FISEVIER

Contents lists available at ScienceDirect

Journal of Infection and Public Health



journal homepage: www.elsevier.com/locate/jiph

Original Article

Knowledge, attitudes, and practices regarding antibiotic use among the population of the Republic of Serbia – A cross-sectional study



Gordana Belamarić ^a, Zoran Bukumirić ^b, Mira Vuković ^c, Rada Sandić Spaho ^{d,*,1}, Marija Marković ^a, Gordana Marković ^e, Dejana Vuković ^f

^a Institute of Public Health of Belgrade, Serbia

^b Institute for Medical Statistics and Informatics, Faculty of Medicine, University of Belgrade, Serbia

^c General Hospital, Valjevo, Serbia

^d Faculty of Nursing and Health Science, Nord University, Norway

^e Primary Health Centre Zemun, Belgrade, Serbia

^f Institute of Social Medicine, Faculty of Medicine, University of Belgrade, Serbia

ARTICLE INFO

Article history: Received 25 September 2023 Received in revised form 3 November 2023 Accepted 3 November 2023

Keywords: Antimicrobial resistance Antibiotics Health knowledge Attitudes Practice

ABSTRACT

Background: Antimicrobial resistance presents one of the most significant threats to public health. This study aimed to examine antibiotic usage within the general population in the Republic of Serbia and their knowledge, attitudes, and behavior concerning this topic.

Methods: We conducted an online cross-sectional study over two weeks in December 2022, on a sample of 1014 respondents, representative of the Republic of Serbia's population. Predictors of the Antibiotic Knowledge Score (composed of four questions) were analyzed by multivariate ordinal logistic regression. *Results:* In 2022, 76.8% of the participants from the Serbian population had taken antibiotics, mostly upon a medical prescription, with the most common reasons being upper respiratory tract infections. Only 31.3% of all respondents received any kind of advice about the rational use of antibiotics and half of them changed their opinions on using antibiotics after receiving this information. The average Antibiotic Knowledge Score was 2.6 out of 4, with 32.5% of respondents answering all knowledge questions correctly. The multivariate ordinal logistic regression analysis showed that female gender, higher education level, and the willingness to change opinions regarding the usage of antibiotics after receiving information about the rational use of antibiotics from any available source were significant predictors of better knowledge about antibiotics use. Respondents who were open to changing their opinion after receiving information about the rational use of antibiotics had 28% higher odds of higher antibiotic knowledge scores.

Conclusion: This is the first population-level study on public knowledge, attitudes, and practices about antibiotic use in Serbia and therefore the baseline for future research and measuring the impact of potential interventions. Our findings underline the importance of taking into account specific population characteristics, knowledge levels, and attitudes when designing educational and intervention strategies for antibiotic use. Policymakers can leverage these findings to target specific groups and enhance the population's knowledge and practices regarding rational antibiotic usage.

© 2023 The Author(s). Published by Elsevier Ltd on behalf of King Saud Bin Abdulaziz University for Health Sciences. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/ 4.0/).

Introduction

The discovery of antibiotics is among the most critical achievements in medicine. However, antimicrobial resistance (AMR) is increasingly being perceived as one of the most significant threats to public health today [1–5]. AMR can be defined as the ability of microorganisms to resist antimicrobials to which they were previously susceptible [6]. It has many consequences, including severe illness,

https://doi.org/10.1016/j.jiph.2023.11.009

1876-0341/© 2023 The Author(s). Published by Elsevier Ltd on behalf of King Saud Bin Abdulaziz University for Health Sciences. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

Abbreviations: AMR, antimicrobial resistance; CAESAR, Central Asian and Eastern European Surveillance of AMR; EU, European Union; CAWI, Computer-Aided Web Interviewing; AKS, Antibiotic Knowledge Score

^{*} Correspondence to: Faculty for Nursing and Health Sciences, Nord University, Universitetsalléen 11, 8026 Bodø, Norway.

E-mail address: rada.sandic-spaho@nord.no (R.S. Spaho).

¹ ORCHID: 0000-0001-7543-3642

hospital admissions, higher costs of second-line drugs, increased overall healthcare costs, and a higher mortality rate [7–9]. AMR is a phenomenon that recognizes no geographical boundaries and poses a substantial threat to public health worldwide. Different factors contribute to the spread of AMR, including self-medication or taking antibiotics without a prescription [2] and the overprescription of antibiotics [8,10,11]. Studies show an increase in the consumption of antibiotics in the past decades [12,13]. Among other reasons, this increasing trend could be related to inappropriate prescription practices in primary healthcare in low- and middle-income countries [11]. The COVID-19 pandemic has brought new challenges to the consumption of antibiotics. Some studies conducted during the pandemic have shown increased irrational use of antibiotics, which may lead to a further increase in AMR [14–16]. Treatment protocols during the COVID-19 pandemic included antibiotic usage, and further studies could provide additional evidence for a better understanding of antibiotic consumption during the pandemic caused by the SARS-CoV-2 virus.

The Republic of Serbia is a middle-income country, with 7.186.862 inhabitants (according to the 2011 Population census). It had adopted the National Antibiotic Resistance Control Programme for the period 2019-2021 (17), with specific objectives, but the implementation of its measures should be further monitored. In Serbia, 80% of all antibiotics are prescribed for outpatient conditions [18]. An established system in Serbia, which is composed of the National Reference Laboratory for the Registration and Monitoring of Bacterial Strains Resistance to Antimicrobial Agents and a national network of 22 clinical laboratories (covering more than 60% of the Serbian population), monitors the susceptibility of invasive isolates from blood and cerebrospinal fluid to antibiotics, using the same methodology as that of the European Union countries, according to applicable international standards [17]. Serbia is a part of the CAESAR network (Central Asian and Eastern European Surveillance of AMR) [19]. According to data from the National Reference Laboratory for AMR, Serbia ranks among European countries with the highest percentage of resistant isolates [19,20]. This highlights the necessity of undertaking more decisive measures for the rational use of antibiotics and conducting research to examine and explain the general population's knowledge, attitudes, and behaviors related to antibiotic use.

Taking into account that people's knowledge, attitudes, and behaviors are of utmost importance for establishing and ensuring the rational use of antibiotics, the Directorate General for Health and Consumers of the European Commission of the European Union has conducted a series of surveys among the general population to monitor their levels of usage and knowledge about antibiotics [6]. Surveys were conducted in 2009, 2013, 2016, and 2018 to track progress on public use of and knowledge about antibiotics [6]. The periodic conduction of such surveys allows for monitoring changes in the public's use of antibiotics over time. This is crucial for assessing the effectiveness of control measures and educational initiatives. By employing similar or partially adapted methodologies as other countries worldwide, we can place our findings in an international context, facilitating the exchange of best practices and experiences [21-24]. This research aims to determine the patterns of antibiotic use among the Serbian population and further explore the specific factors that could be associated with antibiotic usage.

This is the first population-based study on knowledge, attitudes, and practices in Serbia. There was research conducted in 2015 among adults who consulted general practitioners at four health centers in Novi Sad (the second-largest city in Serbia), to investigate the knowledge, attitudes, and behavior regarding antibiotics [25]. This study indicated that larger-scale research is needed where a more heterogeneous population mix would define further scope of antibiotic use and misuse among Serbian adults [25].

Methods

The cross-sectional study was conducted in December 2022, and the 25 questions in the questionnaire refer to the previous 12 months, while there was still a COVID-19 pandemic. The target population was the population of the Republic of Serbia. Demographic attributes in the sample, designed to be representative of the Republic of Serbia, were established based on data from the 2011 census conducted by the Statistical Office of the Republic of Serbia. This included the urban and rural population distribution, with urban populations accounting for 60.0% and rural populations making up the remaining 40.0%. These demographics spanned across four regions in the Republic of Serbia: Vojvodina, Belgrade, Western Serbia with Šumadija, and Eastern and Southern Serbia. Furthermore, the demographic characteristics encompassed gender, age, and educational profiles of the respondents, aligning with the structure of the 2011 census data. A sample size of 634 respondents is necessary to provide a statistically reliable assessment of the frequency of adequate knowledge, with a precision of 2%, a reliability coefficient of 0.95, and an assumed frequency of the researched phenomenon at 7.1% [22]. The method of selecting participants for this study was executed through a robust three-stage stratified sampling approach. The stratification was performed based on geographical and administrative divisions within the Republic of Serbia, ensuring a representative sample from different levels of urbanization and demographic clusters. The first stage included Municipalities and Cities which were chosen as primary sampling units. This stage was crucial for ensuring the regional representation of respondents. The second stage included the selection of the respondents from local communities (where 'local communities' refer to specific areas within cities and municipalities, including rural areas). The probability of choosing a particular local community was directly proportional to its population size, ensuring that larger communities had a greater chance of being selected, but smaller ones were not overlooked. The third stage included the individual respondent selection within each selected local community, where a set number of individuals were chosen with equal probability. This design ensured that every individual within the chosen communities had an equal probability of being selected to participate, minimizing potential biases. The contact details of potential respondents were sourced from a dedicated email address database maintained for surveys. This was done under the strict adherence to national privacy protection standards. The Public Opinion Research Agency entrusted with the study's execution, ensured that the sampling was both randomized and aligned with the sampling requirements.

The research was conducted online using a computer-assisted survey (Computer Aided Web Interviewing - CAWI) method for gathering data, in which the respondent filled out an online survey posted on a website. This approach enabled fast, reliable, and accurate data collection. At the beginning of the questionnaire, respondents were informed that participation was voluntary and anonymous. The flow and sequence of questions were predefined through automatic filter options based on the respondent's answers to previous questions, preventing possible logical errors. Respondents were free to complete the online questionnaire at leisure, without pressure. This method also facilitated data collection from remote geographical areas and access to specific target groups within the general population.

Approval to conduct the research was obtained from the Ethics Committee of the Institute of Public Health of Belgrade (V-2 no. 86/ 2/2022). Before researching a sample of the general population of the Republic of Serbia, the questionnaire was tested on a smaller sample at the Institute of Public Health of Belgrade, enabling us to verify the clarity and comprehensibility of the questions for the respondents.

Research instruments

Our research utilized the Eurobarometer guestionnaire [6] (with the permission of the Directorate-General for Communication Unit -Europe Direct reply no. 457661/2021, stating that the reuse of the document by third parties is permitted according to Commission Decision 2011/833/EU of 12 December 2011, under Article 6 of the Reuse Decision, with reuse subject to acknowledgment of the source). The research covered the following areas: the use of antibiotics in the previous year and their acquisition methods; the reasons for taking antibiotics; whether any test was conducted to determine the cause of the illness before taking antibiotics; the Antibiotic Knowledge Score (AKS) consisting of four items, which measured the levels of knowledge about the nature and effectiveness of antibiotics as well as the risks associated with their unnecessary use; whether the general public has been informed about unnecessary antibiotic use and the influence of this information on their behavior; their interest in learning more about antibiotics, along with perceptions of the most reliable information sources [6]. Given that the research was conducted during the ongoing COVID-19 pandemic, we included questions related to the use of antibiotics during the pandemic to gain a broader insight into antibiotic usage during this specific period.

Respondents demonstrated their knowledge about antibiotics by answering 4 questions - Antibiotics kill viruses (false); Antibiotics are effective against colds (false); The unnecessary use of antibiotics makes them become ineffective (true); Taking antibiotics often has side effects such as diarrhea (true). The Antibiotic Knowledge Score (AKS) is calculated based on participants' responses to these four items. Each respondent is assigned a knowledge score, which reflects the number of correct answers they provided to these items. Knowledge questions had three response options: 'Yes', 'No', and 'I don't know'. Correct knowledge responses were assigned 1 point while incorrect responses scored 0 points - maximum AKS was 4 points and minimum 0 points.

The statement "willingness to change opinions regarding the usage of antibiotics after receiving information about the rational use of antibiotics from any available source" (doctor, nurse, pharmacy, hospital or other health care facility, family or friends, a health-related website, social networks, and mass media) was based on the participants answers on 2 questions – If they have received some information on rational use of antibiotics and whether the information they received influenced a change in their opinion regarding the use of antibiotics.

Statistical Methods

Results were presented as frequency (percent). Datasets for continuous numerical variables were described using mean and standard deviation, while attributive variables were described using frequency and percentage. For testing the hypotheses on the difference between frequencies, the following tests were used: Chi-square Test, Fisher's exact test, and McNemar's Test. Predictors of the number of correct answers of knowledge about antibiotics were analyzed by multivariate ordinal logistic regression. All p-values less than 0.05 were considered significant. Statistical data analysis was performed using IBM SPSS Statistics 22 (IBM Corporation, Armonk, NY, USA) and R-4.0.0 software (The R Foundation for Statistical Computing, Vienna, Austria).

Results

A total of 1014 respondents participated in the research (while 65 did not respond to the survey), with an average age of 43.4 ± 12.9 years, of which 54.2% were women (Table 1). The lowest representation were respondents with very poor and poor health (0.2%

Table 1

Frequency distribution by categories of demographic features, health and social status
of respondents, and antibiotic use in the total study sample (N = 1014).

	Categories	f	%
Gender	Man	464	45.8
	Women	550	54.2
Age category (years)	18 – 29	167	16.5
	30 - 44	387	38.2
	45 – 59	333	32.8
	≥60	127	12.5
Self-rated health	Very bad	2	0.2
	Bad	34	3.4
	Average	261	25.7
	Good	520	51.3
	Very good	197	19.4
Education	Elementary school	17	1.7
	Secondary school	473	46.6
	College and university	524	51.7
Socio-economic status	Very bad	16	1.6
	Bad	73	7.2
	Average	510	50.3
	Good	355	35.0
	Very good	60	5.9
Work status	Employed in the public sector	241	23.8
	Employed in the private	494	48.7
	sector (Entrepreneur)		
	Farmer	13	1.3
	Unemployed	134	13.2
	Student	30	3.0
	Retired (Pensioner)	102	10.1
Region	Vojvodina	280	27.6
	Belgrade	256	25.2
	Eastern and Southern Serbia	212	20.9
	Western Serbia and Šumadija	266	26.2
Use of antibiotics in the last	Yes	779	76.8
12 months	No	226	22.3
	Refusal	1	0.1
	Don't know	8	0.8

f - frequency.

and 3.4%) and respondents who had completed elementary school (1.7%). Most of the participants were individuals with a moderate financial status (50.3%), as well as employees in the private sector (48.7%) (Table 1). Regarding frequency distribution by region (above mentioned four regions in the Republic of Serbia), respondents were evenly represented, ranging from 20.9% in Eastern and Southern Serbia to 27.6% in Vojvodina.

The average Antibiotic Knowledge Score in the population of respondents was 2.6 out of 4. The share of respondents who did not have a single correct answer to these 4 statements is 7.3%, while 32.5% of respondents gave correct answers to all 4 questions. About a quarter of respondents had two correct answers, and almost the same proportion of respondents had three correct answers out of four. (Fig. 1).

The majority of respondents, 779 of them (76.8%), had taken antibiotics in the previous 12 months, 611 of them (78,6%) upon a doctor's prescription, while 57.8% of those respondents who used antibiotics had undergone blood or urine test, or throat swab test before or at the same time with the antibiotic administration (Table 2). The most common reasons for using antibiotics were complaints and symptoms related to upper respiratory tract

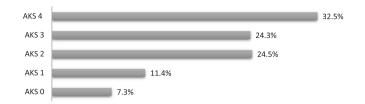


Fig. 1. Knowledge about antibiotic use - Antibiotic knowledge score (AKS).

Table 2

Frequency distribution by categories of application and prescription of antibiotics, medical analyses performed before or with the application of antibiotics, and the reason for their last taking.

Variable	Category	f	%
Use of antibiotics in the last 12 months (orally as tablets, powder, or syrup)	Yes	779	76.8
	No	226	22.3
	Refusal	1	0.1
	Don't know	8	0.8
How did you obtain the last course of antibiotics that you used?	From a medical prescription	611	78.4
	I had some leftovers from a previous course	78	10.0
	Without a prescription from a pharmacy	68	8.7
	Without a prescription from elsewhere	20	2.6
	Don't know	2	0.3
Did you have a test, for example, a blood or urine test, or throat swab, to find out what was causing your illness,	Yes	450	57.8
before or at the same time as you started antibiotics?	No	311	39.9
	Don't know	18	2.3
The reason for last taking the antibiotics	Pneumonia	52	6.7
	Bronchitis	80	10.3
	Rhino pharyngitis	136	17.5
	Flu	111	14.2
	Cold	185	23.7
	Sore throat	231	29.7
	Cough	161	20.7
	Fever	177	22.7
	Headache	78	10.0
	Diarrhea	22	2.8
	Urinary tract infection	87	11.2
	Skin or wound infection	39	5.0
	Other	124	15.9
	Don't know/Don't want to answer	7	0.9

f - frequency.

infections: sore throat 9.7%, cold 22.7%, cough 20.7%, and rhinopharyngitis 17.5%. Diarrhea and skin or wound infections were the least frequent reasons for using antibiotics (2.8% and 5.0%). (Table 2).

Respondents who used antibiotics compared to those respondents who did not use antibiotics were more often female (56.7% vs. 46.0%), were less likely to be in the age category \geq 60 (10.4% vs. 19.5%), and less likely to report very good health (16.8% vs. 29.2%). Respondents who used antibiotics more frequently knew that taking antibiotics often has side effects such as diarrhea (71.5% vs. 58.0%). (Table 3).

Less than a third of our study's participants (318 respondents or 31.3%) reported that they had received any kind of advice about the rational use of antibiotics in 2022, and around half of those participants who received advice (158) reported that the advice contributed to a change in their opinion about antibiotics use. The respondents who used antibiotics more often expressed a need for additional information about resistance to antibiotics, how to use antibiotics, prescribing, and diseases for which antibiotics are used (Table 4).

The multivariate ordinal logistic regression model contains 7 predictors of the level of knowledge about antibiotics listed in Fig. 2. The whole model was statistically significant (p < 0.001).

In the multivariate ordinal logistic regression model, statistically significant predictors of a higher level of knowledge about antibiotics were female gender (OR=0.55; p < 0.001), higher level of education (OR=1.44; p = 0.001) and the openness to changing the opinion after receiving information about the rational use of antibiotics (OR=1.28; p = 0.046). Male respondents have 45% lower odds for each higher level of antibiotics knowledge, controlling for all other factors in the model. With the increasing level of education, the odds for each higher level of antibiotics knowledge increased by 44%, controlling for all other factors in the model. The respondents who changed their opinion after receiving information about antibiotic use have 28% higher odds for a higher level of knowledge about antibiotics while controlling for all other factors in the model.

Discussion

Our research showed a higher prevalence of antibiotic use among the Serbian population (76.8%), compared to the European Union countries where less than half of all respondents have taken antibiotics [6]. However, there is a difference in antibiotic usage between EU countries and while nearly half of respondents in Italy have taken antibiotics (47%), less than a quarter of respondents in Poland and Slovenia (both 24%), Germany (23%), the Netherlands (21%) and Sweden (20%) say that they have done so [6]. Here it must be emphasized that the research in Serbia was conducted during the COVID-19 pandemic, and different studies have already shown increased antibiotic consumption during the pandemic [26–29].

National Antibiotic Resistance Control Programme Republic of Serbia includes activities of continuous education of health professionals on policies for prescribing, dispensing, and using antibiotics as well as updating university curricula to include rational use of antibiotics and antimicrobial resistance [17]. The specific goal of the Action Plan of the Serbian National Antibiotic Resistance Control Programme was that 42% of the population became familiar with the fact that the cold and flu are not treated with antibiotics. According to our results, this goal is achieved, since 49.7% of the participants who used antibiotics knew this fact and even 60.6% of the participants who didn't use antibiotics have that knowledge.

The majority of the respondents who used antibiotics in the last 12 months in Serbia stated that they had a doctor's prescription, which may indicate the effectiveness of measures undertaken by the National Antibiotic Resistance Control Program for 2019–2021, including control of dispensing antibiotics only by prescription [17]. Since nearly 80% of participants used antibiotics by prescription, it is very important to educate health professionals, especially doctors in primary health care who are prescribing antibiotics to patients. However, 21.3% of respondents didn't have a doctor's prescription for taking antibiotics, which is a larger share compared to the average of EU countries [6]. In the EU countries, the vast majority of

Table 3

Demographic characteristics, health and social status, and knowledge about antibiotics.

Variable	Category	Use of antibiotics	p-value (test statistics)	
		Yes (n = 779)	No (n = 226)	-
Gender	Men	337 (43.3%)	122 (54.0%)	p=0.004
	Women	442 (56.7%)	104 (46.0%)	$(\chi^2 = 8.116)$
Age category (years)	18 - 29	142 (18.2%)	23 (10.2%)	p = 0.002
0 0 0 0 0	30 - 44	296 (38.0%)	90 (39.8%)	(U=76635.0)
	45 - 59	260 (33.4%)	69(30.5%)	. ,
	≥60	81 (10.4%)	44(19.5%)	
Self-rated health	Very bad	2 (0.3%)	0 (0.0%)	p = 0.001
	Bad	25 (3.2%)	9 (4.0%)	(U=76071.5)
	Average	213 (27.3%)	46 (20.4%)	(,
	Good	408 (52.4%)	105 (46.5%)	
	Very good	131 (16.8%)	66 (29.2%)	
Educational background	Primary school	13 (1.7%)	4 (1.8%)	p = 0.661
	Secondary school	366 (47.0%)	102 (45.1%)	(U=86556.0)
	College or University	400 (51.3%)	120 (53.1%)	()
Socio-economic status	Very bad	11 (1.4%)	5 (2.2%)	p = 0.725
	Bad	57 (7.3%)	16 (7.1%)	(U=86792.5)
	Average	387 (49.7%)	114 (50.4%)	(0 00/0210)
	Good	278 (35.7%)	77 (34.1%)	
	Very good	46 (5.9%)	14 (6.2%)	
Employment status	Employed	593 (76.1%)	150 (66.4%)	p = 0.002
Employment status	Unemployed	99 (12.7%)	33 (14.6%)	$(\gamma^2 = 14.380)$
	Student	23 (3.0%)	6 (2.7%)	(χ -14.500)
	Retired (Pensioner)	64 (8.2%)	37 (16.4%)	
Region	Vojvodina	196 (25.2%)	78 (34.5%)	p = 0.014
Region	Belgrade	195 (25.0%)	61 (27.0%)	$(\gamma^2 = 10.633)$
	Western Serbia and Šumadija	216 (27.7%)	48 (21.2%)	(χ =10.055)
	East and South Serbia	172 (22.1%)	39 (17.3%)	
Knowledge about antibiotics	Antibiotics kill viruses (false)	460 (59.1%)	130 (57.5%)	p = 0.681
Knowledge about antibiotics	Antibiotics kin viruses (laise)	400 (39.1%)	150 (57.5%)	$(\chi^2 = 0.169)$
	Antibiotics are effective against colds (false)	297 (40 7%)	137 (60.6%)	p = 0.004
	Antibiotics are effective against colus (laise)	387 (49.7%)	157 (00.0%)	p = 0.004 ($\gamma^2 = 8.402$)
	The unnecessary use of antibiotics makes them become	657 (84.3%)	190 (84.1%)	$(\chi = 0.402)$ p = 0.922
	ineffective (true)	037 (04.3%)	190 (04.1%)	$\beta = 0.922$ ($\gamma^2 = 0.010$)
	Taking antibiotics often has side effects such as diarrhea (true)	557 (71.5%)	131 (58.0%)	$(\chi^{-} = 0.010)$ p < 0.001
	Taking anumours onen nas sue effects such as diarmea (true)	557 (71.5%)	151 (58.0%)	$(\gamma^2 = 14.867)$
				(χ =14.807)

 χ^2 – Chi square test; U – Mann-Whitney test.

Table 4

Need for additional information regarding antibiotic use.

Need for additional information regarding	Use of antibio 12 months	p-value (test statistics)	
further antibiotic use	$\begin{array}{llllllllllllllllllllllllllllllllllll$		
Resistance to antibiotics	351 (45.1%)	46 (20.4%)	p < 0.001 ($\chi^2 = 44.735$)
How to use antibiotics	329 (42.2%)	57 (25.2%)	p < 0.001 ($\chi^2 = 21.432$)
Diseases for which antibiotics are used	387 (49,7%)	82 (36,3%)	p < 0.001 ($\chi^2 = 12,630$)
Prescribing antibiotics	175 (22,5%)	35 (15.5%)	p = 0.023 ($\chi^2 = 5160$)
Links between human, animal, and environmental health	216 (27,7%)	70 (31,0%)	p = 0.341 ($\chi^2 = 0906$)

 χ^2 – Chi square test.

respondents obtained antibiotics via medical prescription from a healthcare professional (93%) and around 7% have taken antibiotics without a prescription, but this varies from 1% to 15% in EU countries [6]. Of all participants who used antibiotics without a prescription, the largest number had some left-overs from a previous course (10.0%), but some participants managed to get antibiotics without a prescription from a pharmacy (8.7%), which is against the regulations, and a few took antibiotics without a prescription from elsewhere (2.6%). These results indicate the directions of action to mitigate the growing threat of antimicrobial resistance, which requires comprehensive and coordinated activities in the government control of implementation of regulations, but also the education of

healthcare professionals, the pharmaceutical industry, and the public to ensure the responsible use of antibiotics.

The most common reasons for antibiotic use in the Serbian population were symptoms related to upper respiratory tract infections, including sore throat, cold, cough, and rhinopharyngitis, which is similar to the previous research [6]. In contrast, diarrhea and skin or wound infections were the least common reasons. More than half of our respondents did some test to find out the cause of the illness before or at the same time as starting the antibiotics therapy, but still, there was a large share of respondents who didn't do any test before, or at the same time as starting therapy (39.9%), or didn't know if they had a test (2.3%). This indicates the need for better information and education for the general public and even for medical professionals about the risks associated with unnecessary use of antibiotics.

The average Antibiotic knowledge score in the Serbian population was 2.6 out of 4, which is a higher knowledge score compared to the Japanese population [22] and a very similar average score compared to the EU population. The highest score was reported in Finland and Sweden (3.1 out of 4) and the lowest score was reported in Latvia and Romania (2.1 out of 4). [6] These initial findings enable the monitoring of the change in Antibiotic knowledge scores in the Serbian population in the future. Here, it must be emphasized that the research in Japan was conducted in 2017 while our research was conducted in 2022, which may present a potential limitation for comparison. On the other hand, research in Japan was also conducted online, using the very similar methodology to our research. The knowledge scores of our respondents are more similar to the knowledge scores of the inhabitants of the EU. More of our respondents have knowledge that antibiotics don't kill viruses

G. Belamarić, Z. Bukumirić, M. Vuković et al.

Analyzed variables					OR (95% CI)
Gender (Male/Female)		H - H	1		0.55 (0.44 - 0.69)
Age category			•		0.99 (0.98 - 1.00)
Self-rated health		н	₽-¦		0.86 (0.73 - 1.02)
Education				• •	1.44 (1.16 - 1.80)
Socio-economic status					1.06 (0.90 - 1.25)
Work status					
-Employed		-			1.19 (0.74 - 1.90)
-Unemployed			•		0.96 (0.56 - 1.66)
-Student		•			0.50 (0.21 - 1.19)
-Retired (Pensioner) reference			1		
Has the information you received changed your opinion about the use of antibiotic	:		-	—	1.28 (1.01 - 1.62)
	0.0	0.5	1.0	1.5	2.0

Fig. 2. Graphics presentation of the ordinal logistic regression with the level of knowledge about antibiotics as the dependent variable.

compared to EU and fewer of our respondents know that antibiotics are not effective against colds. There were very close shares of the respondents in the EU and Serbia that provided correct answers to the remaining two knowledge questions (that the unnecessary use of antibiotics makes them become ineffective and that taking antibiotics often has side effects such as diarrhea). Again, we must emphasize that the research in the EU was conducted in 2018 while our research was conducted in 2022, which may present a potential limitation for comparison.

The respondents who were aware that inappropriate use of antibiotics can cause side effects such as diarrhea were more likely to use antibiotics. This finding might confirm that knowledge about appropriate antibiotic use does not always translate into behavior patterns [25]. Studies identified various factors influencing behavior related to antibiotic use, apart from knowledge. These factors include attitudes, beliefs, subjective norms, opinions of persons in one's social network, self-efficacy, and ability to obtain antibiotics [30,31]. Even though it was demonstrated that knowledge influences behavior, the relation is not direct, and recent research attempted to test mechanisms linking knowledge and behavior related to antibiotic use based on various models of health behavior such as the Health Belief Model, Theory of Planned Behavior, and Patient-Centered Communication Theory [31–33]. However, tested models explain a relatively small part of the variance in behavior. On the other hand, the research on prescribing is very important too, since many factors may affect prescribing behaviors, such as socio-cultural context, financial incentives, personal beliefs, patients' attitudes, and AMR awareness [11]. Therefore, it is crucial to develop targeted educational and other specific interventions to bridge this knowledge-behavior gap [8]. Experiences from different countries show the importance of the implementation of specific interventions aimed at combating AMR and monitoring their effects [8,34]. Although the long-term effects and effects on behavior are uncertain, some educational interventions were proven to be successful in knowledge transfer among different age groups [35]. The use of video in health promotion topics can bring a positive change in the knowledge of the public since videos are easy to watch and listen to, so the study from Lo et al. recommended educational intervention on the elderly utilizing multimedia in knowledge transfer concerning AMR [35]. Those findings should also be considered in the light of wide use of the internet and social networks as potentially important tools for the population's educational interventions.

Our research showed that older individuals (60 years and older) used antibiotics less frequently in the previous year compared to other age groups. This is contrary to another survey, which identified the elderly as heavy users of antibiotics [36]. Among other factors

that may influence antibiotic usage, the measures during the COVID-19 pandemic aimed at protecting the health of older citizens should be mentioned here.

Respondents who reported very good health were less likely to use antibiotics, which emphasizes the importance of prevention and health improvement in general, but also shows the significance of establishing antimicrobial stewardship as a strategy, and a coherent set of actions that promote the responsible use of antimicrobials in the whole population [37]. While in our research we relied on the participants' self-assessment of their health status, future studies could further explore the specific health-related factors that might be associated with antibiotic use. The qualitative studies conducted after the quantitative could explore more deeply the potential directions of changing views about the use of antibiotics after different educational interventions.

Since less than a third of study participants were informed about the proper use of antibiotics in 2022, it underscores the need for campaigns to raise awareness about the rational use of antibiotics and antimicrobial resistance. As a significant predictor of a higher level of knowledge about antibiotics our study results showed: female gender, higher level of education, and willingness to change their opinion after receiving information about the rational use of antibiotics. The respondents in our research who changed their opinion after receiving information about antibiotics have higher odds of better knowledge about antibiotic use. This finding shows that when people receive information and their views on antibiotics change as a result, it may lead to a better overall understanding and awareness. This is an important positive incentive for future educational interventions. It may emphasize the need for more personalized patient care and intervention strategies in antibiotic consumption, which is already cited as an important future trend [38,39]. In line with these findings, the respondents who used antibiotics compared to those who did not, were more open to learning about the antibiotic's usage, more frequently wanted additional information about resistance to antibiotics, and about the diseases for which antibiotics are used.

Strengths and limitations

The cross-sectional design of the study requires scrutiny of the potential risk of bias [40]. While the study's strengths include the large and comprehensive sample of the general population, the overrepresentation of higher educational levels in the study sample indicates potential selection bias. An online questionnaire, as a survey tool, enables data gathering from respondents who live in remote geographical areas of the country and provides access to specific target groups of the general population. However, potential limitations of online data gathering are the lack of internet

connection in some areas, and the absence of an interviewer to assist the respondent and clarify questions in person when necessary. It potentially may result in lower quality or incomplete surveys. Selfadministered surveys present challenges in interpreting questions as it is a "one-way communication" that can introduce measurement error [41]. As self-administered questionnaires were used, there is also a possibility that participants may have over- or under-reported in a socially desirable manner. Given that the questions refer to a period of 12 months prior, there is also the potential for recall bias. However, a three-stage random representative stratified sample of the general population of the Republic of Serbia and a high number of respondents partially overcomes these limitations.

Conclusions and future implications

This study aimed to investigate the use of antibiotics among the population of the Republic of Serbia and identify associated factors. It is the first population-level study on public knowledge, attitudes, and practices about antibiotics and AMR in Serbia and it provides baseline data for future studies. Findings may contribute to the existing knowledge by clarifying the multifaceted factors influencing antibiotic use. Certain specific factors should be considered when planning actions and educational interventions on antibiotic use, such as population characteristics (gender, education, health status) and the level of knowledge concerning antibiotic utilization patterns. Repeating this research at specific intervals could allow for the monitoring of changes in the population's knowledge about antibiotic use and track the impact of educational and other potential interventions in the Republic of Serbia. Educating the general public can lead to more informed decisions about antibiotic use, contributing to efforts to address the global challenge of antimicrobial resistance.

Considering the study's limitations, its key findings may assist policymakers in Serbia to strategize and implement actions for specific target groups to increase the population's knowledge about the rational use of antibiotics. National Antibiotic Resistance Control Programme already defines that the training of doctors, dentists, pharmacists, and veterinarians on the principles of rational antibiotic therapy should be carried out continuously. Education of health professionals on the rational use of antibiotics implies raising awareness and the level of knowledge, primarily raising awareness on the importance of the issue of antibiotic resistance at the undergraduate and graduate levels. Here it must be emphasize that the National Program was for the period 2019-2021, and the new program isn't yet adopted but our results shows that targeted educational interventions about antibiotic use both for the general public and for health professionals should be incorporated for the following period too.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

 Tacconelli E, Sifakis F, Harbarth S, Schrijver R, van Mourik M, Voss A, et al. Surveillance for control of antimicrobial resistance. Lancet Infect Dis 2018;18(3):e99–106. https://doi.org/10.1016/S1473-3099(17)30485-1. Epub 2017 Nov 5. PMID: 29102325.

- [2] Christaki E, Marcou M, Tofarides A. Antimicrobial resistance in bacteria: mechanisms, evolution, and persistence. J Mol Evol 2020;88(1):26–40. https://doi. org/10.1007/s00239-019-09914-3. Epub 2019 Oct 28. PMID: 31659373.
- [3] Morrison L, Zembower TR. Antimicrobial resistance. Gastrointest Endosc Clin N Am 2020;30(4):619–35. https://doi.org/10.1016/j.giec.2020.06.004. Epub 2020 Aug 1. PMID: 32891221.
- Marston HD, Dixon DM, Knisely JM, Palmore TN, Fauci AS. Antimicrobial resistance. JAMA 2016;316(11):1193–204. https://doi.org/10.1001/jama.2016. 11764. PMID: 27654605.
- [5] Majumder MAA, Rahman S, Cohall D, Bharatha A, Singh K, Haque M, et al. Antimicrobial stewardship: fighting antimicrobial resistance and protecting global public health. Infect Drug Resist 2020;13:4713–38. https://doi.org/10. 2147/IDR.S290835. PMID: 33402841; PMCID: PMC7778387.
- [6] Special Eurobarometer 478: antimicrobial Resistance (in the EU), Report 2018–11–13 doi:10.2875/92205 Available from: https://data.europa.eu/data/datasets/s2190_90_1_478_eng?locale=en). [Accessed July 19, 2021].
- [7] World Health Organization. Turning plans into action for Antimicrobial Resistance (AMR). Working paper 2.0: implementation and coordination. Geneva: World Health Organization; 2019.
- [8] Public Health Group. Tackling Antimicrobial Resistance 2019– 2024: The UK's Five-Year National Action Plan. London: HM Government; 2019. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/ attachment_data/file/784894/UK_AMR_5_year_national_action_plan.pdf [Accessed August 10, 2021].
- [9] Dadgostar P. Antimicrobial resistance: implications and costs. Infect Drug Resist 2019;12:3903–10. https://doi.org/10.2147/IDR.S2346108
- [10] Papenburg Jesse, Fontela Patricia S, Freitas Raphael R, Burstein Brett. Inappropriate antibiotic prescribing for acute bronchiolitis in US emergency departments, 2007–2015. J Pediatr Infect Dis Soc 2019;8(6):567–70. https://doi. org/10.1093/jpids/piy131
- [11] Sulis G, Adam P, Nafade V, Gore G, Daniels B, Daftary A, et al. Antibiotic prescription practices in primary care in low- and middle-income countries: a systematic review and meta-analysis. PLoS Med 2020;17:e1003139. https://doi. org/10.1371/journal.pmed.1003139
- [12] Van Boeckel TP, Gandra S, Ashok A, Caudron Q, Grenfell BT, Levin SA, et al. Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data. Lancet Infect Dis 2014;14(8):742–50. https://doi.org/10.1016/S1473-3099(14)70780-7
- [13] Klein EY, Van Boeckel TP, Martinez EM, Pant S, Gandra S, Levin SA, et al. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. Proc Natl Acad Sci U S A 2018;115(15):E3463–70. https://doi.org/10. 1073/pnas.1717295115
- [14] Langford BJ, So M, Raybardhan S, Leung V, Soucy JR, Westwood D, et al. Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis. Clin Microbiol Infect 2021;27(4):520–31. https://doi.org/10.1016/j.cmi.2020.12.018
- [15] Ghosh S, Bornman C, Zafer MM. Antimicrobial resistance threats in the emerging COVID-19 pandemic: where do we stand. J Infect Public Health 2021;14(5):555–60. https://doi.org/10.1016/j.jiph.2021.02.011
- [16] Segala FV, Bavaro DF, Di Gennaro F, Salvati F, Marotta C, Saracino A, et al. Impact of SARS-CoV-2 epidemic on antimicrobial resistance: a literature review. Viruses 2021;13(11):2110. https://doi.org/10.3390/v13112110
- [17] National Antibiotic Resistance Control Programme for the period 2019–2021 Republic of Serbia February 2019. Available from: (https://cdn.who.int/media/ docs/default-source/antimicrobial-resistance/amr-spc-npm/nap-library/serbia_ national-antibiotic-resistance-control-programme-2019–2021.pdf?sfvrsn= 7e2eb9c0_1&download=true). [Accessed May 16, 2023].
- [18] Horvat O, Mijatović V, Milijasevic B, Tomás A, Kusturica MP, Tomic Z, et al. Are there striking differences in outpatient use of antibiotics between South Backa District, Serbia, and some Scandinavian countries. Front Public Health 2018;6:91. https://doi.org/10.3389/fpubh.2018.00091
- [19] European Centre for Disease Prevention and Control and World Health Organization; 2023. Antimicrobial resistance surveillance in Europe 2023 - 2021 data. Available from: https://www.ecdc.europa.eu/en/publications-data/antimicrobial-resistancesurveillance-europe-2023-2021-data). [Accessed 10 June, 2023].
- [20] Medić D, Milosavljević B, Gusman V, Smieško G, Trudić A, Devrnja M, et al. Antimicrobial resistance of invasive isolates in Serbia – CAESAR annual report 2018. 14th Serbian Congress of Pharmacologists and 4th Serbian Congress of Clinical Pharmacology; 2019. Abstract book: p123-p124.
- [21] Anderson A. Online health information and public knowledge, attitudes, and behaviours regarding antibiotics in the UK: multiple regression analysis of Wellcome Monitor and Eurobarometer Data. PLoS One 2018;13(10):e0204878. https://doi.org/10.1371/journal.pone.0204878
- [22] Kamata K, Tokuda Y, Gu Y, Ohmagari N, Yanagihara K. Public knowledge and perception about antimicrobials and antimicrobial resistance in Japan: a national questionnaire survey in 2017. PLoS ONE 2018;13(11):e0207017. https:// doi.org/10.1371/journal.pone.0207017
- [23] Berdida DJE, Grande RAN, Lopez V, Ramirez SH, Manting MME, Berdida MME, et al. A national online survey of Filipinos' knowledge, attitude, and awareness of antibiotic use and resistance: a cross-sectional study. Nurs Forum 2022;57(6):1299–313. https://doi.org/10.1111/nuf.12803. Epub 2022 Sep 26. PMID: 36161465.
- [24] Tangcharoensathien V, Sommanustweechai A, Chanvatik S, Kosiyaporn H, Tisocki K. Addressing the threat of antibiotic resistance in Thailand: monitoring population knowledge and awareness. WHO South East Asia J Public Health 2018;7(2):73–8. https://doi.org/10.4103/2224-3151.239417. PMID: 30136664.

- [25] Horvat OJ, Tomas AD, Paut Kusturica MM, Savkov AV, Bukumirić DU, Tomić ZS, et al. Is the level of knowledge a predictor of rational antibiotic use in Serbia. PLoS One 2017;12(7):e0180799. https://doi.org/10.1371/journal. pone.0180799
- [26] Sulayyim HJA, Ismail R, Hamid AA, Ghafar NA. Antibiotic resistance during COVID-19: a systematic review. Int J Environ Res Public Health 2022;19(19):11931. https://doi.org/10.3390/ijerph191911931
- [27] Malik SS, Mundra S. Increasing consumption of antibiotics during the COVID-19 pandemic: implications for patient health and emerging anti-microbial resistance. Antibiotics 2022;12(1):45. https://doi.org/10.3390/antibiotics12010045
- [28] Hurtado IC, Valencia S, Pinzon EM, Lesmes MC, Sanchez M, Rodriguez J, et al. Antibiotic resistance and consumption before and during the COVID-19 pandemic in Valle del Cauca, Colombia. Rev Panam De Salud Publica 2023;47:e10. https://doi.org/10.26633/RPSP.2023.10
- [29] Markovskaya Y, Gavioli EM, Cusumano JA, Glatt AE. Coronavirus disease 2019 (COVID-19): secondary bacterial infections and the impact on antimicrobial resistance during the COVID-19 pandemic. Antimicrob Steward Healthc Epidemiol 2022;2(1):e114. https://doi.org/10.1017/ash.2022.253
- [30] Hawkings NJ, Butler CC, Wood F. Antibiotics in the community: a typology of user behaviours. Patient Educ Couns 2008;73(1):146–52. https://doi.org/10. 1016/j.pec.2008.05.025
- [31] Mallah N, Badro DA, Figueiras A, Takkouche B. Association of knowledge and beliefs with the misuse of antibiotics in parents: a study in Beirut (Lebanon). PLoS One 2020;15(7):e0232464.
- [32] Byrne MK, Miellet S, McGlinn A, Fish J, Meedya S, Reynolds N, et al. The drivers of antibiotic use and misuse: the development and investigation of a theory driven community measure. BMC Public Health 2019;19(1):1425. https://doi.org/10. 1186/s12889-019-7796-8
- [33] Sobeck J, Smith-Darden J, Gartner D, Kaljee L, Pieper B, Kilgore P, et al. Antibiotic knowledge, beliefs, and behaviors: testing competing hypotheses using an urban community sample. Health Commun 2022;37(7):862–71. https://doi.org/10. 1080/10410236.2021.1875557

- [34] Godman B, Egwuenu A, Wesangula E, Schellack N, Kalungia AC, Tiroyakgosi C, et al. Tackling antimicrobial resistance across sub-Saharan Africa: current challenges and implications for the future. Expert Opin Drug Saf 2022;21(8):1089–111. https://doi.org/10.1080/14740338.2022.2106368
- [35] Lo ACY, Li JTS, Chau JPC, Wong SYS, Hui DSC, Lee VWY. Impact of interprofessional service-learning on the effectiveness of knowledge transfer of antimicrobial resistance to Hong Kong elders: a quasi-experiment. Antimicrob Resist Infect Control 2021;10(1):145. https://doi.org/10.1186/s13756-021-01011-9
- [36] Malo S, José Rabanaque M, Feja C, Jesús Lallana M, Aguilar I, Bjerrum L. High antibiotic consumption: a characterization of heavy users in Spain. Basic Clin Pharmacol Toxicol 2014;115(3):231–6. https://doi.org/10.1111/bcpt.12211
- [37] Dyar OJ, Huttner B, Schouten J, Pulcini C. ESGAP (ESCMID Study Group for Antimicrobial stewardshiP). What is antimicrobial stewardship. Clin Microbiol Infect 2017;23(11):793-8. https://doi.org/10.1016/j.cmi.2017.08.026
- [38] Moser C, Lerche CJ, Thomsen K, Hartvig T, Schierbeck J, Jensen PØ, et al. Antibiotic therapy as personalized medicine - general considerations and complicating factors. APMIS 2019;127(5):361–71. https://doi.org/10.1111/apm.12951
- [39] Johnson KB, Wei WQ, Weeraratne D, Frisse ME, Misulis K, Rhee K, et al. Precision medicine, AI, and the future of personalized health care. Clin Transl Sci 2021;14(1):86–93. https://doi.org/10.1111/cts.12884
- [40] Mallah N, Figueiras A, Takkouche B. Comparison of longitudinal and cross-sectional approaches in studies about knowledge, attitude, and practices related to antibiotic misuse. Drug Saf 2021;44(7):797–809. https://doi.org/10.1007/ s40264-021-01075-x
- [41] Kosiyaporn H, Chanvatik S, Issaramalai T, Kaewkhankhaeng W, Kulthanmanusorn A, Saengruang N, et al. Surveys of knowledge and awareness of antibiotic use and antimicrobial resistance in the general population: a systematic review. PloS One 2020;15(1):e0227973. https://doi.org/10.1371/journal. pone.0227973