

# EVALUATION OF ANTIBIOTIC CONSUMPTION AT RAKOVICA COMMUNITY HEALTH CENTER FROM 2011 TO 2015

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## EVALUACIJA POTROŠNJE ANTIBIOTIKA U DOMU ZDRAVLJA RAKOVICA U PERIODU 2011\_2015. GODINA

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### ABSTRACT

Antibacterial drugs are among the major discoveries of the 20<sup>th</sup> century because they significantly reduced the rate of morbidity and mortality as well as the risk of infections related to invasive medical procedures. Indiscriminate and wrongful use of these powerful life-saving drugs has led to the development of resistance of numerous microorganisms, resulting in an increase in the number of hospital-acquired infections with a fatal outcome. Thus, it is very important to establish the volume of antibiotic consumption and surveillance of antimicrobial resistance in order to rationalize the use of this important group of medications. The usage unique ATC/DDD methodology results expressed as Defined Daily Doses (DDD)/1000 inhabitants per day (DID) has enabled the comparison of antibiotic consumption in Serbia to that in other countries for a better understanding of our results. The community health center in Rakovica provides treatment for approximately 70,820 patients. The volume of overall antibiotic consumption has been calculated as well as the use of certain antibiotics in the total consumption and comparison of the guides for good clinical practice. The most prescribed antibiotics were antibiotics for diseases of the respiratory system. The most prescribed groups of antibiotics were penicillin drugs, which are an optimal choice as per the guides for good clinical practice. Amoxicillin are the most frequently prescribed individual antibiotic. A yearly increase in prescribing penicillin was observed. A rise in consumption of all generations of quinolones was observed, particularly for levofloxacin, which is not in accordance with the recommendations.

**Keywords:** Rational use of antibiotics, DID, antibiotic consumption

### SAŽETAK

Antibakterijski lekovi su među najvećim otkrićima 20. veka, jer su znatno smanjili stopu obolevanja i smrtnosti od infektivnih bolesti i rizik od infekcije kod invazivnih medicinskih procedura. Neodgovorna i pogrešna upotreba ovih moćnih lekova koji spasavaju život dovela je do razvoja rezistencije mnogih mikroorganizama na njih, a rezultat toga je i porast bolničkih infekcija sa smrtnim ishodom. Veoma je važno utvrđivanje obima potrošnje antibiotika i nadzora nad antimikrobnom rezistencijom, radi racionalizacije upotrebe ove važne grupe lekova. Primenjena je jedinstvena ATC/DDD metodologija, rezultati su izraženi kao broj upotrebljenih definisanih dnevnih doza (DDD)/1000 stanovnika /dan (DID) omogućila je poređenje potrošnje antibiotika u Srbiji sa drugim zemljama i bolje razumevanje naših rezultata. U Domu zdravlja Rakovica leči se oko 70820 pacijenata. Izračunat je obim ukupne potrošnje antibiotika kao i učešće pojedinih antibiotika u ukupnoj potrošnji i poređenje sa vodičima dobre kliničke prakse.

Najviše su propisivani antibiotici za bolesti respiratornog sistema. Najpropisivanija grupa antibiotika su penicilini, što je u skladu sa vodičima dobre kliničke prakse. Zapažen je porast propisivanja penicilina iz godine u godinu sa dominacijom amoksicilina. Zapaža se i porast propisivanja hinalona, posebno levofloksacina, što nije u skladu sa preporukama vodiča dobre kliničke prakse.

**Ključne reči:** racionalna upotreba antibiotika, DID, potrošnja antibiotika





## INTRODUCTION

In 1985, the World Health Organization (WHO) defined the rational use of drugs as a process in which the patients obtain medications that suit their needs, in doses suitable for them, within an appropriate length of time and at the lowest cost for them and the society they live in (1).

Currently, the irrational use of medications, with all of its negative implications, represents a continuing process that takes on increasing proportions and is thus considered to be one of the biggest global public health issues (2).

Of all the drugs, antibiotics have played the greatest role in indiscriminate drug prescriptions. The discovery and use of antimicrobial drugs for the treatment of infections constitutes the biggest success of modern medicine. Approximately 80 % of all antibiotics prescribed in health care institutions are being prescribed within primary health care settings and most frequently for respiratory tract infections. A non-clinical factor, such as the pressure that is exerted on doctors by the patients, also has a large impact on antibiotic prescriptions, but the doctors themselves prescribe antibiotics quite often and unjustifiably (3). A study has been performed involving patients with symptoms of cough where antibiotics are quite frequently administered, showing that there is no difference in the degree of recovery between the patients treated with antibiotics and the ones who did not receive them (4).

The introduction of a mandatory continuing medical education (CME) requirement for health workers in the Republic of Serbia regulated by the Law on Health Care and Rules will probably have an impact on solving this problem.

Apart from other public health measures that have led to the extension of life expectancy, the use of antibiotics is certainly of great importance. However, the success in treatment of infections is compromised by their irrational use, which has led to bacterial resistance of these medications. Irrational use is defined as microbiologically inefficient antimicrobial therapy that can have adverse effects on the outcome of treatment. The irrational use of antimicrobial drugs is important not only from the clinical aspect, i.e. because of the outcome of the patient treatment, but also from the public health aspect since it represents one of the main factors for the emergence of resistance of infectious agents (5).

With an aim at preventing resistance, antimicrobial drugs should be administered rationally, which according to current concepts means that their usage should not be empirical but rather targeted and based on diagnostic evidence.

Over the last 30 years, the development of new antibiotics has considerably decreased, while the options to treat infections caused by resistant agents, which are increasingly on the rise, have become increasingly limited. Tens of thousands of people die each year from infections caused by resistant bacteria. The reasons for delayed development of antibiotics are simple: drug development is risky and expensive, while medicines used to treat infections are not

as profitable as the ones that treat chronic illnesses. Indiscriminate use of antibiotics has led to the emergence of multidrug resistant microorganisms—MRSA, VRSA, VRE, etc. The problem of the increasing resistance of microorganisms to antibiotics has become a global health issue (6).

The choice of therapy should rely either on the culture and identification of bacterial pathogens and the results of the sensitivity test (directed therapy) or on the familiar common pathogens in the given state and their common forms of resistance (empirical therapy).

The basic principles of the rational use of antibiotics are as follows:

- Based on the localization of the infection, the causative agent that is in question can be assumed.
- An empirical antibiotic choice during the initial patient contact should be made.
- Sampling for microbiological survey should be conducted prior to administering antibiotics.
- Within 48-72 hours, the effectiveness of antibiotics should be reconsidered, and in view of microbiological findings, the choice of whether to continue or change the application of antibiotics should be decided.
- Apply the antibiotic for a sufficient length of time to treat the infection in question.

One of the ways to achieve this goal is to evaluate and correct the antibiotic prescribing habits in all health care institutions, principally in the primary health care system such as community health centers (7). This study has examined the protocols on antibiotic prescribing at Rakovica Community Health Center, Belgrade.

## GOAL

The main goal of this study is to provide insight into the volume of consumption of antibiotics and the participation of certain antibiotics in their overall consumption at Rakovica Community Health Center, as well as to compare the volume to the national guidelines effective in Serbia and the ESAC (European Surveillance of Antimicrobial Consumption) recommendations.

## METHODOLOGY

The monitoring of antibiotic use refers to a five-year period (2011 -2015) involving patients over 18 years of age at the adult health care service at Rakovica Community Health Center. The community health center in Rakovica provides treatment for approximately 70,820 patients (30,016 male and 40,657 female).

In order to assess the quality of medicinal treatment (type and scope of unreasonable pharmacotherapy), multiple and varied objective methods have been established in practice, several of which have been standardized and structured by the World Health Organization and International Network for Rational Use of Drugs (INRUD) (8).



Consumption is expressed by the Anatomical Therapeutic Chemical (ATC) /Defined Daily Doses (DDD) methodology recommended by WHO and by the number of DDD/1000 inhabitants per day (DID). The internationally accepted classification system for medicines is the Anatomical Therapeutic Chemical (ATC) classification prescribed by the World Health Organization. Each non-proprietary name of the drug code corresponds to seven alphanumeric characters that are divided into five levels of classification. J01 is a subgroup of the System for Anatomical Therapeutic Chemical (ATC) classification. These are antibiotics that are intended for systemic use. Subgroup J01 is a part of anatomical group J (anti-infective drugs for systemic use). Subgroup J01 is furthermore divided into J01A - tetracyclines, J01C - beta lactam antibiotics and penicillins, J01D - other beta lactam antibiotics and cephalosporins, J01F - macrolides, J01M - quinolone antibiotics, J01E - sulfonamides and trimethoprim, and J01G - aminoglycoside antibiotics.

ATC/DDD methodology has been proven beneficial in overcoming the differences, and the WHO proposed that this methodology should become a European criterion in 1981, whereas it became a world criterion in 1993.

Data from the community health center in Rakovica have been obtained by the Heliant programme. The Heliant programme has enabled us to gain insight into overall antibiotic consumption, which serve as an overview of indications for which antibiotics were prescribed as well as an insight into antibiotic consumption according to the age and gender of patients.

Within the framework of the ATC/DDD methodology, the existing (real) and expected consumption of medications can be compared. Moreover, the ATC/DDD methodology enables us to compare the use and consumption of drugs among various healthcare institutions, regions and states.

Additionally, the rate of adherence to national guidelines and the rate of consumption of the recommended antibiotics is calculated in compliance with the European Surveillance of Antimicrobial Consumption (ESAC) recommendations.

The ESAC has proposed a list of disease-specific quality indicators (DSQI) for outpatient antibiotic prescriptions: 1. acute bronchitis/bronchiolitis, 2. acute upper-respiratory infection, 3. cystitis, 4. acute tonsillitis, 5. sinusitis, 6. acute otitis media, and 7. pneumonia (10).

The rate of adherence to national guides and ESAC recommendations for pneumonia has been calculated in this study.

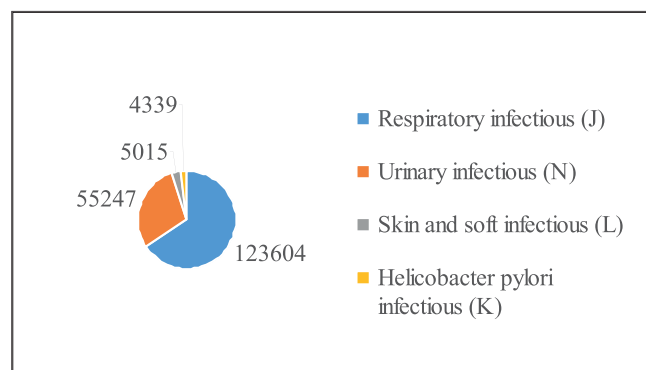
## RESULTS

In the period from 2011-2015, at Rakovica Community Health Center, the most prescribed antibiotics were for diseases of the respiratory system, followed by urinary infections, and then skin and soft tissue infections (Figure

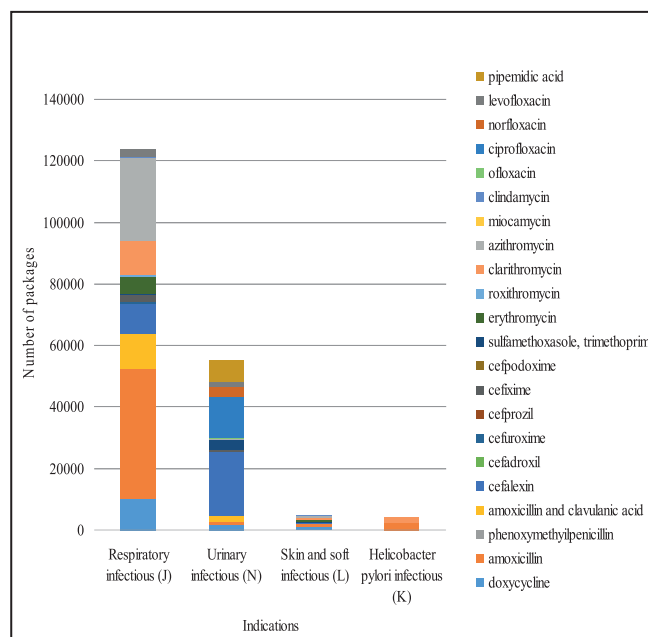
1). As for respiratory system infections, amoxicillin was the most frequently prescribed individual antibiotic, followed by azithromycin, then amoxicillin and clavulanic acid (Figure 2). These prescriptions for respiratory system infections were most frequently prescribed for diagnosis of J02 (acute pharyngitis), then J20 (acute bronchitis) and J03 (acute tonsillitis). For urinary tract infections, the most widely prescribed medications were cephalexin, ciprofloxacin and piperimide acid (Figure 2).

When considering the use of antibiotics in relation to age, the most widely prescribed antibiotics were penicillin and macrolides for patients under 65, whereas cephalosporins and penicillin drugs were predominant for those over 65 years of age.

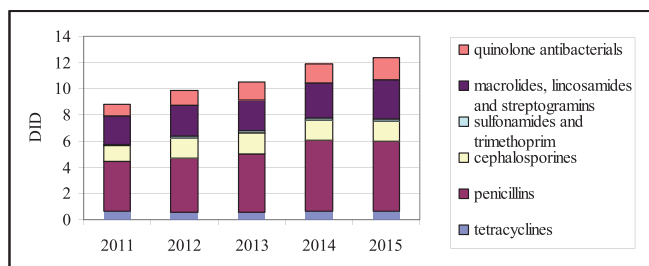
Overall use of antibiotics (ATC group J01) is expressed in the form of DID at Rakovica Community Health Center. An increase in total antibiotic consumption can be noticed in the period from 2011 to 2015 (from 8,7 DID in 2011 up to 12,4 DID in 2015). Consumption per year for the last five years has been calculated for each group and subgroup of antibiotics. The most prescribed groups of antibiotics



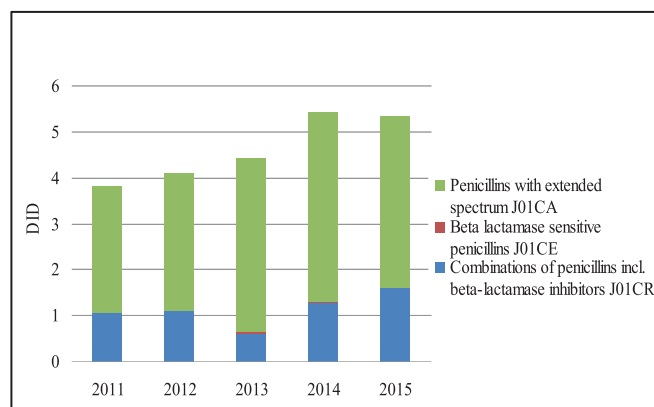
**Figure 1.** Number of dispensing packages according to indications over the period 2011-2015



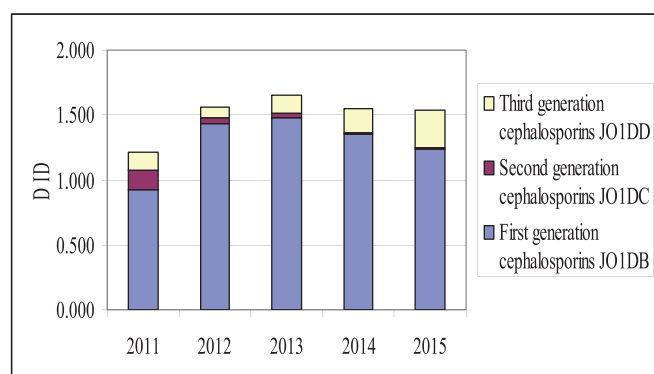
**Figure 2.** The most frequently prescribing antibiotics according to indications over the period 2011-2015



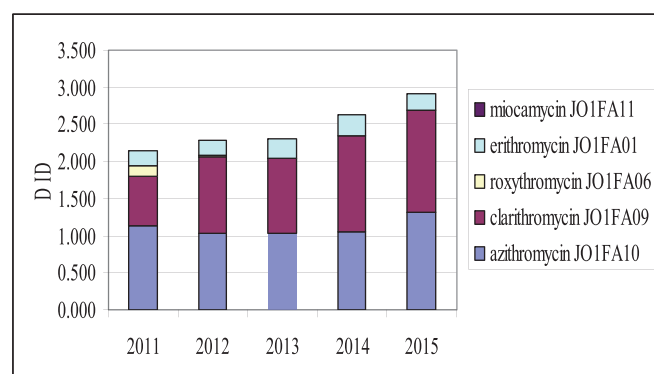
**Figure 3.** Consumption of antibiotics for systemic use -J01 (3<sup>rd</sup> level of ATC) defined as DID over the period 2011-2015



**Figure 4.** Consumption of penicillins -J01C (4<sup>th</sup> level of ATC) defined as DID over the period 2011-2015



**Figure 5.** Consumption of cephalosporins -J01D (4<sup>th</sup> level of ATC) defined as DID over the period 2011-2015



**Figure 6.** Consumption of macrolides -J01F (5<sup>th</sup> level of ATC) defined as DID over the period 2011-2015

were penicillin drugs, then macrolides, followed by cephalosporins (Figure 3).

As for tetracyclines (ATC group J01A), a decrease in consumption was evident in 2013 (0,57 DID), with a new increase in 2015 (0,62 DID). The most widely used tetracycline was doxycycline.

Penicillin drugs (ATC group J01C) were the most prescribed antibiotics in all respective years, and an increase in prescribing penicillin every year was observed, with amoxicillin being the predominant drug (Figure 4).

As for cephalosporins, the most frequently prescribed medication was cephalosporins of the 1<sup>st</sup> generation (J01DE). In the previous period, a decline in the use of cephalosporins of the 2<sup>nd</sup> generation and a rise in prescribing of cephalosporins of the 3<sup>rd</sup> generation were evidenced (Figure 5).

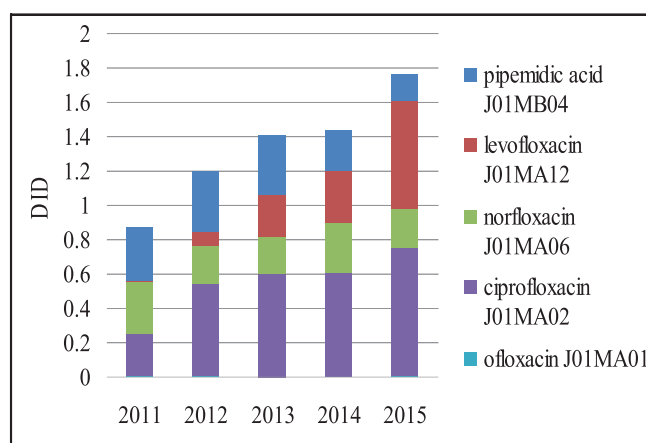
With regard to sulfamethoxazole trimethoprim, its consumption was nearly doubled in the period from 2011 to 2015 (from 0.08 DID up to 0.18 DID).

In relation to the group of macrolides, an increase in prescribing these medications is also noticeable from 2.17 DID in 2011 up to 2.95 DID in 2015. The most frequently prescribed macrolides were azithromycin, whereas the use of clarithromycin nearly doubled (from 0.06 DID in 2011 up to 1.3 DID in 2015) (Figure 6).

The most widely prescribed quinolones were fluoroquinolones, with the leading position being that of ciprofloxacin. A rise in consumption of all generations of quinolones was observed, but the most noticeable increase was an increase in the use of levofloxacin. (from 0.01 DID in 2011 up to 0.62 DID in 2015) (Figure 7).

## DISCUSSION

In comparison with other European countries, Serbia is among the countries with an above average antibiotic use, a finding that was published in *The Lancet Infectious Diseases*.<sup>11</sup> The use of antibiotics at Rakovica Community Health Center has been increasing over the years (from 8.7 DID in 2011 up



**Figure 7.** Consumption of quinolones -J01M (5<sup>th</sup> level of ATC) defined as DID over the period 2011-2015



**Table 1.** Top INN used for pneumonia treatment in comparison with National Serbian Guideline (NSG)

ATC	INN	DID	% from total antibiotics use for pneumonia	NSG recommended as first choice	NSG recommended as second choice
J01MA12	levofloxacin	0.0617	49.04		X
J01DD08	cefixime	0.0199	15.82		
J01FA09	clarithromycin	0.0119	9.42	X	
J01CA04	amoxicillin	0.0074	5.86		
J01FA10	azithromycin	0.0072	5.69	X	
J01AA02	doxycycline	0.0055	4.33		X
J01MA02	ciprofloxacin	0.0050	4.00		X
J01CR02	amoxicillin and clavulanic acid	0.0031	2.43		
J01FA01	erythromycin	0.0010	0.79		
J01EE01	sulfamethoxazole, trimethoprim	0.0008	0.65		
J01FA06	roxithromycin	0.0006	0.46		
J01DD13	cefpodoxime	0.0005	0.40		
J01FF01	clindamycin	0.0004	0.35		
J01DC02	cefprozil	0.0003	0.28		
J01DB01	cefalexin	0.0002	0.17		
J01DC02	cefuroxime	0.0002	0.15		
J01CE02	phenoxymethylpenicillin	0.0001	0.10		
J01MA01	ofloxacin	0.0001	0.06		
	total	0.1259	100	15.11%	57.37%

**Table 2.** Top INN used for pneumonia treatment in comparison with ESAC disease specific quality indicators (DSQI)

ATC	INN	DID	% from total antibiotics use for pneumonia	DSQI7b*	DSQI7c**
J01MA12	levofloxacin	0.0617	49.04		X
J01DD08	cefixime	0.0199	15.82		
J01FA09	clarithromycin	0.0119	9.42		
J01CA04	amoxicillin	0.0074	5.86	X	
J01FA10	azithromycin	0.0072	5.69		
J01AA02	doxycycline	0.0055	4.33	X	
J01MA02	ciprofloxacin	0.0050	4.00		X
J01CR02	amoxicillin and clavulanic acid	0.0031	2.43		
J01FA01	erythromycin	0.0010	0.79		
J01EE01	sulfamethoxazole, trimethoprim	0.0008	0.65		
J01FA06	roxithromycin	0.0006	0.46		
J01DD13	cefpodoxime	0.0005	0.40		
J01FF01	clindamycin	0.0004	0.35		
J01DC02	cefprozil	0.0003	0.28		
J01DB01	cefalexin	0.0002	0.17		
J01DC02	cefuroxime	0.0002	0.15		
J01CE02	phenoxymethylpenicillin	0.0001	0.10		
J01MA01	ofloxacin	0.0001	0.06		
	total	0.1259	100	10.18%	53.04%





to 12.4 DID in 2015). Antibiotics are most frequently used for treating respiratory tract infections, followed by urinary tract infections and then skin and soft tissues infections. The consumption of penicillin drugs is prevailing, which is an optimal choice as per the guides for good clinical practice. The use of beta lactamase sensitive penicillins (cliacil) is very low, which is considered to be irrational use. It is likely that the lack of this drug's availability on the market has led to its reduced consumption. However, the use of macrolides is high both at Rakovica Community Health Center and in the whole of Serbia, which differs from other countries. Physicians decide to prescribe macrolides more frequently probably because of their good compliance (once a day regimen) and due to their good safety profile. In the previous period, an increase in prescribing cephalosporins of the 3<sup>rd</sup> generation and quinolones (of all generations) has been observed, which is not in accordance with the recommendations because these are reserve antibiotics.

In order to evaluate the approximate prescribing habits and adherence to the national and European guidelines, testing has been conducted with antibiotics that are prescribed to treat pneumonia.

Over the observed period from 2011-2015, the average use of antibiotics to treat pneumonia in a patient population over the age of 18 at Rakovica Community Health Center was 0.13 DID. The most prescribed antibiotic to treat pneumonia at Rakovica Community Health Center was levofloxacin (approximately 49%), which is not consistent with the guides for good clinical practice as a first-line therapy. Levofloxacin was followed by cefixime, clarithromycin, amoxicillin, azithromycin, doxycycline, ciprofloxacin, amoxicillin and clavulanic acid, erythromycin and sulfamethoxazole, and trimethoprim. Adherence to the principles of good clinical practice amounted to 15 % for first-line therapies that are used to treat pneumonia, whereas it was cca 57 % for alternative therapy (Table 1).

The ESAC recommended antibiotic use (doxycycline and amoxicillin) in CAP at Rakovica Community Health Center was 10 %, in contrast to the recommended range of 80-100 %. The consumption of fluoroquinolones was 53 %, which exceeded the recommended range of 0-5%, pursuant to ESAC recommendations (Table 2).

Apart from well-known factors influencing the choice and efficacy of antibiotic therapy, these drugs are not being used rationally in our country.

These results indicate the need for a more detailed analysis and monitoring of antibiotic consumption (considering not only quantity-wise but also disease-specific quality indicators), with an aim at the rationalization of prescribing practices.

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