antibiotic consumption 2000 - 2005**

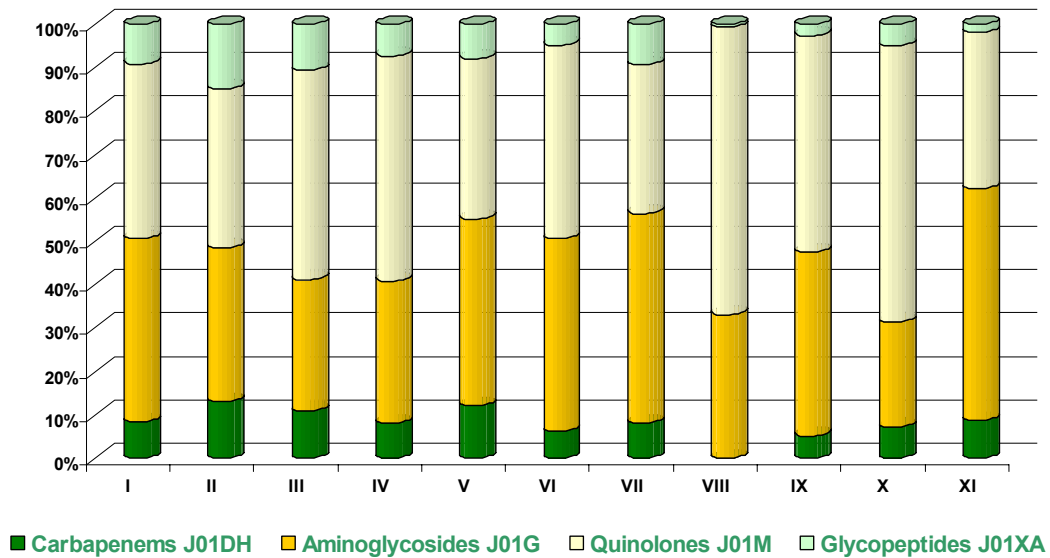


**Slika 2 Figure 2**  
**Udio pojedinih grupa antibiotika u potrošnji antibiotika u 11 bolnica, 2004**  
**Relative frequency of antibiotic consumption in 11 hospitals, 2004**



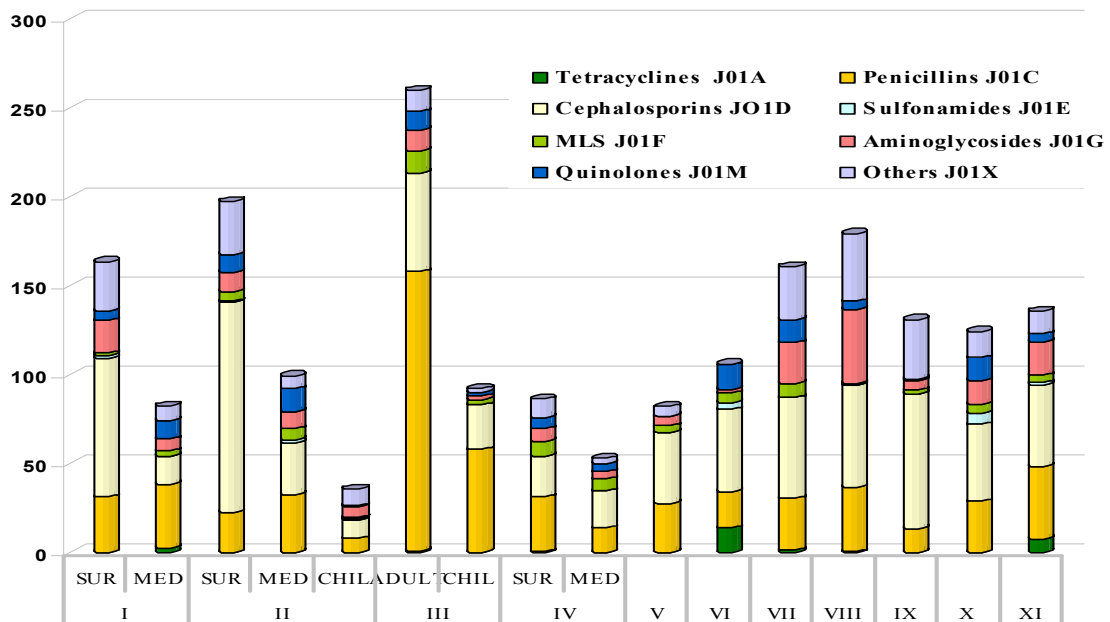
**Slika 3 Figure 3**

**Udio pojedinih grupa za bolnicu specifičnih antibiotika u 11 bolnica, 2004**  
**Relative frequency of hospital specific antibiotics in 11 hospitals, 2004**



**Slika 4 Figure 4**

**Udio pojedinih grupa za bolnicu specifičnih antibiotika u 11 bolnica, 2004**  
**Relative frequency of hospital specific antibiotics in 11 hospitals, 2004**



**Tablica 1. Table 1****Izvanbolnička potrošnja antibiotika (DDD/TID)****Ambulatory antibiotic consumption (DDD/TID)**

ATC šifra ATC code	ANTIBIOTIK ANTIBIOTIC	2001	2002	2003	2004	2005
JO1AA	Tetraciklini Tetracyclines	1.39	1.82	1.90	1.91	2.01
JO1CA	Penicilini širokog spektra Broad spectrum penicillins	4.09	4.95	4.82	5.10	5.07
JO1CE	Penicilini uskog spektra Narrow spectrum penicillins	1.18	1.78	1.85	1.71	1.42
JO1CF	Beta-laktamaza rezistentni penicilini Beta-lactamase resistant penicillins	0.06	0.06	0.06	0.06	0.05
JO1CR	Kombinacije s beta- laktamaza inhibitorima	3.77	5.21	5.9	5.29	5.39
JO1DA	Cefalosporini I gen. I gen. cephalosporins	1.65	1.99	1.94	1.87	1.85
	Cefalosporini II gen. II gen. cephalosporins	1.14	1.34	1.37	1.29	1.39
	Cefalosporini III gen. III gen. cephalosporins	0.38	0.35	0.44	0.35	0.42
JO1EE	Sulfonamides + trimethoprim	1.70	1.85	1.72	1.64	1.57
JO1F	Macrolides, lincosamides	1.88	1.92	2.07	2.27	2.82
JO1G	Aminoglycosides	0.06	0.04	0.01	0.01	0.01
JO1MA	Fluoroquinolones	1.34	1.52	1.53	1.47	1.57
<b>UKUPNO TOTAL</b>		<b>18.65</b>	<b>22.86</b>	<b>23.61</b>	<b>22.97</b>	<b>23.57</b>

**Tablica 2. Table 2**

**Bolnička potrošnja antibiotika (DDD/TID)  
Hospital antibiotic consumption (DDD/TID)**

ATC šifra ATC code	ANTIBIOTIK ANTIBIOTIC	2001	2002	2003	2004	2005
JO1AA	Tetracyclines	0.07	0.12	0.15	0.08	0.09
JO1CA	Penicilini širokog spektra Broad spectrum penicillins	0.27	0.30	0.33	0.15	0.15
JO1CE	Penicilini uskog spektra Narrow spectrum penicillins	0.08	0.24	0.35	0.20	0.14
JO1CF	Beta-laktamaza rezistentni penicilini Beta-lactamase resistant penicillins	0.03	0.04	0.04	0.03	0.03
JO1CR	Kombinacije s beta-laktamaza inhibitorima	0.52	0.64	0.79	0.40	0.36
JO1DA	Cefalosporini I gen. cephalosporins	0.14	0.20	0.17	0.09	0.11
	Cefalosporini II gen. cephalosporins	0.26	0.28	0.19	0.27	0.25
	Cefalosporini III + IV gen. cephalosporins	0.09	0.09	0.12	0.09	0.12
JO1DH	Carbapenems	0.01	0.02	0.02	0.02	0.02
JO1EE	Sulfonamides + trimethoprim	0.09	0.14	0.20	0.09	0.08
JO1F	Macrolides, lincosamides	0.13	0.14	0.16	0.10	0.12
JO1G	Aminoglycosides	0.11	0.15	0.12	0.10	0.11
JO1MA	Fluoroquinolones	0.16	0.18	0.22	0.15	0.18
JO1XA	Glycopeptides	0.02	0.02	0.02	0.02	0.02
JO1XD	Metronidazole	0.03	0.06	0.06	0.01	0.06
<b>UKUPNO TOTAL</b>		<b>2.04</b>	<b>2.52</b>	<b>2.94</b>	<b>1.80</b>	<b>1.84</b>