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## Change in parental knowledge, attitudes and practice of antibiotic use after a national intervention programme

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**Background:** Nation-wide multifaceted interventions to improve antibiotic use were undertaken in the former Yugoslav Republic of Macedonia in September 2014. This study aimed to assess the parental knowledge and attitudes about antibiotics, and self-medication practices in children, and evaluate the impact of interventions on these parameters. **Methods:** Pre–post-intervention surveys were conducted in May 2014–16 in three administrative regions in the country. Data were collected by interviewing parents of children younger than 15 years of age through a questionnaire. The analysis of knowledge, attitudes and antibiotic use involved descriptive quantitative statistics. The effects of interventions were assessed by a logistic and linear regression analysis. **Results:** Data from 1203 interviewees showed that 80% of parents knew that antibiotics could kill bacteria, while 40% believed antibiotics could kill viruses. One third of parents expressed potential dissatisfaction with doctors who would not agree with them on antibiotic use. More parents received information about not taking antibiotics unnecessarily after the interventions, but the rates decreased one year later. At baseline, 20% of the parents and 10% of the children who received antibiotics in previous year, took them without prescriptions. Parental self-medication rates did not change over time, while children rates decreased only in 2015. **Conclusion:** The insignificant and short-term changes in knowledge, attitudes and self-medication demonstrate that interventions need to be implemented for a longer period of time, at a large scale, with active health providers’ engagement, and accompanied by inspections to promote appropriate use of antibiotics and discourage self-medication.  
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## Introduction

Irrational use of antibiotics includes self-medication by patients, which means taking antibiotics without consulting a doctor,

either by getting antibiotics at the pharmacy without a prescription, or by using leftover antibiotics from previous treatments.<sup>1</sup> Although the emergence of antimicrobial resistance (AMR) is a natural biological phenomenon, it is exacerbated by the inappropriate use

of antibiotics, including unnecessary use in nontherapeutic situations.<sup>2,3</sup> Children are particularly prone to high rates of antibiotic use due to greater frequency of respiratory tract infections (RTIs), and (often unnecessary) concerns about possible complications.<sup>4,5</sup>

Self-medication with antibiotics is an existing problem worldwide, mainly in low- and middle-income countries. However, it has been also documented in high-income countries, in particular for cold and upper respiratory tract symptoms (URTI).<sup>1,6,7</sup> Research indicates that self-medication with antibiotics in such context is driven by a variety of determinants on different levels.<sup>8</sup> Individual attitudes toward use of antibiotics, poor knowledge of indications for antibiotic use, and non-awareness of AMR have all been associated with higher rates of self-medication.<sup>8</sup> Over the counter (OTC) sales of antibiotics at pharmacies are often related to customer's pressure, weak regulatory mechanism, and professional conflicts of interest.<sup>8,9</sup> The prevalence of self-medication in, for example, the European Union (EU) varies between 2 and 20 per 100 respondents among different countries, with the highest rates in eastern and southern European countries, and the lowest in northern and western European countries.<sup>10</sup> Given the complexity of the phenomenon of self-medication, simultaneous employment of multiple different interventions is needed to target all stakeholders. Multifaceted managerial and training strategies have proved effective in changing suboptimal prescribing practices.<sup>11,12</sup> As part of a broader strategy, promising interventions at population level include mass education campaigns on the rational use of antibiotics that change public attitudes and perhaps also behaviour, especially in countries with high antibiotic use.<sup>13</sup>

In contrast to the EU where self-medication with antibiotics has regularly been measured in Eurobarometer surveys, antibiotic use including self-medication has not been systematically studied in the non-EU countries in South-Eastern Europe.<sup>10,14</sup> Yet, recent studies have raised awareness of high resistance levels and inappropriate antibiotic use, including widespread, but under-reported OTC sales of antibiotics across this region.<sup>15,16</sup>

This may be of particular relevance in the former Yugoslav Republic (FYR) of Macedonia, where a recent study revealed that 18% of the respondents self-medicated themselves with antibiotics for URTI, and public knowledge on antibiotics was relatively low.<sup>17</sup> The national government has made recent efforts to decrease the overuse of antibiotics by implementing nation-wide multifaceted antibiotic interventions.<sup>18,19</sup> The impact of these interventions on public knowledge and behaviour regarding antibiotics has not been assessed so far, while this might provide a useful guidance for future activities on the improvement of appropriate antibiotic use. Since children are an important target group with common RTI in need of appropriate treatment, and because the occurrence of AMR must be limited, part of the interventions was directed at parents. This study aimed to: (i) assess parental knowledge, attitudes and behaviours regarding use of antibiotics for RTI in children (and parents), and (ii) evaluate the changes in parental awareness and practice of antibiotic use after the implementation of national interventions.

## Methods

### Setting

The FYR Macedonia is a middle-income country with 2 million inhabitants, situated in the Balkan peninsula in Southeast Europe. The country has an universal access to healthcare, and its citizens register with primary healthcare doctors/paediatricians where they get free medical consultations.<sup>20,21</sup> National evidence-based guidelines have been developed for the management of most diseases, including RTIs.<sup>22</sup> Antibiotics are regulated as prescription-only medicines, and those on a positive list are reimbursed by the Health Insurance Fund.<sup>23</sup> The country adopted its national AMR action plan in 2011, and conducted several nation-wide

interventions to improve antibiotic use in 2014/15, as described in Supplementary table S1a.<sup>18,19</sup>

### Design

The impact of the national interventions has been evaluated through three community-based surveys, conducted in May 2014 (baseline), 2015 (post-1) and 2016 (post-2). The timeline of the three measurement points and related interventions are presented in Supplementary table S1b.

The study was conducted in three out of eight administrative state regions (East Region, Southeast Region and Vardar Region), inhabited by half a million people (about 25% of the country population).<sup>24</sup> Each May, respondents were recruited during ten randomly assigned days from people leaving shops and markets, pharmacies, paediatric consultation offices, schools, kindergartens and playgrounds until the sample size of 40 respondents/day was reached. The eligible study participants were defined as parents with at least one child below 15 years of age. Healthcare professionals (e.g. doctors, nurses, pharmacists and lab technicians), more than one member of the same family, and inhabitants from other regions were excluded from the survey. A sample size of 400 respondents was determined using a 95% confidence level and 5% margin of error for an assumed 50% response distribution for self-medication.<sup>25</sup>

### Data collection

Data were collected through a structured questionnaire developed with validated questions from other studies, including the European Commission's Eurobarometer 407 on AMR.<sup>14</sup> The questionnaire was translated from English into national language, pre-tested on a small pilot population and finalized in early 2014. The questionnaires were distributed to trained volunteers during three consecutive years who conducted face-to-face interviews. Respondents' verbal consent was obtained at the beginning of the survey. The confidentiality of the information was maintained by excluding personal identifiers, and all the data collected were processed and analysed anonymously. The interviewees did not receive any financial or other compensation for participation in the study.

The questionnaire consisted of 33 questions divided broadly into three sections: (i) socio-demographic characteristics of parents and their youngest child, (ii) knowledge, attitudes and beliefs regarding antibiotic use and RTI and (iii) self-reported practices related to antibiotic use, including self-medication, in the preceding year. Answers to questions were either 'yes, no, don't know' or multiple-choice answers. Commonly used terms to describe infectious conditions were used without providing a particular definition of the term, e.g. cold, sore throat, flu etc. The questionnaire is included as a Supplementary material S2.

### Analysis

Questionnaire data were checked and coded identically in all three surveys. Collected data were recorded in Excel (Version 2007, Microsoft Office; USA), and the descriptive analysis was done in SPSS (Version 20; SPSS Inc., Chicago, IL, USA). Categorical data were summarized and reported as frequencies and simple proportions. Continuous data were summarized and reported as medians or means.

Differences in participants' socio-demographic characteristics between 2014 and 2015, and 2014 and 2016 were tested with the  $\chi^2$  test or Fisher's exact test for categorical variables, and with the unpaired Student's *t*-test and Mann-Whitney test for continuous variables. In the section on knowledge, 'don't know' replies were grouped with the incorrect answers.

The changes after the interventions were assessed by comparing the differences in knowledge, attitudes and behaviour between 2014 and 2015, and between 2014 and 2016, using a logistic and linear regression analysis in Stata (version 14, StataCorp., TX, USA). In the model, years 2015 and 2016 were entered as dummies and year 2014

**Table 1** Study participants and their children's characteristics: demography and information related to antibiotics in the previous year, 2014–2016

Characteristics	2014 (n = 403)	2015 (n = 400)	2016 (n = 400)
Parents			
Mean age in years (SD)	33 (6.4)	32.3 (6.3)	32.5 (6.5)
Female gender	308 (76%)	312 (78%)	298 (75%)
Minorities	51 (13%)	45 (11%)	51 (13%)
Urban residents	290 (72%)	273 (68%)	312 (78%)*
Married	381 (95%)	381 (95%)	371 (93%)
University degree	143 (36%)	147 (37%)	167 (42%)
Employed	277 (69%)	284 (71%)	297 (74%)
Youngest child in family			
Median age in years (IQR)	5.9 (3; 10)	4.5 (2.5; 8)*	5 (2.5; 9)
Younger than 5 years	195 (48%)	210 (53%)	196 (49%)
Female gender	181 (45%)	206 (52%)	186 (47%)
In kindergarten	105 (26%)	129 (33%)	131 (33%)*
With siblings (<18years)	181 (45%)	199 (50%)	176 (44%)

\*:  $P < 0.05$ .

as a reference variable. The results were corrected for the differences in samples' socio-demographic composition. The statistical significance was determined at  $P < 0.05$ .

## Results

### Participant characteristics

In total, data of 1203 parents and their (youngest) child below 15 years of age were analysed over the three years study period ( $n = 403$  in 2014,  $n = 400$  in 2015 and  $n = 400$  in 2016). Although the parents were different for each of the surveys, their socio-demographic characteristics were similar over the years (table 1). The average parents' age at baseline was about 33 years, and three-quarters of the respondents were females. More than 90% of parents were married, and lived in urban areas. Around half of the children in all the surveys were below 5 years of age.

### Knowledge of antibiotics

Parental knowledge of antibiotics was tested with four statements about the nature and effectiveness of antibiotics and the risks associated with their unnecessary use (table 2). At baseline, 82% of parents knew that antibiotics were effective against bacteria, and their percentage rose slightly over the years. Around 30% of parents understood that antibiotics were not effective against viruses in 2014, with a 9% (statistically insignificant) improvement over the years. Similar or higher percentages of parents expected that colds and flu improve faster with antibiotics (cold: 38, 37 and 38%, and flu: 45, 40 and 48% in 2014, 2015 and 2016, respectively). In 2014, 76% of the respondents were aware of the possibility that antibiotics become ineffective if they are used inappropriately, and 85% knew about antibiotics' side effects. Both percentages increased in 2015, but dropped in 2016 lower than at baseline. The average number of correct answers out of 4 increased significantly from 2.7 to 2.9 between 2014 and 2015, and dropped again to 2.7 in 2016.

### Attitudes towards antibiotics

Figure 1 presents parental attitudes towards antibiotic prescribing and use. At baseline, 20% of parents preferred to give antibiotics—even if unnecessarily—to their children over wait and see if the symptoms would resolve spontaneously. Around 30% of parents were unsatisfied if no antibiotic was prescribed to their children when they considered it necessary, and similar percentage would seek another doctor as a result of that. About a quarter of parents would stop the antibiotic treatment when the symptoms of their

**Table 2** Parental knowledge on antibiotics 2014–16

Statements on antibiotics with correct answers	2014 (n = 403)	2015 (n = 403)	2016 (n = 400)
1. Antibiotics kill bacteria Answer: Yes	330 (82%)	336 (84%)	336 (84%)
2. Antibiotics kill viruses Answer: No	124 (31%)	157 (39%)	158 (40%)
3. If used inappropriately, antibiotics may become ineffective Answer: Yes	307 (76%)	326 (82%)	290 (73%)
4. Antibiotics may have side effects Answer: Yes	342 (85%)	359 (90%)	314 (79%)*
Average correct answers (out of 4)	2.7	2.9*	2.7

\*:  $P < 0.05$ .

child improve. The percentages of parents holding these attitudes did not change significantly over time.

### Information and appropriate use of antibiotics

At baseline, 65% of parents received information about not taking antibiotics unnecessarily in the previous year. There was a significant increase to 78% in 2015, but a decrease 1 year later (63%).

At baseline, 79% of children were given antibiotics in the last year, while the corresponding figures were 84% in 2015 and 70% in 2016 (table 3). In 2014, 89% of children that received antibiotics, were given antibiotics prescribed by doctors, while 6% and 4% were given antibiotics that were either purchased OTC, or kept at home from previous treatments, respectively. The percentage of children that were given antibiotics with prescriptions rose (significantly) to 95% in 2015, but decreased to 91% in 2016.

As for the parents, half of them took antibiotics in the last years at baseline, similarly to 2015 and 2016. In 2014, around 79% of those that used antibiotics took them with prescriptions, while the rest of the parents self-medicated themselves either with OTC (9%) or left-over (11%) antibiotics. The ways of obtaining antibiotics by parents did not change over the years.

## Discussion

We found that over 80% of parents knew that inappropriate use of antibiotics could lead to their inefficacy or side effects, and that antibiotics could kill bacteria. In contrast, 30–40% erroneously believed that antibiotics were effective against viruses and common URTIs. One third of the parents expressed potential dissatisfaction with doctors who would not agree with them on antibiotic use. At baseline, 20% of the parents and 10% of the children who received antibiotics in previous year, used OTC or left-over antibiotics. In comparison to the baseline results, there was a significant increase in the percentage of parents stating to be informed about not taking antibiotics unnecessarily, and a significant drop in the percentage of children self-medicated with antibiotics. Parental irrational patterns of antibiotic provision did not change during or after any of the interventions.

Our study findings should be interpreted within the context of several limitations. First, the study was confined to the southeast and central regions which have their own socio-demographic and health particularities, thereby possibly limiting the generalizability of the results to the whole country. However, a recent baseline study conducted in one western town mainly highlighted the overarching national healthcare culture and infrastructure.<sup>26</sup> Second, the results are based on self-reported practices, which may not represent the actual behaviour, as they have the potential for recall bias, underreporting or overreporting. Future research should therefore combine other methods (i.e. focus groups, observational studies, and pharmacy exit interviews) to validate and triangulate self-reported

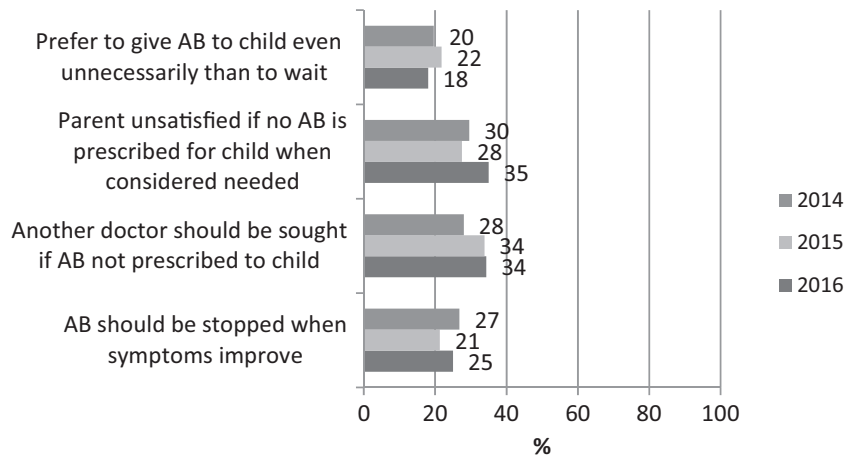


Figure 1 Parents' attitudes towards AB prescribing and use, 2014–16

Table 3 Patterns of antibiotic provision for children and parents in the last year, 2014–16

	2014 (n = 403)	2015 (n = 400)	2016 (n = 400)
<b>Children</b>			
Antibiotic use in last year	n = 319 (79%)	n = 334 (84%)	n = 279 (69%)*
Sources of antibiotics for children that took antibiotics in the last year			
Doctor's prescription	283 (89%)	317 (95%)*	254 (91%)
OTC sale in pharmacies	18 (6%)	4 (1%)	12 (4%)
Left-over AB at home	14 (4%)	13 (4%)	12 (4%)
Don't remember/Don't know	4 (1%)	0 (0%)	1 (0%)
<b>Parents</b>			
Antibiotic use in last year	n = 203 (50%)	n = 211 (53%)	n = 201 (50%)
Sources of antibiotics for parents that took antibiotics in the last year			
Doctor's prescription	160 (79%)	167 (79%)	155 (77%)
OTC sale in pharmacies	18 (9%)	19 (9%)	20 (10%)
Left-over AB at home	22 (11%)	25 (12%)	26 (13%)
Don't remember/Don't know	3 (2%)	0 (0%)	0 (0%)

\*:  $P < 0.05$ .

data. Third, by following the Eurobarometer 407 methodology, we have not ascertained whether the respondents have had a correct idea about antibiotics. Yet, earlier studies have shown that antipyretics and painkillers were often confused with antibiotics.<sup>27</sup>

The parental knowledge of antibiotics in our study is similar to average knowledge levels in adults across the EU. Yet, the parental rates of non-prescribed antibiotic use are in line with highest levels of self-medication in the EU (Greece–21% and Romania–16%), pointing out at certain knowledge, attitudes and practice (KAP) gaps, i.e. inconsistencies between parental knowledge and their own self-medication behaviour.<sup>10</sup>

Our data show relatively lower prevalence of self-medication with antibiotics in children compared with 12–23% of parents in Greece, 36% in China, and 42% in Mongolia that used non-prescribed antibiotics to treat symptoms in their children.<sup>28–31</sup> However, for many developed countries, including the EU, the non-prescribed use of antibiotics in children is less often described in the literature, probably because of its infrequency in such contexts. Besides, findings may vary considerably among countries, because of different study methodologies, or differences in the disease burden and health-care delivery systems.

Although the non-prescription sale of antibiotics is illegal in the country, our results show that pharmacies were an important source of antibiotics for self-medication. Such antibiotic dispensing malpractice calls for more in-depth exploration around the OTC sales. Community pharmacists are the first point of contact in the health system, and are thereby, crucial in demystifying to patients the need to use antibiotics for minor ailments. Thus, more structured

education for pharmacists, their active engagement in public health interventions, and innovative pharmacy service remuneration based on patient care may be effective strategies to improve antibiotic use in the community.<sup>32</sup>

Keeping leftover antibiotics at home is another important factor linked to the non-prescription use of antibiotics.<sup>1,8,33</sup> We found that the percentages of children and parents self-medicated with home-stored antibiotics were as high as those using OTC purchased antibiotics. This practice has also been described in other European countries (Austria: 5%, Estonia and Latvia: 4%).<sup>14</sup> A global survey found that living in a country where antibiotics are dispensed in fixed-count packs rather than as the exact numbers of pills was a strong predictor of the use of left-over antibiotics.<sup>8</sup> Stopping treatment earlier than prescribed is another source of leftover antibiotics.<sup>34</sup> In our study, 25% of parents believed that antibiotics should be stopped when symptoms improve. This practice can increase the risk of relapse, the development of resistant pathogens and produces leftovers for future self-medication. Thus, dispensing of antibiotics in exact numbers of doses should be recommended in addition to the development of information campaigns addressing the importance of completing antibiotic treatment, and discarding any leftover drugs.

Our results show that the national media campaign can lead to elevated percentage of parents informed about not taking antibiotics unnecessary. This is important, because surveys done after campaigns showed that those exposed to the campaigns were more likely to agree with standards of appropriate use of antibiotics and were less likely to expect antibiotics.<sup>35</sup> However, the available literature demonstrates that educating the public about the



differences between infections caused by viruses or bacteria seems difficult. For example, in France, after successive campaigns over 5 years, 54% of the public still did not know that most upper RTIs are of viral origin and do not need treatment with antibiotics.<sup>36</sup> These findings mirror those in our study: parental knowledge on the use of antibiotics for viral infections did not significantly improve after the media campaign, and may need to be addressed with better targeted education on specific indications for antibiotics (e.g. the lack of need for antibiotics for treatment of cold and flu) rather than on the use of antibiotics in general.

Our post-intervention data also revealed the short-term sustainability of the media campaign, as both improvements in terms of more informed parents about not taking antibiotics unnecessarily; and less children self-medicated with antibiotics tended to revert to previous levels after 2015. This suggests the need for continuous educational initiatives to improve knowledge, or at least of longer duration or repetitive actions, followed by regular evaluation of their effects and fine-tuning of key messages to the public.

It was also evident that the introduction of legal penalties to further control the OTC dispensing of antibiotics in 2015 did not immediately reduce self-medication practices in 2016. Perhaps combining the regulatory measures with strict enforcement, including inspections would be more beneficial to ultimately reduce the possibility of getting antibiotics from the pharmacies without prescription. Earlier interventions that succeeded in reducing the OTC antibiotic sales may offer some lessons. Sales of antibiotics without prescription in Zimbabwe decreased after a strict enforcement of the law against OTC sales, when pharmacists expressed fear of losing their licenses for a noncompliance to the rules.<sup>37</sup> Several Latin American countries have also implemented policies to enforce existing laws of restricting consumption of antibiotics only to patients presenting a prescription. An immediate and moderate decrease in the level of antibiotics consumption was documented in Colombia, Brazil and Mexico.<sup>38,39</sup> The effect was even stronger in Chile, where the prohibition of OTC sales of antibiotics was accompanied by a simultaneous public education campaign and involvement of pharmacists. However, these actions were not sustained and the consumption in Chile increased again, highlighting the importance of multifaceted campaigns repeated over several years.<sup>40</sup>

In conclusion, this study is a good starting point to make recommendations to fill some of the knowledge gaps, highlight inappropriate practices and help the planning of future initiatives. It signals the need to implement similar media campaigns for a longer period of time, at a large scale and with active providers' engagement to promote more appropriate use of antibiotics and discourage self-medication practices. The study also calls for an enforcement of certain aspects of dispensing practices, such as inspection of OTC sales, and a limitation of the number of antibiotic tablets dispensed in pharmacies. Finally, monitoring systems that track the implementation of the regulation in terms of antibiotic use (such as part of our data), in addition to AMR and infections rates shall be core components of a more comprehensive strategy.

## Supplementary data

Supplementary data are available at *EURPUB* online.

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*Conflicts of interest:* None declared.

## Key points

- Non-prescribed antibiotic use in FYR Macedonia was comparable to the EU countries with highest levels of antibiotic self-medication.
- Poor parental knowledge on the use of antibiotics for viral infections did not significantly improve after the media campaign.
- The introduction of legal penalties to discourage over-the-counter dispensing of antibiotics did not immediately reduce self-medication practices.
- Media campaigns need to be implemented for a longer period of time, at a large scale, and combined with active health providers' engagement, and inspections.

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