FACTORS INFLUENCING CONSUMERS' USE OF ANTIBIOTICS IN THE WHO EUROPEAN REGION

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List of abbreviations

AB(s) - Antibiotic(s)

AMR- Antimicrobial Resistance

DDD- Defined Daily Dose

EAAD- European Antibiotic Awareness Day

ECDC- European Center for Disease Prevention and Control

EEA- European Economic Area

EU- European Union

MAS- Masculinity

MRSA- Methicillin-Resistant Staphylococcus Aureus

OTC- Over The Counter

PDI- Power Distance Index

SAR- Self- medication with Antibiotics and Resistance

UAI- Uncertainty Avoidance Index

UK- United Kingdom

URTIs- Upper Respiratory Tract Infections

WHO- World Health Organization

List of figures and tables

Abstract

Background: Antimicrobial resistance is a growing threat for public health globally, and this is also the case in Europe. It is not only a medical problem but also socio- economic and ecological problem. In addition to prescribers and dispensers, consumers also are the main players in reducing inappropriate and excessive antibiotic use which develop bacterial resistance to antibiotics. The analysis of consumer related factors in the EU has not been performed. Therefore, this thesis is focusing on the consumers.

Objective: The overall objective of this study is to explore factors influencing consumers' use of antibiotics in the WHO European region.

Methods: A literature review was performed using broad search terms that were defined by the study objective. 37 relevant peer- reviewed articles, searched using database PubMed, were analyzed.

Results: The problem of inappropriate antibiotic use in the WHO European region exists. It is more significant in Southern- Eastern than in Northern- Western Europe. The key underlying factors, outside the health care service delivery, influencing antibiotic use are: insufficient knowledge about antibiotics, especially among respondents from rural area, Southern- Eastern Europe and immigrants; weakness of drug legislation in Southern- Eastern countries, influencing the using antibiotics over the counter; and cultural factors which are rather different in the analyzed region.

Conclusions: The results of this study can be a basis for further studying on the issue of the antibiotic use in the WHO European region. However, the findings should be interpreted within the context of the limitations of the study.

Key words: Antibiotic use; WHO European region; Consumers

Word count: 248

Introduction

Antimicrobial resistance (AMR) is a growing threat for public health at the global level, and this is also the case in Europe. Resistance patterns vary per organism and country. In some countries of the World Health Organization (WHO) European region more than 50% of Staphylococcus aureus is methicillin-resistant (MRSA). Moreover, new mechanisms of resistance appear and spread quickly (1).

Incidence and mortality are considerable. For example, in Norway and Iceland, about 400 000 resistant infections arise annually. It in turn leads to about 25 000 deaths per year. The problem already can be identified at the local levels in hospitals: reducing effectiveness of antibiotics (ABs) in treatment serious life-threatening diseases. It decreases people's chances of survival (1).

Antimicrobial resistance is not only a problem of the health care sector. It has great economic consequences. The economic loss in the European Union (EU) due to antimicrobial resistance is over €1.5 billion every year. These estimations have been done by the European Centre for Disease Prevention and Control (ECDC) in 2011 (1). According to the prediction of Jim O'Neill, the chairman of the Review on AMR in 2014, drug-resistant infections could kill an extra 10 million people across the world every year by 2050 if they are not tackled. By this date they could also cost the world around $100 trillion in lost output: more than the size of the current world economy, and roughly equivalent to the world losing the output of the United Kingdom (UK) economy every year, for 35 years (2).

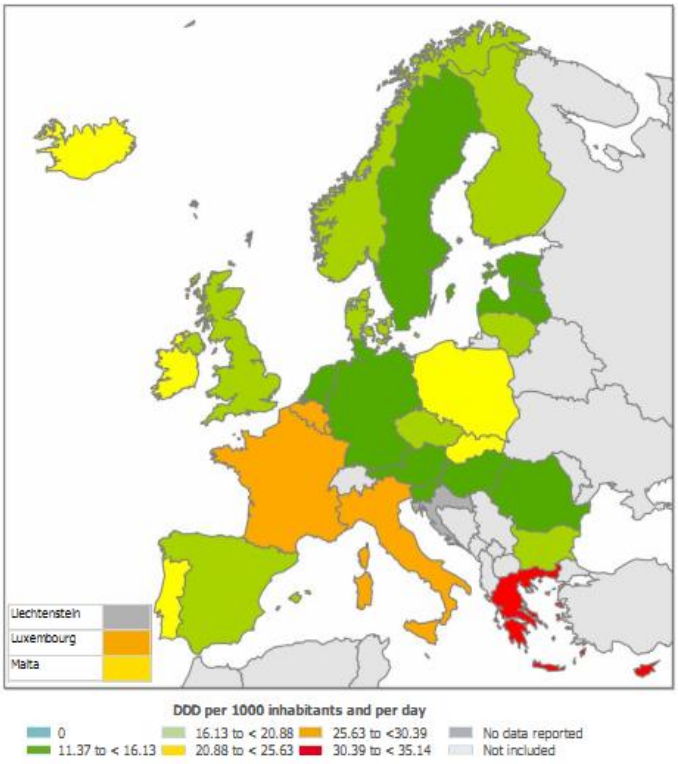
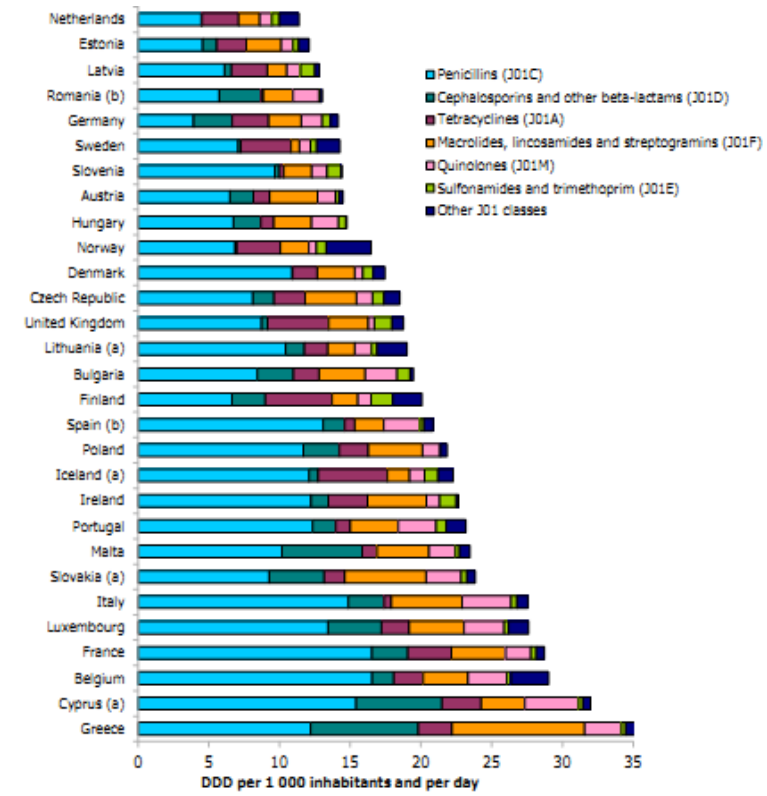


Figure 1. Consumption of antibiotics in EU/European Economic Area (EEA) countries, expressed as DDD per 1000 inhabitants and per day, 2011 (9).

Antibiotic resistance is the resistance of bacteria to antibacterial medicines to which it was sensitive previously. Bacteria's mutations or acquirement a resistance gene lead to resistance development. It in its turn leads to inefficiency of standard prevention and treatment, and persistence of infections which may spread to other persons (1). Antibiotics (antibacterial drugs) - medicines which use for prevention and treatment bacterial infections (e.g. tuberculosis, bloodstream, some respiratory tract infections, etc.). Their inappropriate as well as appropriate use has led to emergence and growth in resistant bacteria (1). Appropriate antibiotic use requires that "patients receive medications appropriate to their

clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community" (3). Inappropriate antibiotic use includes self- medication, sharing antibiotics with other people, failure to complete treatment and saving leftovers for another occasion (4). Self-medication is defined by the WHO as "the autonomous decision to use a medication without medical advice in order to treat self-diagnosed symptoms" (5). Antibiotics are used not only in treatment of humans but also in animal treatment and in the food animal production. The use of antibiotics in humans as well as in animals may lead to resistance of bacteria. Moreover, resistance can be transmitted between them and the environment (e.g. some water supplies) (6).



(a) Cyprus, Iceland, Lithuania and Slovakia provided total care data, i.e. including the hospital sector.
(b) Romania and Spain provided reimbursement data, i.e. not including consumption without a prescription and other non-reimbursed courses.

Figure 2. Total antibiotic use in EU/EEA countries, expressed as DDD per 1000 inhabitants and per day, 2011 (9).

The level of antibiotic use in the WHO European region is different: lower consumption is in Northern Europe compared to Southern- Eastern Europe (7- 9). Data from Eastern Europe are not reported (see Figure 1). The consumption of antibiotics is expressed in defined daily dose (DDD) per 1000 inhabitants and per day. Indices vary from country to country and also depend on the strength of monitoring system (6). According to the report of the European Antibiotic Resistance Surveillance network, antimicrobial resistance of Gram-negative bacteria (e.g. Escherichia coli and Klebsiella pneumonia) to new- generation antibiotics (e.g. third-generation cephalosporins,

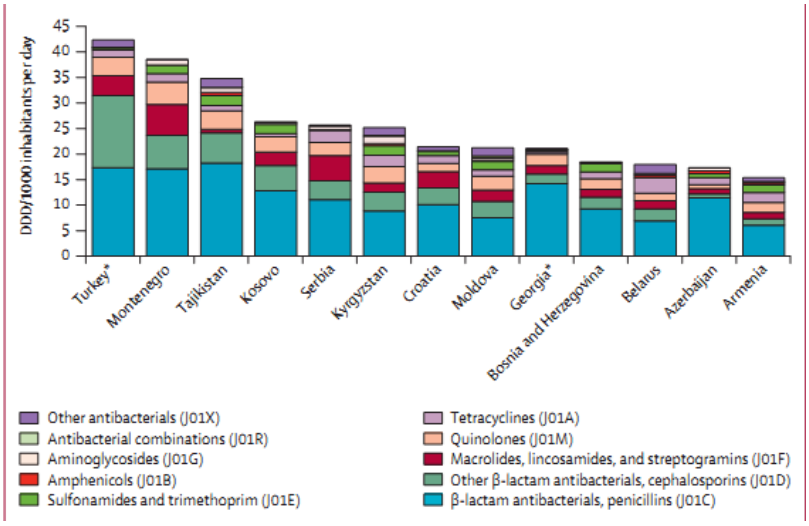


Figure 3. Total antibiotic use in non- EU southern and eastern European countries and newly independent states, expressed as DDD per 1000 inhabitants and per day, 2011 (10).
*Reported only outpatient antibiotic use.

fluoroquinolones, and carbapenems) is increasing in Europe. At the same time, development of new antibiotics is not expected (6, 10). The mainly used antibiotic in both EU and non-EU countries is penicillin (see Figures 2, 3).

Background information

The WHO European region includes 53 Member States: both European Union and non- European Union countries (see Appendix 1). There are many differences in the WHO European region: geography, political forces, economy, demographic situation, languages, cultures, etc. This territory is divided into some regions: Northern (e.g. Iceland, Sweden, etc.), Southern (e.g. Spain, Malta, etc.), Western (United Kingdom, France, etc.) and Eastern (e.g. the former Soviet Union countries: Ukraine, Belarus, Russia, etc.) (see Figure 4). Also, some sources (11) consider Central region (e.g. Switzerland, Estonia, etc.). Countries with different income are presented: from high income countries (e.g. Sweden, the Netherlands, Austria, etc.) to the countries with lower- middle- income economies (e.g. Armenia, Moldova, Uzbekistan, etc) (12). The European Union countries are a part of the WHO European region. For statistical data about the EU see Table 1.

Figure 4. Map of the WHO European region and the surrounding region, 2015 (11).

Capital	Brussels
Official languages	24 languages
Type	Politico- economic union
Member states	24 states
Total area	4,324,782 km2
Population	506,913,394 (2014)
GDP	$16.449 trillion (2015)

Table 1. Statistical data about the European Union, 2015 (13).

Immediate actions of both government sectors and society are required worldwide to improve the situation. Moreover, the collaboration of the main stakeholders (policy makers, health workers, pharmacists, general population, patients, food animal industry, etc.) is needed.

Problem Statement, Justification, Objective, and Methodology

Problem Statement

Antibiotics are important medicines used all over the world (4, 14). However, their inappropriate and excessive use has led to increasing antimicrobial resistance, which is becoming an extremely important public health issue worldwide (7, 15- 29). This problem also affects the WHO European region. Moreover, there are evidences of aggravation of the situation in some countries from this region (19, 22, 29). The emergence of antimicrobial

resistance is multicausal. The contribution of health professionals at this process is well established. Doctors contribute by inappropriate antibiotic prescribing (14, 24, 29, 30) and pharmacists and drug stores contribute by selling antibiotics over the counter (OTC) (17, 19, 21, 22, 31- 33). However, inappropriate use among consumers also plays a role in development of bacterial resistance to antibiotics (7, 8, 14- 17, 19- 21, 23- 25, 27- 32, 34- 44). Hence it is essential important to understand what can be done to minimize inappropriate use of antibiotics (8, 17, 18).

As indicated above, European countries have different level of antibiotic self- medication among general population: from 5% to 45% (7, 8, 21, 23, 29, 30). It is stated that the problem is more significant for Southern- Eastern European countries (e.g. Romania, Lithuania, Russia, Malta, Spain and Italy) compared to Northern- Western Europe due to possibility of purchasing antibiotics over the counter (17, 19, 21, 22, 32, 39, 43). The role of consumer related factors however has not been studied. Moreover, in some countries of Southern-Eastern Europe (19, 22, 29) the level of antibiotic self- medication has increased. For example, in Lithuania there is a clear upward trend: self- medication has increased by 10% since 2006 and makes 31% in 2015 (29). The reasons for this increased trend are likely partly due to consumer related factors. Self- medication is likely also dependent on the condition for which the antibiotics are taken. According to the studies (17, 20- 22, 24, 25, 27, 31, 36, 43, 45), upper respiratory tract infections (URTIs), which usually are caused by viruses, were the most common reason for antibiotic self- medication in Europe. For example, it was found that expectation of antibiotic efficacy for common cold symptoms was about 48% among Europeans (45).

Antibiotic misuse as well as their inappropriate use may lead to negative medical consequences due to insensitivity of bacteria to the standard treatment of infectious diseases. Some articles indicated a transition from the old narrow-spectrum to the new broad-spectrum antibiotics (17, 25). Also, it is an additional risk of appearing of side effects which may appear because of drug interactions in treatment multidrug resistant bacterial infections (19, 21, 30, 43). Moreover, resistance to antibiotics leads to increasing morbidity, mortality and costs of health-care services (7, 16, 25, 36). As indicated antibiotic resistance is both a medical and economic problem. It however also relates to social and ecological factors (4, 16, 22, 26, 28, 30, 36). Globalization and migration increase the spread of the AMR problem (10).

Antibiotic resistance is a global problem. For this reason countries individually cannot confront this issue and international collaboration is needed (7). The WHO report "Antimicrobial resistance: global report on surveillance 2014" indicated that antimicrobial resistance is a danger for everyone everywhere. "A post-antibiotic era – in which common infections and minor injuries can kill – far from being an apocalyptic fantasy, is instead a very real possibility for the 21st Century." (46). The World Health Day's topic in 2011 was "Combat drug resistance: no action today means no cure tomorrow" (47). A strategic action plan against the antibiotic resistance was developed in 2011 by WHO European Region (47). According to the WHO report, consumers can help to overcome the antibiotic resistance by using only prescribed antibiotics, completing the full prescribing course, stop using leftover prescriptions and avoiding sharing antibiotics with other people whom drugs were not

prescribed. There are examples of interventions in Europe aimed to improve the situation of antibiotic resistance. Educational campaigns (e.g. e-Bug project, national media campaigns in Belgium, Sweden, etc.) were conducted to increase the awareness about antibiotic resistance and decrease the level of inappropriate antibiotic use among general population and patients in Europe (23, 34, 45).

Justification

As indicated above there are three main players regarding the issue of antibiotic resistance. In addition to prescribers and dispensers, consumers also influence on the level of inappropriate and excessive antibiotic use (7, 8, 14- 17, 19- 21, 23- 25, 27- 32, 34- 44). The analysis of consumer related factors in the EU has not been performed. Therefore, this thesis is focusing on the consumers. The exploration of the underlying factors, influencing on the use of antibiotics among consumers, is essentially important in order to understand further interventions to improve the situation according to inappropriate antibiotic use (15). There are clear differences among countries that influence on the use of antibiotics among consumers. Comparative analysis of the studies lead in different countries may shed light on the interplay between the factors.

Objective

The overall objective of this study is to explore factors influencing consumers' use of antibiotics in the WHO European region. Identification of factors influencing the use of antibiotics could help developing targeted interventions to reduce inappropriate use.

The following research questions motivated the study:

1) What are the underlying factors associated with antibiotic use among consumers in the WHO European region?

and

2) How can we use research findings to improve an antibiotic use practices among consumers in the WHO European region?

Methods

Search strategy

A literature review was performed using broad search terms that were defined by the study objective. Search terms from four main fields (factors, consumers, antibiotics and geography) were combined with OR and AND (see Appendix 2). Relevant published peer- reviewed articles were searched using database PubMed and electronic search engine Google Scholar. Also, 'grey' literature was used for extra information for a better focus in the subject (e.g. WHO website, Wikipedia, etc.). It was identified 1667 peer- reviewed articles using the search terms in the title/ abstract fields. The following filters were applied: humans, 10 years and languages (English and Russian). Eventually, 647 articles were screened for relevance. There were three stages of screening process: screening of title, abstract and full text. Each stage was based on the inclusion and exclusion criteria of the review. The reference lists of the selected articles were searched for other relevant articles. This resulted in 37 full text

articles that were assessed for eligibility (see Appendix 3). The detailed search strategy is presented in Figure 5.

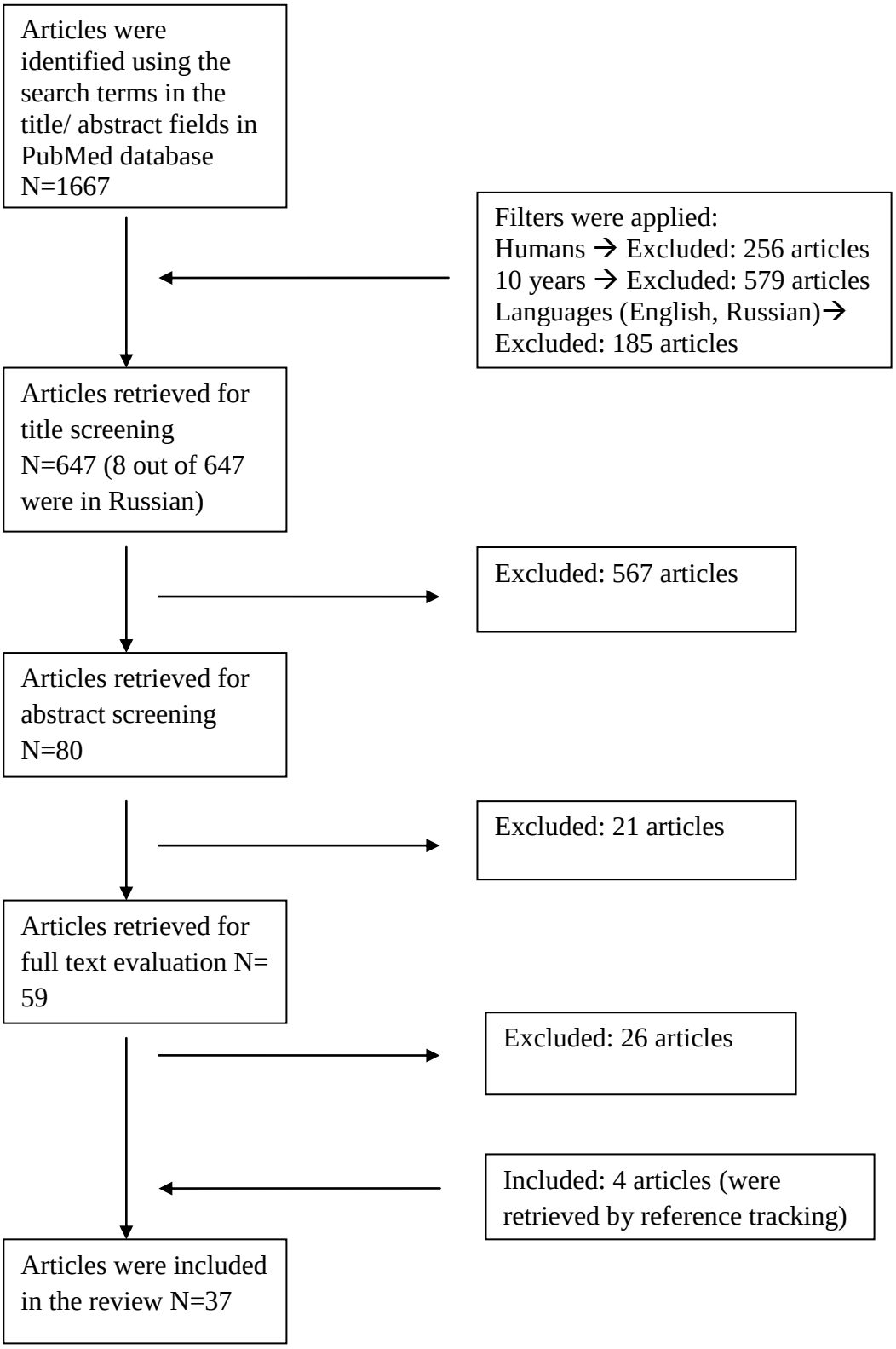


Figure 5. Flow diagram of the article selection process.

Study Inclusion and Exclusion Criteria

Articles were included if they (1) reported about factors regarding antibiotic use among consumers; (2) provided the required data about the countries of the WHO European region. The filter on time (10 years) was used to find out the current situation regarding antibiotic use in the WHO European region. However as the main search articles on the subject had limited information about some regions of the WHO European region, additional articles have been searched for expanding the geography of the literature review via reference tracking including older articles. The reference tracking resulted in 4 articles published in 2002- 2003 from the countries that were originally not represented in the search. The filter "languages" allowed retrieving for screening articles only in the suitable languages: English and Russian. The filter "humans" was caused by the need to analyze antibiotic use among consumers. 614 articles were excluded due to:

- Articles were not about factors influencing consumers'/ patients' use of antibiotics (e. g. evaluation of the programs' implementation, antimicrobial susceptibility, bacterial resistance, etc.): 337 articles;
- Articles focused on prescribers or dispensers not on consumers/ patients: 216 articles;
- Articles were not about the WHO European region: 36 articles;
- Articles were about medication in general, not about ABs: 23 articles;
- It was not possible to find full text: 2 articles.

Conceptual framework

This literature review discusses the influence of the underlying factors on the consumers' antibiotic use, and bases their analysis on the Dahlgren and Whitehead's model of health determinants presented at Figure 6.

This framework has been chosen as it allows analyzing the study results in order to explore the underlying determinants that pose key barriers and motivators regarding antibiotic use among consumers. The findings should help to understand further interventions to improve the situation according to inappropriate antibiotic use. The conceptual framework is used in the result and the discussion sections of the literature review for a better structure. However, this framework is too limited and it is needed to adapt it regarding to the aim of the study.

The framework allows exploring results consistently: from micro to macro. There are five layers of social and economic determinants which interact with individual factors: (1) age, sex and hereditary factors, (2) individual lifestyle factors, (3) social and community networks, (4) living and working conditions and (5) general socio- economic, cultural and environmental conditions.

In the first layer individual factors are analyzed: sex, age and health condition. The health condition factor was added to the model, while hereditary factor was excluded.

Knowledge and the use of sources of information about antibiotics are linked to individual lifestyle and discussed here in the second layer.

In the third layer on social and community networks the role of migration on the social networks will be discussed.

In the fourth layer agriculture and food production, work environment, water and sanitation, housing and environmental condition were excluded from the review of living and working conditions because they are not associated with antibiotic use among consumers. The influence of curative health care services are described but not studied in detail in this thesis. However, the impact of educational campaigns by the health care services will be discussed here as this has not been studied extensively before. Also, the role of education on the consumers' antibiotic use is analyzed in this layer.

Geographical context, socio- economic status, implementation of drug legislation and cultural factors are discussed under general socio-economic, cultural and environmental conditions in the fifth layer.

This adaptation of the model was done for more thorough analysis of the influence of the underlying factors on the consumers' antibiotic use.

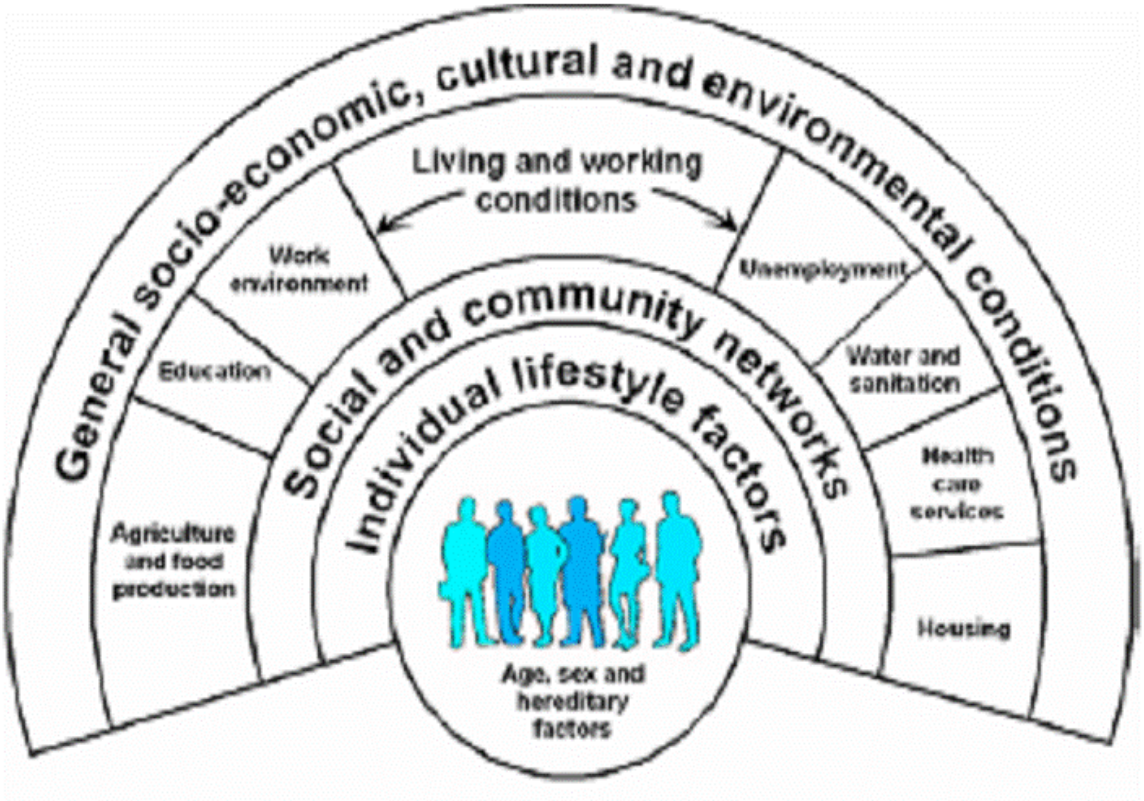


Figure 6. Dahlgren and Whitehead's model of health determinants, 1991 (48).

Study results

1. Individual demographic factors

According to some of the articles, which were included in the review, consumers' demographic factors, like age and sex, influence on the antibiotic use. These factors are presupposed to be connected with other determinants like gender, geographical context, health status, socio- economic situation as well as education.

1.1 Sex

Ambiguous conclusions regarding the connection between sex and antibiotic use were provided by the studies. Some studies stated that there is no difference in inappropriate antibiotic use including self- medication between men and women (7, 19, 25, 32, 39, 43, 44).

However, some studies (28- 30, 41) found that men are more inclined to use antibiotics inappropriately than women. And another number of the studies (5, 14, 34) reported these data in the opposite way. According to the studies, these differences had different ranges. On the one hand, the level of self- medication with antibiotics among men was 1,24- 2,91 times higher than among women. On the other hand, women used antibiotics as self- medication 2-3,44 times more often compared to men. Some studies stated that these differences were not significant. The information about the studies and their limitations is summarized at Table 2.

The 'sex- knowledge- antibiotic use' relation was discussed in some studies (see section 'Knowledge'). The documentary evidences of links between 'sex- antibiotic use' and other underlying factors (access to health care services, socio- economic status, gender roles, etc.) were not found in the reviewed articles.

Sex	Reference	Country	Study	Year(s)	Nr. participants	Limitations/ Strengths
Men > women	30	Portugal	Descriptive, cross- sectional, epidemiological study (self-medication)	February - April 2011	1192	- area of selection (one region) - patient self-reporting + high response rate + large sample size
	28	Turkey	Descriptive, questionnaire survey by face to face interview (self-medication)	30 January-9 February 2006	2696	- area of selection (healthcare centers in the capital) + high response rate + large sample size
	29	Lithuania	Prospective cross- sectional study (self-medication)	2015	1005	- patient self-reporting - obtained ↓ % of the respondents over 60 + high response rate + large sample size + study population characteristics are comparable with general population
	41	Greece	Cross- sectional study, questionnaire survey (inappropriate	January-July 2007	5312	- time (months) of the survey (antibiotic overuse) - patient self-reporting

			AB use)			+ high response rate + large sample size
Women > men	34	Great Britain	Questionnaire survey (inappropriate AB use)	February, March, June, July 2003	7120	- patient self-reporting + high response rate + large sample size + random sampling represent the whole population
	5	Greece	Cross- sectional, survey by face to face interview (self-medication)	January-February 2011	150	- area of selection (rural area) - small sample size + random sampling
	14	Italy	Questionnaire-based survey (self-medication)	October 2009-October 2010	1269	- area of selection (urban area) - patient self-reporting + large sample size

Table 2. Link sex with inappropriate antibiotic use/ self- medication.

1.2 Age

There is contradictory information about the influence of age on the antibiotic use. On the one hand, seven studies (7, 19, 25, 32, 39, 43, 44) didn't find any association of the age of the respondents with self- medication.

On the other hand, in the studies, where such a connection has been found, there was no general consensus on the question of the age of people inclined to self- medication with antibiotics. The notes were made in the six studies that the age of a person is connected with antibiotic use. Jorgji et al. (31) restricted the interviewees to a mid aged group between 21-49 years old in two districts in Albania. The study found that 78% of respondents of 21- 49 years old used antibiotics for self- medication. However, the study had small sample size (350 respondents). High level of self- medication among mid-aged people of approximately the same age groups of people was found by the other two studies: Grosso et al. (14) indicated that about 40% of the interviewees, who self- medicated with antibiotics, were aged 25- 44, in Italy; and Ilhan et al. (28) found that about 45% among the respondents of 30-49 years old in Turkey used antibiotic self- medication. The population over 18 years old was analyzed in these two studies. The samples' sizes were large: 1269 and 2696 respectively. However, only urban population was examined. One more survey was done in Italy. Napolitano et al. (16) showed that the participants of 28- 39 years old self- medicated with antibiotics more often compared to another age group of 40- 60. However, the study was conducted among 419 parents of pupils 5- 18 years old in two districts. One study found a higher level of self medication among elderly: Pavyde et al. (29) found that in Lithuania the respondents of 41- 79 years old were more likely to use antibiotics for self- medication than 18- 40 years old respondents. However, it was stated that it was low representation of the participants over 60. At the same time, the sample size of the study was large: 1005; and population characteristics of the participants were comparable with general population of Lithuania. Finally, in Portugal the age groups of the highest risk were identified by

Ramalhinho et al. (30) as 18- 34 and 50- 64 while the individuals of 18-79 years old were analyzed. The risk age groups compared with the age group over 65. The risk of self-medication was 4,57 times higher in the 18- 34 years group and 2,33 times higher in the 50-64 years group. Despite a large size of sample (1192), the study was conducted in one Portugal region. The evidence of strict compliance between particular age group and self-medication could not be found. Links between age and self- medication, which were found in the articles, are summarized in the Table 3.

Age of self-medication	Reference	Country	Study	Year(s)	Nr. participants	Limitations/ Strengths
21-49	31	Albania	Descriptive, questionnaire based study	December 2012-March 2013	350	age (21- 49) - area of selection (2 districts) - patient self- reporting - small sample size - a part of questionnaires were sent by E-mail
25-44	14	Italy	Questionnaire- based survey	October 2009-October 2010	1269	age (over 18) - area of selection (urban area) - patient self- reporting + large sample size
30-49	28	Turkey	Descriptive, questionnaire survey by face to face interview	30 January - 9 February 2006	2696	age (over 18) - area of selection (healthcare centers in the capital) + high response rate + large sample size
28-39	16	Italy	Cross-sectional, questionnaire- based, epidemiologic survey	December 2011	419	age (28- 60 years old parents of students 5- 18 years old) - area of selection (9 schools at 2 regions) - patient self- reporting - small sample size - study's design precludes any conclusion regarding the causal relationships between variables + high response rate + random sample
41-79	29	Lithuania	Prospective cross-sectional study	2015	1005	age (18- 79) - obtained ↓ % of the respondents over 60 - patient self- reporting

						+ high response rate + large sample size + study population characteristics are comparable with general population
18-34 50-64	30	Portugal	Descriptive, cross-sectional, epidemiological study	February- April 2011	1192	age (18- 79) - area of selection (one region) - patient self-reporting + high response rate + large sample size

Table 3. Link age and self- medication.

1.3 Health condition

As indicated in the introduction, viral URTIs were mentioned in the reviewed articles as the most common reason for self- medication with antibiotics among Europeans.

According to the large European project "Self- medication with Antibiotics and Resistance" (SAR project) (25), absence of chronic disorders linked with the high level of antibiotic self-medication among general population in Lithuania: individuals without chronic conditions used self- medication approximately two times more often compared to chronically sick persons. The same conclusion was reached in a study among rural population in Greece (5). There were no explanation of the connection between health condition and antibiotic self-medication in the articles.

There were a limited number of studies (two) which described association between health status of individuals and their use of antibiotics. Moreover, the size of the study's sample in Greece was small: 150 participants from rural area only. The study in Lithuania analyzed 746 participants from rural and urban areas, but it should be stated that the response rate was low (25.4%). For more information about the studies see Appendix 3.

2. Individual lifestyle factors

2.1 Knowledge

Knowledge has an impact on antibiotic use. According to some studies (24, 26, 27, 34, 44), there was no a simple link between knowledge and actual use of antibiotics. For example, McNulty et al. (34) found that British people had enough knowledge about antibiotic resistance but in spite of that used them inappropriately. Moreover, Buke et al. (26, 33) stated that even specific knowledge (pharmacology lessons) didn't lead to appropriate antibiotic use among university students and academic staff in Turkey. On the one hand, people at the Faculties of Dentistry and Pharmacy had better knowledge and lower level of self-medication with antibiotics compared to other faculties. On the other hand, they still often practiced self- medication with antibiotics. Also, the articles (26, 33) stated that in Turkey the weakness of implementation of drug legislation existed. It led to availability of antibiotics without prescriptions. Additionally, there were two independent studies and there was no

comparison between them regarding socio- economic statuses of academic staff and students of the University.

A lot of studies found a direct relation between better knowledge about antibiotics and their appropriate use (5, 7, 15, 16, 22, 23, 25, 29, 34, 37, 44, 45). This data was obtained from 21 countries of different regions of the WHO European region. For example, the findings of the study in Spain suggested that patients, who actively discussed potential drug interactions with their doctors more often, were less likely to self-medicate due to better knowledge (44).

Despite this fact, there was no a simple influence of knowledge on antibiotic use. According to the studies, knowledge about antibiotics is multifaceted (e.g. knowledge about resistance, use, side effects, etc.). For example, respondents in Macedonia had high knowledge about antibiotic resistance and about allergic reactions as a side effect, while poor knowledge about antibiotic effectiveness existed (38). Some studies (19, 23) indicated a direct relation between knowledge about antibiotic resistance and the level of self- medication: in Uzbekistan less knowledge was associated with high antibiotic self- medication, while in Sweden more than 80% of respondents knew about antibiotic resistance and the country had a low level of self-medication. Also, in Poland was found that low level of knowledge about antibiotic effectiveness led to high level of self- medication (36).

Moreover, in Lithuania was found that people with low level of knowledge about antibiotics were inclined to overestimate their knowledge (29). Such conclusion was reached after the comparison of self-evaluation of knowledge about antibiotics before answering the surveys' questions with actual correct answers related to antibiotic use among the respondents. Also, overestimation in turn increased the level of self- medication (29). Additionally, Godycki-Cwirko et al. (37) found that the rural population in Poland was less convinced in their knowledge about antibiotics. It led to a more accurate following the doctors' advices compared to the urban population. At the same time, the study stated that in fact in rural area people had less knowledge, while in cities the level of knowledge was enough. It in turn showed the association between better knowledge and inappropriate antibiotic use in cities and the opposite situation in villages: less knowledge led to a more appropriate antibiotic use. Radosevic et al. (7) and McNulty et al. (34) also found that better knowledge associated with higher antibiotic self- medication in both six countries of Southeastern Europe and the United Kingdom as well.

There were evidences of interaction of knowledge with demographic factors as well as education, which influenced on antibiotic use.

Six studies (23, 34, 35, 41, 44, 49) made a note of gender specific knowledge about antibiotics: less knowledge about antibiotics (effectiveness, resistance, etc) was found among men.

There was no common opinion about the influence of age on the knowledge about antibiotics as well as on antibiotic use. On the one hand, low level of knowledge was found among young generation (16- 24 years old persons) in Britain (34). It is not always associated with their educational level as the lack of knowledge about antibiotics was detected also among

young school teachers in Uzbekistan (19). On the other hand, people of 41- 50 years old (49, 38) and individuals aged more than 75 (34) associated with the lack of knowledge.

Comparative pan- European study (15) found that inappropriate knowledge as well as the level of self- medication was higher among the population of Southern- Eastern Europe than in Northern- Western one. For example, in Malta 87% of respondents didn't know about antibiotic resistance and there was the highest index of self- medication compared with the other countries. Knowledge about antibiotic resistance was the lowest in South- Eastern Europe where prevalence of self- medication was high (15).

Many studies have shown a link between lower education and a poor knowledge about antibiotics (16, 30, 34, 38, 49). However, two studies (26, 33) indicated that better education and knowledge didn't necessary lead to appropriate antibiotic use. The researchers found inappropriate antibiotic use and lack of knowledge among academic stuff and university students from different Faculties (including Dentistry and Pharmacy) in Turkey.

2.2 Source of information about antibiotics

Doctors (general practitioners, pediatricians) were the main source (53,6%- 90%) of the information about antibiotics for consumers in studies in various countries and settings (7, 16, 24, 29, 35, 37, 40, 49). Also, Napolitano et al. (16) stated that information from other sources increased the level of self- medication with antibiotics. The same finding was done in Russia: low quality information from the media sources and the Internet was associated with high level of antibiotic self- medication (22). At the same time, the relations between findings and gender, education or socio- economic status were not explained in the articles.

3. Social and community networks

3.1 Migration

Some studies (18, 32, 39- 41) indicated that immigrants had an inappropriate knowledge and practices regarding to antibiotics. Low level of education, the limited access to health care services and to the sources of reliable information, cultural beliefs often led to the inappropriate antibiotic use among immigrants. Also, the difficulty in communication with doctors because of non- native language affected immigrants' antibiotic use (41).

Moreover, immigrants gave antibiotics to their children more often compared to the non-immigrants as believed that such a treatment should help kids to recover faster. It was important because parents had to get back to work earlier due to the low socio- economic status (18, 41). Additionally, they were away from the native country and had less support of relatives, which made parents more worried about a sick child (41). For example, the immigrants in Cyprus more often treated their children of 4-7 years old with antibiotics purchased over the counter more often compared to parents which were born in Cyprus (40). Also, Mangrio et al. (32) conducted a population-based cross-sectional survey in Sweden among parents of 8- month- old children. It was found that children whose parents were immigrants consumed antibiotics more often compared to families from Sweden. Additionally, the studies which analyzed practices regarding antibiotics among non-immigrants parents (24, 38, 40), found that even adults, who used antibiotics for self-

medication, were less likely to treat their children without doctors' advices due to trusting relationship with their pediatricians (21, 24, 29, 38, 43).

Also, Vaananen et al. (39) found that Finnish immigrants changed their antibiotic use habits and practiced antibiotic self- medication when poor implementation of drug legislation in Spain allowed them to purchase antibiotics over the counter.

4. Living and working conditions

4.1 Education

14 articles indicated the connection between the level of education and antibiotic use. However, the information about this relationship was ambiguous. Six of them (19, 31, 32, 36, 40, 41) from Poland, Albania, Uzbekistan, Sweden, Cyprus and Greece found a link between the low educational level and inappropriate usage of antibacterial drugs. However, the studies had a number of limitations. For example, 31- had small sample size (350 respondents) and a part of questionnaires was send by e- mail; 19, 40- analyzed only urban population; 36- compared rural and urban population, however, the representation of the urban people was approximately two times higher; the participants of different age groups have been represented.

On the contrary, in the Great Britain, Greece, Italy and Turkey (5, 14, 28, 34) higher education led to the high level of self- medication. But these studies also had limitations. For example, two studies (14, 28) were conducted among urban population, while the study in Greece (5) analyzed small number of respondents (150 respondents) from rural area only. Also different age groups were presented: in the Great Britain the respondents over 16 have been selected, while the people over 18 have been included in the other studies.

Moreover, according to the analytical studies in Ege University in Turkey among the academic staff and students, it was found that the level of self- medication was high despite the higher education of the respondents: 45.8% and 44.1% respectively (26, 33). However, the people with different socio- economic status and different age groups were included in the studies: 26- 48 years old academic staff and students aged 18- 24.

Additionally, in Portugal and Lithuania any association between self- medication and the level of education was not found (25, 30). For more information about the studies see Table 3 and Appendix 3.

Also, the association of education and antibiotic use can be linked with other determinants: knowledge, geographical context, socio- economic status, cultural factors and drug legislation. The evidences of most of these relations were not found in the reviewed articles. However, the associations between antibiotic use with education and knowledge as well as with education and residence area were found (see sections 'Knowledge' and 'Geographical context' respectively).

4.2 Health care system: prevention through educational campaigns

As indicated above, prescribers and dispensers are the key health care players regarding to the antibiotic use. The role of pharmacists in antibiotic use is important. They should be one

of the barriers for inappropriate use. However, the articles stated that people in Southern-Eastern Europe still can purchase antibiotics over the counter without prescriptions (7, 15, 17, 28, 29, 31, 38). As far as prescribers are concerned, it should be stated that they can influence on the antibiotic use not only by the amount of prescribed antibiotics but also by providing information (7, 16, 24, 29, 35, 37, 40, 49). The limited trust in relationship between doctors and patients as well as low levels of quality, availability and accessibility of the health care services can lead to self- medication (39, 41, 44).

The impact of the e- Bug project among school students in Portugal was analyzed in one study (45). The level of knowledge among pupils was improved: the knowledge about antibiotic effectiveness increased from 43% to 76% and the knowledge about antibiotic resistance increased from 48% to 74% (45). The e-Bug project is an international campaign which unites 29 countries. It is held among junior, senior students and young adults in order to increase knowledge about appropriate antibiotic use and awareness about antibiotic resistance. The goal is achieved by interactive lessons, website hosting games, quizzes, etc. (50). As indicated above, the relation between knowledge about antibiotics and their use is not simple: increased knowledge may even increase self medication. The results, which were assessed in the study, were short term results of the educational campaign. The long term results of the campaign were not mentioned in the article.

Also, in some articles were mentioned about educational campaigns in Europe: 'Andybiotic' in the United Kingdom (34) and 'Strama' in Sweden (23). However, the impact of these projects was not analyzed. The data about public- education campaigns in Eastern Europe was not found in the reviewed articles.

All the campaigns mentioned above are the interventions of the ECDC. One of the aims of the ECDC is to fight against inappropriate antibiotic use. Also, this European Union agency conducts the European Antibiotic Awareness Day (EAAD). It is an annual event on the 18th of November which aimed to increase awareness about antibiotic resistance and antibiotic appropriate use. For example, in 2014 the major theme of the EAAD was antibiotic self-medication. ECDC has launched a number of national campaigns in Europe in order to decrease inappropriate antibiotic use (51). The effects of the interventions were not explained in the reviewed articles. However, it should be stated that such activities have long term results.

5. General socio- economic, cultural and environmental conditions

5.1 Geographical context

Some studies found a link between the residence area and inappropriate antibiotic use. As it was mentioned in the introduction, the level of self- medication with antibiotics varies between the European countries. According to the comparative pan- European study (15), the highest level of antibiotic self- medication was among the population in Southern- Eastern Europe (e.g. in Italy, Malta, Croatia, Lithuania, etc.) compared to Northern- Western one (e.g. in Sweden, The Netherlands, Belgium, etc).

Additionally, there were found differences between rural and urban areas within countries. Muras et al. (36) stated about high level of antibiotic self- medication in Poland (more than

41% of respondents), especially in the southern- eastern part of the country and rural areas. 62.2% of rural respondents used antibiotics inappropriately compared to 32.1% of respondents from urban area. However, among 891 the study's participants 69.1% was urban population and 30.9% was rural population. Approximately the same conclusion was reached in the studies in Lithuania (25, 29): the rural respondents used antibiotics for self- medication about twice often compared to the urban residents. Also, it should be stated that the adults over 18 were included in the studies and studies' sample sizes were large: 746 (25) and 1005 (29). Moreover, characteristics of the respondents' and the general population in Lithuania were comparable.

The opposite situation was found in Macedonia. 36.8% of rural participants used over the counter antibiotics while this index among urban population was higher: it made 63.2% (43). However, there were 402 respondents from 3 administrative regions. Also, youth and women were over represented compared to the general population in Macedonia.

It was fond a limited number of studies (five) about association between antibiotic use and residence area. Moreover, the studies had their own limitations (see Appendix 3). For example, some studies didn't compare the situation of self- medication between rural and urban areas. At the same time, articles analyzing a link between the places of residence (rural or urban as well as location in the WHO European region) and socio- economic differences between them or differences in organization of health care services (their availability and quality) could not be found. However, a link between place of a resident and cultural factors was analyzed in pan- European study which is described in detail in the section 'Cultural factors' (18). Also, in the analyzed articles it was mentioned about the associations of the place of residence (rural/ urban) with knowledge about antibiotics (5, 29, 41, 44) and the level of education (36). Additionally, in some articles the different level of self- medication between the European countries was explained by the different implementation of the drug legislations (17, 19, 21, 22, 32, 39, 42).

5.2 Socio- economic status

Ivanovska et al. (43) found that respondents form the Republic of Macedonia with high socio- economic status (employed, with good financial situation and health insurance) used purchased over the counter antibiotics and antibiotic leftovers more often. The main limitations of the study were small sample size, limited area of the study and incomparable characteristics of respondents and general population of the country. Also, in Italy was found that high socio- economic situation associated with higher level of antibiotic self- medication (14). It was a large study among the respondents over 18 years old in the urban area.

On the contrary, in Turkey the unemployed interviewees were more likely to use antibiotics for self- medication (28). However, it was a large sample size study among adults in the capital of Turkey.

It was found an insufficient number of studies (three) regarding the influence of socio-economic status on consumers' antibiotic use. Also, the studies had limitations (see also Appendix 3). Studies which explored associations between socio- economic factors and residence area, cultural factors, education or knowledge could not be found.

5.3 Drug legislation

Approximately half of the reviewed articles (18 out of 37) stated that respondents purchased antibiotics for self- medication in pharmacies without prescriptions. According to the articles, it was a common thing in Southern and Eastern Europe. Usually it was possible due to the weakness of drug legislations (7, 15, 17, 28, 29, 31, 38). According to the drug legislations, in the analyzed countries antibiotics can be purchased only on the doctors' prescriptions. However, in Southern- Eastern Europe people can buy antibiotics over the counter due to the weak implementation of the drug legislations.

5.4 Cultural factors

According to some researchers, cultural beliefs and different traditions in treatment of infectious diseases influenced on antibiotic use (7, 8, 15, 18, 19, 32). For example, it was stated that disease labeling, family strategy of treatment, religious traditions influenced on differences of antibiotic consumption in two neighboring cities of the Netherlands and Belgium (8). Socio- economic situation in these studied cities was approximately the same except the prevailing religions: Reformism in the Netherlands and Catholicism in Belgium.

Also, Deschepper et al. (18) analyzed how cross- national differences in antibiotic use linked to the differences between national cultures. The data from three large European studies were used: 27 countries were analyzed for the period of six years. European countries were compared regarding the results at the end of the study. It was found that such cultural dimensions as Power Distance Index (PDI) and Uncertainty Avoidance Index (UAI) could explain differences between countries regarding antibiotic use. PDI determines 'patient-doctor' relationship: in countries where doctors discussed treatment with their patients, antibiotics were used appropriately more often (e.g. in Northern- Western Europe). At the same time, UAI can clarify patients' expectation in antibiotic prescription in order to reduce uncertainty, which in turn led to high antibiotic consumption. It can explain the low level of antibiotic use in Nordic countries and the opposite situation in Southern- Eastern Europe. Also, such a cultural dimension as Masculinity (MAS) can explain the attitude and practice regarding to antibiotics among immigrants and population in the rural area. They perceive antibiotics as medications that help to recover and back to work faster (5, 18). It is important for them due to their low socio- economic status.

Vaananen et al. (39) confirmed that the influence of cultural factors on antibiotic use should be analyzed in combination with the organization of health care services, drug legislation in specific countries and individual demographic factors.

Discussion

The literature review has analyzed 37 articles in order to explore the factors influencing consumers' use of antibiotics in the WHO European region. Most of the studies focused on self- medication as a form of inappropriate antibiotic use. Evidences of other forms of inappropriate use are limited. Also, all types of rational use (using only prescribed antibiotics, completing the full prescribing course, stop using leftover prescriptions and avoiding sharing antibiotics with other people whom drugs were not prescribed) were not described in the studies.

The following determinants have been analyzed: sex, age, health condition, knowledge, source of information about antibiotics, migration, education, the role of the health system through specific educational campaigns, geographical context, socio- economic status, implementation of drug legislation and cultural factors. A number of studies' limitations exist: small size of studies, different methods used, low response rate, etc. They lead to local interest of the provided data and don't allow generalizing the findings. Despite it, the studies have identified and analyzed the underlying factors associated with antibiotic use and when combined they do assist in better understanding of the complex that determines consumer antibiotic use.

The factors with the clear evidence from this review are: knowledge about antibiotics and residence area as well as cultural factors and drug legislation. These seem to be the factors, outside the health care service delivery, most clearly influencing consumers' antibiotic use in the WHO European region. These determinants need to be analyzed and addressed first in order to see the effect of the other factors. However, there are often ambiguous results. Moreover, there is limited number of articles analyzing these underlying factors. Thus, these determinants have not been studied enough. In the following sections these key factors will be discussed and related to the effect of the other factors.

Discussing associations between knowledge and inappropriate antibiotic use

A lot of studies stated that better knowledge associated with appropriate use of antibiotics. However, it was found that there was no a simple relationship between knowledge and actual use of antibiotics. Better knowledge separately didn't always correlate with appropriate antibiotic use. For example, in Britain respondents with high level of knowledge didn't usually use antibiotics appropriately. There was another evidence to support this assumption. Two studies in Ege University in Turkey showed that the students and the academic stuff used antibiotics as self- medication in spite of having the specific knowledge due to pharmacology lessons. Also, there was a complicated influence of knowledge on antibiotic use because knowledge was a multicomponent determinant: knowledge about resistance, about effectiveness, about side effect, etc. Knowledge about one aspect didn't associate with knowledge about others and didn't necessary lead to the appropriate antibiotic use. It was an example in Macedonia (38). A lot of knowledge about resistance and side effect can be presented with poor knowledge about antibiotic effectiveness. These results cannot be generalized due to limitations of the studies, but they showed the complicity of the issue.

At the same time, there were evidences of interaction of demographic factors with knowledge, which influenced on antibiotic use. Overall, according to the articles, men had less knowledge about antibiotics. One article in Poland explained it by the fact that women usually had more visits to the doctors due to their kids. As a result, they received more reliable information from pediatricians compared to men. At the same time, it was assumed: the more children the better chance of visiting the doctors and discussing with them the appropriate use of antibiotics (37). Also, it was found in Spain that trusting relationship between patients and their doctors as well as active discussion of potential drug interaction led to a better knowledge and more appropriate antibiotic use (44). However, it was noted in the Netherlands that even women, who didn't have children, showed more accurate knowledge about antibiotics compared to mothers (35). Nevertheless, a strong connection

was not found between sex and appropriate antibiotic use. It confirms the assumption that knowledge doesn't always correlate with the actual use of antibiotics.

The information about association of age with knowledge and antibiotic use also was ambiguous. In Britain young respondents had insufficient knowledge about antibiotics. At the same time, the people of 16- 24 years old and women were more aware about educational campaign 'Andybiotic' in the United Kingdom (34). This could be one more explanation of a better knowledge about antibiotics among women (34). However, it can't explain the reason of low level of knowledge among young respondents. It was also found in Uzbekistan that young respondents had insufficient knowledge about antibiotics (19). On the contrary, in Austria and Macedonia respondents about 41-50 years old had lack of knowledge. It seems that there is no clear connection and age separately doesn't play an important role in antibiotic knowledge and use. The contradicting results on the role of age can be explained by the links with the other factors: education, access to health care services, cultural factors, socio- economic status, etc.

Such complicated influence of knowledge on the use of antibiotics can also be explained by weakness of drug legislation in the analyzed countries. It is stated by some articles. It can be assumed that knowledge is not so important if self- medication is impossible due to the strict drug legislation. At the same time, the difference of the role of knowledge can be linked to interplay with culture gender norms, socio- economic factors and the organization of health care system (availability and quality of health care services). These associations were not discussed in the reviewed articles. For example, a poor single woman with the children, living in the rural area, in spite of her knowledge about antibiotics will have to use self-medication than try to access the health care services which may be of the bad quality and far away from her place of residence.

Discussing urban/rural influences on antibiotic use

According to the reviewed literature, antibiotic self- medication was done more often in the rural area comparing to the urban area. Some articles (5, 29, 41, 44) assumed that it happened due to the lack of knowledge among rural population. A study in Poland explained it by lower educational level of villagers compared to citizens (36). In Spain it is linked with more passive role in communication with the doctors on the topic of drug interactions among rural population (44). However, in Macedonia, urban population used antibiotics for self-medication more often than rural population. The explanation of this fact was not found in the article. Also, the same finding was done in the studies which analyzed six countries of the Southeastern European region.

It is possible to assume that the relationship between urban/ rural areas and antibiotic self-medication also depend on socio- economic situation (higher in urban area), availability and quality of health care services (worth in rural area). The evidences of such links were not found in the reviewed articles. However, the evidence that cultural factors influence on the antibiotic use among rural population was found in one large pan- European study (18).

Discussing differences between regions in the WHO European region

Also, the inappropriate knowledge and practice of self- medication took place more often in Southern- Eastern European countries compared to Northern- Western ones (15). One of the possible explanations may be weakness of drug legislations in South- Eastern Europe, which led to availability of antibiotics over the counter in spite of the law (26, 33). A lot of articles indicated that pharmacies were the main source of antibiotics for self- medication in this region. Also, knowledge about antibiotics was low in South- Eastern Europe where prevalence of self- medication was high (15). Different socio- economic situations can influence on the use of antibiotics among the population of different countries in Europe. At the same time, the contradicting results can be linked to interplay geographical context with different availability and accessibility of health care services in the countries. However, these links could not be found in the articles. Nevertheless, the influence of cultural factors on antibiotic use in the European countries was explained in some studies (see 'Discussing Culture and antibiotic use').

Discussing Culture and drug legislation influences on the antibiotic use

According to some studies, different cultural beliefs and traditions in treatment with antibiotics existed in different countries. Even the neighboring countries such as the Netherlands and Belgium had a sufficient number of cultural differences (e.g. disease labeling, family strategy of treatment, religious traditions, etc) in relation to antibiotic use (8). One large study (18) among 27 European countries confirmed and explained the cross-national difference in antibiotic use by diversity between national cultures. For example, the findings can explain the fact of inappropriate antibiotic use among immigrants, different use of antibiotics between Southern- Eastern and Northern- Western Europe as well as between rural and urban area. Thus, the reviewed articles show that cultural factors may play an important role in antibiotic use among consumers. However, the determinant is still not studied enough. More studies on this issue are needed to explore the link better and to reach the final conclusion.

At the same time, cultural beliefs are mentioned as one of the factor influencing on the inappropriate antibiotic use among immigrants. Additionally, according to the studies, insufficient knowledge about antibiotics and the low level of education, access to health care services and socio- economic status explained the tendency to self- medication among immigrants. Nevertheless, a limited number of studies about immigrants have been found. It doesn't allow reaching a clear conclusion.

Moreover, there was evidence from Spain (39) that influence of cultural factors on antibiotic use should be analyzed in combination with individual demographic factors, organization of health care services and drug legislation in a specific country. The authors found that Finnish immigrants could purchase antibiotics over the counter in Spain, while in Finland they didn't use antibiotic self- medication due to the strict drug legislation. Also, a study in Sweden (32) found that immigrants used antibiotics more often compared to native population. At the same time, the level of self- medication among both groups was low in the country. It can be explained by strict drug legislation in Sweden.

Thus, a weak implementation of drug legislation also seems to be one of the important motivators for the inappropriate antibiotic use. Approximately half of the reviewed articles mentioned about the link between self- medication and availability of antibiotics over the counter. However, the associations of this determinant with the others were not explored enough. Thus, the influence of drug legislation on the antibiotic use is needed to be analyzed more thoroughly.

Other factors

The information about the influence of sex, age, socio- economic status and education on the use of antibiotics among consumers in the WHO European region was contradictory. At the same time, a small number of studies and their limitations didn't allow applying the findings to the general population of the countries. Also, more evidences are needed to reach the conclusions about the links between antibiotic use and such factors as health condition, source of information about antibiotics and educational campaigns.

As far as the difference of the interplay of sex and antibiotic use is concerned, it can be assumed that the sex of a person doesn't have any direct causal relation to the use of antibiotics. This association can be explained by confounding factors. It can be linked with the other determinants such as education, knowledge, access to health care services, cultural gender norms, socio- economic status, etc. Thus, the relation between sex and use of antibiotics is indirect. Despite the fact that 'sex- knowledge- antibiotic use' link was discussed in some studies, clear conclusions were not been reached. Moreover, the associations of sex and antibiotic use with the other determinants were not explained in the reviewed articles. It makes a comparison of different parts of Europe regarding 'sex- antibiotic use' association unreliable.

The contrast results on the role of age can be linked to different methods used in the studies. A lot of them didn't analyze all age groups. Also, the association between age and self-medication can be explained by confounding factors: education, knowledge, access to health care services, cultural factors, socio- economic status, etc. These relations were not analyzed enough in the studies. All the above makes it unreliable to generalize the findings of the studies.

The contradictory results on the influence of socio- economic status on the antibiotic use may have some explanations. On the one hand, it can be linked to bias in the studies. For example, in the studies the consumers' socio- economic statuses were not analyzed regarding different age groups or places of residence. It is less likely that young people at the age of 18 in the rural area have the same socio- economic status like people of working age in the cities (or in the capital). Also, the issue on socio- economic status could be sensitive for some respondents. It can lead to additional biases due to self- reporting questionnaires. On the other hand, it can be assumed that confounding factors (e.g. cultural factors, education, knowledge and residence area) may explain the differences in antibiotic use among consumers with the same socio- economic status. It was an example in the study comparing antibiotic use in the Netherlands and Belgium. The socio- economic status of respondents was approximately the same. However, different religions influenced on the antibiotic use: Protestants in the Netherlands used antibiotics rarely than Catholics in Belgium.

The results on association of education with antibiotic use among consumers are ambiguous. It can be explained by the influencing of the other underlying factors: knowledge, geographical context, socio- economic status, cultural factors and drug legislation. For example, people in rural area are less likely to have higher education. According to some articles, it can increase inappropriate antibiotic use. However, better education may also lead to inappropriate antibiotic use. High education can be linked with both actual better knowledge and with overestimation the knowledge about antibiotics, which may increase the level of self- medication. Additionally, the studies conducted in Southern- Eastern Europe indicated the high level of antibiotic self- medication among respondents with different education levels. It can be explained by the availability of the antibiotics without prescriptions in pharmacies in spite of the drug legislation. The influences of confounding factors were not analyzed enough in the reviewed articles but they are essentially important to reach the conclusion.

The association between consumers' health conditions and their antibiotic use can be explained by relationship between doctors and patients. People with chronic conditions may have a trust relationship with their doctors and thus seek their advice more easily. It in its turn can explain the studies' outcomes: chronically sick persons were less likely to use antibiotic self- medication. Nevertheless, more evidences are needed to reach a clear conclusion.

Despite the fact that all the articles, which analyzed the source of information about antibiotics, mentioned that doctors play the main role, more studies are needed. No attention was given to socio- economic status, gender, education and place of residence in addressing the issue. For example, maybe the people with a low income or immigrants are more likely to consult the Internet than a doctor due to their low socio- economic status (bad financial situation or absence of health insurance). Also, rural people may prefer to advice the family members or friends due to difficulties with the access to the health care services or their bad quality. These aspects were not analyzed in the articles although they may have an influence on the studies' conclusions.

A limited number of studies, exploring the impact of education campaigns on the knowledge about antibiotics and their use, did not allow evaluating their influence. Moreover, such interventions usually have long term results.

Strengths and limitations of this literature review

This literature review has limitations as well as strengths. One of the limitations is that only one database (PubMed) was used. A further limitation is that only articles published since 2005 (and additional four articles published in 2002- 2003) have been reviewed. At the same time, there is language restriction: only articles in the English and Russian languages have been included in screening for relevance at the literature search about the WHO European region. Also, it is possible that the relevant studies have been excluded automatically (e.g. studies, which have no publication year). Additionally, not all countries of the WHO European region have been presented at the articles included in the literature review. Eastern Europe has been analyzed only in two articles. Finally, this literature review is focusing on self- medication as a form of inappropriate antibiotic use. All types of rational antibiotic use are not described, too. Despite number of limitations, there are strengths of the literature review. One of the strength is that only peer reviewed articles have been analyzed. A further

strength is that interactions of different underlying factors, influencing consumers' use of antibiotics, have been analyzed in the literature review.

Conclusions and recommendations

The problem of inappropriate antibiotic use in the WHO European region exists. Consumers are one of the key players who influence the level of inappropriate antibiotic use in the region. The consumers' antibiotic use in its turn is influenced highly by the other key players (prescribers and dispensers) and the legislation. Within the frames of freedom that consumers have (which differs per country) their antibiotic use may be modified by addressing the mentioned factors. Taking into account the results of this literature review and further discussion, it seems that the key underlying factors, outside the health care service delivery, influencing antibiotic use are: insufficient knowledge about antibiotics, especially among respondents from rural area, from Southern- Eastern Europe and immigrants; weakness of drug legislation in Southern- Eastern countries, influencing the using antibiotics over the counter; and cultural factors which are rather different in the analyzed region. The literature review provides data which can be basic for further studying on the issue of the antibiotic use in the WHO European region. However, limitations of the study do not allow generalizing the findings to the whole population of the region. Thus, the findings should be interpreted within the context of the limitations of the literature review.

The following recommendations can be given:

- Carry out studies in the countries of Southern- Eastern Europe, particularly in those which are not in the European Union. The main aim of the studies should be an investigation of the main motivators for the inappropriate antibiotic use among consumers: level of knowledge, cultural factors, influence of drug legislation's implementation.
- Carry out more studies in the countries of the WHO European region in order to study the influence of cultural factors on the consumers' use of antibiotics better.
- Apply a multisectoral approach based on the studies' results to solving the issue of inappropriate antibiotic use: cooperation of health-care professionals, pharmacists, health authorities and consumers.
- Conduct educational campaigns and targeted interventions to improve knowledge about antibiotics and their appropriate use among rural population in the WHO European region, immigrants and general population in Southern- Eastern Europe.
- Strengthen the control over the implementation of the drug legislation in Southern-Eastern Europe.

References

1. World Health Organization Europe. Antimicrobial resistance [Internet]. 2015 [cited 2015 Aug 01]. Available from: http://www.euro.who.int/en/health-topics/disease-prevention/antimicrobial-resistance/antimicrobial-resistance
2. Review on Antimicrobial Resistance. Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations [Internet]. 2014 Dec 11 [cited 2015 Aug 01]. Available from: http://amr-review.org/
3. World Health Organization. The Pursuit of Responsible Use of Medicines: Sharing and Learning from Country Experience [Internet]. 2012 Mar [updated 2015; cited 2015 Aug 01]. Available from: http://who.int/medicines/areas/rational_use/en/
4. Azevedo MM, Pinheiro C, Yaphe J, et al. Portuguese students' knowledge of antibiotics: a cross-sectional study of secondary school and university students in Braga. BMC Public Health [Internet]. 2009 Sep 23 [cited 2015 Jun 20];9:359. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2759931/ doi: 10.1186/1471-2458-9-359.
5. Papakosta M, Zavras D, Niakas D. Investigating factors of self-care orientation and self-medication use in a Greek rural area. Rural Remote Health [Internet]. 2014 [cited 2015 Jun 12];14:2349. Available from: http://www.rrh.org.au/articles/subviewnew.asp?ArticleID=2349.
6. World Health Organization Europe. Antimicrobial resistance: data and statistics [Internet]. 2015 [cited 2015 Aug 01]. Available from: http://www.euro.who.int/en/health-topics/disease-prevention/antimicrobial-resistance/data-and-statistics
7. Radosevic N, Vlahovic- Palcevski V, Benko R, et al. Attitudes towards antimicrobial drugs among general population in Croatia, FYROM, Greece, Hungary, Serbia and Slovenia. Pharmacoepidemiol Drug Saf [Internet]. 2009 Aug [cited 2015 Jun 9];18(8):691-6. Available from: http://onlinelibrary.wiley.com/doi/10.1002/pds.1768/abstract DOI: 10.1002/pds.1768.
8. Deschepper R, Vander Stichele RH, Haaijer-Ruskamp FM. Cross-cultural differences in lay attitudes and utilisation of antibiotics in a Belgian and a Dutch city. Patient Educ Couns [Internet]. 2002 Oct –Nov [cited 2015 Jun 9];48(2):161-9. Available from: http://www.sciencedirect.com/science/article/pii/S0738399102000174 doi:10.1016/S0738-3991(02)00017-4.
9. European Centre for Disease Prevention and Control. Surveillance of antimicrobial consumption in Europe 2011 [Internet]. 2014 Feb 04 [cited 2015 Aug 01]. Available from: http://ecdc.europa.eu/en/publications/_layouts/forms/Publication_DispForm.aspx?List=4f55ad51-4aed-4d32-b960-af70113dbb90&ID=1016
10. Versporten A, Bolokhovets G, Ghazaryan L et al. Antibiotic use in eastern Europe: a cross-national database study in coordination with the WHO Regional Office for Europe. Lancet Infect Dis [Internet]. 2014 [cited 2015 Aug 01]; 14 (5): 381–87. Available from: http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(14)70071-4/fulltext?dialogRequest= DOI: http://dx.doi.org/10.1016/S1473-3099(14)70071-4.
11. Wikipedia. Europe [Internet]. 2015 [cited 2015 Aug 01]. Available from: https://en.wikipedia.org/wiki/Europe

12. The World Bank. Country and Lending Groups [Internet]. 2015 [cited 2015 Aug 01]. Available from: http://data.worldbank.org/about/country-and-lending-groups#Lower_middle_income
13. Wikipedia. European Union [Internet]. 2015 [cited 2015 Aug 01]. Available from: https://en.wikipedia.org/wiki/European_Union
14. Grosso G, Marventano S, Ferranti R, et al. Pattern of antibiotic use in the community: von-adherence and self-prescription rates in an Italian urban population. Mol Med Rep [Internet]. 2012 May [cited 2015 Jun 20];5(5):1305-10. Available from: http://www.spandidos-publications.com/mmr/5/5/1305 doi: 10.3892/mmr.2012.818.
15. Grigoryan L, Burgerhof JG, Degener JE, et al. Attitudes, beliefs and knowledge concerning antibiotic use and self-medication: a comparative European study. Pharmacoepidemiol Drug Saf [Internet]. 2007 Nov [cited 2015 Jun 9];16(11):1234-43. Available from: http://onlinelibrary.wiley.com/doi/10.1002/pds.1479/abstract;jsessionid=E65B10970CA15D7024F6BC7C66761BCA.f02t03 DOI: 10.1002/pds.1479.
16. Napolitano F, Izzo MT, Di Giuseppe G, et al. Public knowledge, attitudes, and experience regarding the use of antibiotics in Italy. PLoS One [Internet]. 2013 Dec 23 [cited 2015 Jun 9];8(12):e84177. Available from: http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0084177 doi: 10.1371/journal.pone.0084177.
17. Skliros E, Merkouris P, Papazafiropoulou A, et al. Self-medication with antibiotics in rural population in Greece: a cross-sectional multicenter study. BMC Fam Pract [Internet]. 2010 Aug 8 [cited 2015 Jun 10];11:58. Available from: http://www.biomedcentral.com/1471-2296/11/58 doi: 10.1186/1471-2296-11-58.
18. Deschepper R, Grigoryan L, Lundborg CS, et al. Are cultural dimensions relevant for explaining cross-national differences in antibiotic use in Europe? BMC Health Serv Res [Internet]. 2008 Jun 6 [cited 2015 Jun 11];8:123. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2430199/ doi: 10.1186/1472-6963-8-123.
19. Belkina T, Al Warafi A, Hussein Eltom E, et al. Antibiotic use and knowledge in the community of Yemen, Saudi Arabia, and Uzbekistan. J Infect Dev Ctries [Internet]. 2014 Apr 15 [cited 2015 Jun 12]; 8(4):424-9. Available from: http://www.jidc.org/index.php/journal/article/view/24727507/1039 doi: 10.3855/jidc.3866.
20. Grigoryan L, Burgerhof JG, Haaijer-Ruskamp FM, et al. Is self-medication with antibiotics in Europe driven by prescribed use? J Antimicrob Chemother [Internet]. 2007 Jan [cited 2015 Jun 13];59(1):152-6. Available from: http://jac.oxfordjournals.org/content/59/1/152.full.pdf+html doi:10.1093/jac/dkl457.
21. Raz R, Edelstein H, Grigoryan L, et al. Self-medication with antibiotics by a population in northern Israel. Isr Med Assoc J [Internet]. 2005 Nov [cited 2015 Jun 13];7(11):722-5. Available from: http://www.ima.org.il/IMAJ/ViewArticle.aspx?year=2005&month=11&page=722.
22. Stratchounski LS, Andreeva IV, Ratchina SA, et al. The inventory of antibiotics in Russian home medicine cabinets. Clin Infect Dis [Internet]. 2003 Aug 15 [cited 2015 Jun 14];37(4):498-505. Available from: http://cid.oxfordjournals.org/content/37/4/498.full.pdf+html.

23. André M, Vernby A, Berg J, et al. A survey of public knowledge and awareness related to antibiotic use and resistance in Sweden. J Antimicrob Chemother [Internet]. 2010 Jun [cited 2015 Jun 20];65(6):1292-6. Available from: http://jac.oxfordjournals.org/content/65/6/1292.full.pdf+html doi: 10.1093/jac/dkq104.
24. Panagakou SG, Spyridis N, Papaevangelou V, et al. Antibiotic use for upper respiratory tract infections in children: a cross-sectional survey of knowledge, attitudes, and practices (KAP) of parents in Greece. BMC Pediatr [Internet]. 2011 Jul 5 [cited 2015 Jun 20];11:60. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3141508/ doi: 10.1186/1471-2431-11-60.
25. Berzanskyte A, Valinteliene R, Haaijer-Ruskamp FM, et al. Self-medication with antibiotics in Lithuania. Int J Occup Med Environ Health [Internet]. 2006 [cited 2015 Jun 20];19(4):246-53. Available from: http://www.degruyter.com/view/j/ijmh.2006.19.issue-4/v10001-006-0030-9/v10001-006-0030-9.xml doi: 10.2478/v10001-006-0030-9.
26. Cagri Buke A, Ermertcan S, Hosgor-Limoncu M, et al. Rational antibiotic use and academic staff. Int J Antimicrob Agents [Internet]. 2003 Jan [cited 2015 Jun 21];21(1):63-6. Available from: http://www.sciencedirect.com/science/article/pii/S0924857902002728 doi:10.1016/S0924-8579(02)00272-8.
27. Emslie MJ, Bond CM. Public knowledge, attitudes and behaviour regarding antibiotics- a survey of patients in general practice. Eur J Gen Pract [Internet]. 2003 Sep [cited 2015 Jun 21];9(3):84-90. Available from: http://www.ncbi.nlm.nih.gov/pubmed/14712905.
28. Ilhan MN, Durukan E, Ilhan SO, et al. Self-medication with antibiotics: questionnaire survey among primary care center attendants. Pharmacoepidemiol Drug Saf [Internet]. 2009 Dec [cited 2015 Jun 21];18(12):1150-7. Available from:http://onlinelibrary.wiley.com/doi/10.1002/pds.1829/abstract;jsessionid=DD2BC3A141376B80C91F36A1A7767DDF.f04t04 doi: 10.1002/pds.1829.
29. Pavydė E, Veikutis V, Mačiulienė A, et al. Public Knowledge, Beliefs and Behavior on Antibiotic Use and Self-Medication in Lithuania. Int J Environ Res Public Health [Internet]. 2015 Jun 17 [cited 2015 Jun 25];12(6):7002-16. Available from: http://www.mdpi.com/1660-4601/12/6/7002 doi: 10.3390/ijerph120607002.
30. Ramalhinho I, Cordeiro C, Cavaco A, et al. Assessing determinants of self-medication with antibiotics among Portuguese people in the Algarve Region. Int J Clin Pharm [Internet]. 2014 Oct [cited 2015 Jun 14];36(5):1039-47. Available from: http://link.springer.com/article/10.1007%2Fs11096-014-9992-z doi: 10.1007/s11096-014-9992-z.
31. Jorgji K, Bebeci E, Apostoli P, et al. Evaluation of use of antibiotics without prescription among young adults in Albania case study: Tirana and Fier District. Hippokratia [Internet]. 2014 Jul-Sep [cited 2015 Jun 11];18(3):217–220. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4309140/.
32. Mangrio E, Wremp A, Moghaddassi M, at al. Antibiotic use among 8-month-old children in Malmö, Sweden- in relation to child characteristics and parental sociodemographic, psychosocial and lifestyle factors. BMC Pediatr [Internet]. 2009 May 8 [cited 2015 Jun 13];9:31. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2685137/ doi: 10.1186/1471-2431-9-31.

33. Buke C, Hosgor-Limoncu M, Ermertcan S, et al. Irrational use of antibiotics among university students. J Infect [Internet]. 2005 Aug [cited 2015 Jun 21];51(2):135-9. Available from: http://www.sciencedirect.com/science/article/pii/S0163445304002762 doi:10.1016/j.jinf.2004.12.001.
34. McNulty CA, Boyle P, Nichols T, et al. Don't wear me out—the public's knowledge of and attitudes to antibiotic use. J Antimicrob Chemother [Internet]. 2007 Apr [cited 2015 Jun 9];59(4):727-38. Available from: http://jac.oxfordjournals.org/content/59/4/727.long doi: 10.1093/jac/dkl558.
35. Cals JW, Boumans D, Lardinois RJ, et al. Public beliefs on antibiotics and respiratory tract infections: an internet-based questionnaire study. Br J Gen Pract [Internet]. 2007 Dec 1 [cited 2015 Jun 9];57(545):942-7. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2084132/ doi: 10.3399/096016407782605027.
36. Muras M, Krajewski J, Nocun M, et al. A survey of patient behaviours and beliefs regarding antibiotic self-medication for respiratory tract infections in Poland. Arch Med Sci [Internet]. 2013 Oct 31 [cited 2015 Jun 11];9(5):854–857. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3832809/ doi: 10.5114/aoms.2012.29217.
37. Godycki-Cwirko M, Cals J, Francis N, et al. Public Beliefs on Antibiotics and Symptoms of Respiratory Tract Infections among Rural and Urban Population in Poland: A Questionnaire Study. PLoS One [Internet]. 2014 Oct 2 [cited 2015 Jun 11];9(10): e109248. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4183578/ doi: 10.1371/journal.pone.0109248.
38. Alili-Idrizi E, Dauti M, Malaj L. Validation of the parental knowledge and attitude towards antibiotic usage and resistance among children in Tetovo, the Republic of Macedonia. Pharm Pract (Granada) [Internet]. 2014 Oct [cited 2015 Jun 11];12(4): 467. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4282763/.
39. Väänänen MH, Pietilä K, Airaksinen M. Self-medication with antibiotics--does it really happen in Europe? Health Policy [Internet]. 2006 Jul [cited 2015 Jun 21];77(2):166-71. Available from: http://www.sciencedirect.com/science/article/pii/S0168851005001612 doi:10.1016/j.healthpol.2005.07.001.
40. Rousounidis A, Papaevangelou V, Hadjipanayis A, et al. Descriptive study on parents' knowledge, attitudes and practices on antibiotic use and misuse in children with upper respiratory tract infections in Cyprus. Int J Environ Res Public Health [Internet]. 2011 Aug [cited 2015 Jun 25];8(8):3246-62. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3166740/ doi: 10.3390/ijerph8083246.
41. Panagakou SG, Papaevangelou V, Chadjipanayis A, et al. Risk factors of antibiotic misuse for upper respiratory tract infections in children: results from a cross-sectional knowledge-attitude-practice study in Greece. ISRN Pediatr [Internet]. 2012 [cited 2015 Jun 25];2012:685302. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3503327/ doi: 10.5402/2012/685302.
42. Fernandes M, Leite A, Basto M, et al. Non-adherence to antibiotic therapy in patients visiting community pharmacies. Int J Clin Pharm [Internet]. 2014 Feb [cited 2015 Jun 29];36(1):86-91. Available from: http://link.springer.com/article/10.1007%2Fs11096-013-9850-4 doi: 10.1007/s11096-013-9850-4.

43. Ivanovska V, Zdravkovska M, Bosevska G, et al. Antibiotics for upper respiratory infections: public knowledge, beliefs and self-medication in the Republic of Macedonia. Prilozi [Internet]. 2013 [cited 2015 Jun 29];34(2):59-70. Available from: http://www.ncbi.nlm.nih.gov/pubmed/?term=ANTIBIOTICS+FOR+UPPER+RESPIRATORY+INFECTIONS%3A+PUBLIC+KNOWLEDGE%2C+++BELIEFS+AND+SELF-MEDICATION+IN+THE+REPUBLIC+OF+MACEDONIA
44. Mira JJ, Navarro I, Huttner B, et al. What do Spaniards read about the prudent use of antimicrobial agents and what do they really do? Psychol Health Med [Internet]. 2014 [cited 2015 Jun 29];19(2):201-10. Available from: http://www.tandfonline.com/doi/abs/10.1080/13548506.2013.793370?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%3dpubmed doi: 10.1080/13548506.2013.793370.
45. Azevedo MM, Pinheiro C, Yaphe J, et al. Assessing the impact of a school intervention to promote students' knowledge and practices on correct antibiotic use. Int J Environ Res Public Health [Internet]. 2013 Jul 15 [cited 2015 Jun 13];10(7):2920-31. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3734468/ doi: 10.3390/ijerph10072920.
46. World Health Organization. Antimicrobial resistance: global report on surveillance 2014 [Internet]. 2014 Apr [updated 2015; cited 2015 Aug 01]. Available from: http://www.who.int/drugresistance/documents/surveillancereport/en/ Antimicrobial resistance: global report on surveillance 2014
47. World Health Organization. World Health Day 2011: Policy Briefs [Internet]. 2011 [updated 2015; cited 2015 Aug 01]. Available from: http://www.who.int/world-health-day/2011/policybriefs/en/
48. Model of Health Determinants. The Dahlgren-Whitehead model. Dahlgren G, Whitehead M. Policies and Strategies to Promote Social Equity in Health. Stockholm, Sweden: Institute for Futures Studies [Internet]. 1991 [cited 2015 Jun 13]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK221240/
49. Hoffmann K, Ristl R, Heschl L, et al. Antibiotics and their effects: what do patients know and what is their source of information? The European Journal of Public Health [Internet]. 2014 Jun [cited 2015 Jun 9];24(3):502-7. Available from: http://eurpub.oxfordjournals.org/content/24/3/502.long doi: 10.1093/eurpub/ckt112.
50. Project e- Bug [Internet]. 2015 [cited 2015 Aug 01]. Available from: http://www.e-bug.eu/
51. European Centre for Disease Prevention and Control. European Antibiotic Awareness Day [Internet]. 2015 [cited 2015 Aug 01]. Available from: http://ecdc.europa.eu/en/eaad/Pages/Home.aspx
52. Wikipedia. WHO European Region [Internet]. 2014 [cited 2015 Aug 01]. Available from: https://en.wikipedia.org/wiki/WHO_regions#WHO_European_Region

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Appendices

Appendix 1. The WHO European region Member States.

The WHO European region includes: Albania, Andorra, Armenia, Austria, Azerbaijan, Belarus, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Georgia, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Luxembourg, Malta, Monaco, Montenegro, Netherlands, Norway, Poland, Portugal, Republic of Moldova, Romania, Russian Federation, San Marino, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Tajikistan, The former Yugoslav Republic of Macedonia, Turkey, Turkmenistan, Ukraine, United Kingdom, Uzbekistan (52).

Appendix 2. Search terms.

knowledge OR belief* OR behavio* OR (behavio* AND intervention*) OR (behavior* AND determinant*) OR (behavior* AND factor*) OR (behavio* AND change*) OR (behavio* AND change*) OR awareness OR expectation* OR misconception* OR experience OR (cultural AND factor*) OR perception OR (health AND motivation*) OR (theory AND planned AND behavio*) OR (theory AND reasoned AND action) OR (theory AND reasoned AND consumer AND behavior*) OR (reasoned AND action AND approach) OR (health AND belief AND model) OR appropriate OR inappropriate OR proper OR improper OR correct OR incorrect OR rational OR irrational OR non-rational OR reasonable OR unreasonable OR over-use OR safe OR unsafe OR wrong OR adequate OR inadequate OR acceptable OR unacceptable OR advisable OR inadvisable OR nonadherence
AND
(community AND member) OR people OR population OR consumer* OR patient* OR community
AND
self-treatment OR self-medication OR (antibacterial AND usage) OR (antimicrobial AND usage) OR (antimicrobic AND usage) OR (antibiotic AND usage) OR (antibacterial AND use) OR (antimicrobial AND use) OR (antimicrobic AND use) OR (antibiotic AND use) OR (antibiotic AND consuming) OR (antimicrobic AND consuming) OR (antimicrobial* AND consuming) OR (antibacterial AND consuming) OR (antibiotic AND consumption) OR (antimicrobic AND consumption) OR (antimicrobial* AND consumption) OR (antibacterial AND consumption) OR (antibiotic AND resistance) OR (antimicrobic AND resistance) OR (antibacterial AND resistance) OR (antimicrobial AND resistance) OR antibiotics OR antimicrobial* OR (antibiotic AND drug*) OR (antimicrobic AND drug*) OR (antimicrobial AND drug*) OR (antibacterial AND drug*) OR (antibacterial AND agent*) OR (antibacterial AND preparation*) OR (antibacterial AND medication*)
AND
(former AND soviet AND union AND countr*) OR (post AND soviet AND countr*) OR (eastern AND europe) OR (european AND countr*) OR (european AND region) OR albania OR andorra OR armenia OR austria OR azerbaijan OR belarus OR belgium OR bulgaria OR croatia OR cyprus OR denmark OR estonia OR finland OR france OR georgia OR germany OR greece OR hungary OR iceland OR ireland OR israel OR italy OR kazakhstan OR kyrgyzstan OR latvia OR lithuania OR luxembourg OR malta OR monaco OR montenegro OR netherlands OR norway OR poland OR portugal OR romania OR russia OR serbia OR slovakia OR slovenia OR spain OR sweden OR switzerland OR tajikistan OR macedonia OR turkey OR turkmenistan OR ukraine OR uzbekistan OR (former AND yugoslav AND republic AND macedonia) OR (united AND kingdom) OR (san AND marino) OR (russian AND federation) OR (czech AND republic) OR (bosnia AND herzegovina) OR (republic AND moldova) OR (republic AND belarus)

Appendix 3. Analyzed full text articles.

#	Ref	Articles	Country Year Participants	Factor(s)	Effect (s)
1	49	Hoffmann K, Ristl R, Heschl L, et al. Antibiotics and their effects: what do patients know and what is their source of information?	• Austria; • November 2010-July 2011; • 3280 participants.	• Explore an influence of demographic factors on knowledge about ABs.	• Education, language, sex, age had the influence on knowledge about ABs; • General practitioners were the main source of information for patients.
2	7	Radosevic N, Vlahovic-Palcevski V, Benko R, et al. Attitudes towards antimicrobial drugs among general population in Croatia, FYROM, Greece, Hungary, Serbia and Slovenia.	• Croatia, FYROM, Greece, Hungary, Serbia and Slovenia; • January-February 2007; • 838 participants.	• Explore components of patients' attitudes (cognitive, affective and behavioral) on AB use; • Explore a link between demographic factors and AB use.	• Behavior regarding ABs complied with emotions and knowledge in all countries; • All components of attitudes towards ABs had links with the level of education; • Gender and age did not have any impact on any attitudes; • General practitioners have a large influence on patients' attitudes towards ABs; • Accessibility of ABs in pharmacies was an important factor increasing self-medication.
3	8	Deschepper R, Vander Stichele RH, Haaijer-Ruskamp FM. Cross-cultural differences in lay attitudes and utilisation of antibiotics in a Belgian and a Dutch city.	• The NL (Middelburg) and Belgium (Bruges); • January 1997-October 1998; • 30 participants.	• Explore influence of cultural factors and organization of health care on AB use.	• Cultural factors (labeling of URTIs, religion, family style of ABs use) and organization of health care influenced on AB use.
4	15	Grigoryan L, Burgerhof JG, Degener JE, et al. Attitudes, beliefs and knowledge	• 12 countries; • October 2003-May 2004;	• Explore knowledge, attitudes and practices regarding ABs.	• Southern and Eastern countries had less appropriate attitudes, beliefs or knowledge and higher prevalence of AB resistance compared

		concerning antibiotic use and self-medication: a comparative European study.	• 1101 participants.		to Northern and Western countries. ❖ 12 countries: Northern/Western (Austria, The Netherlands, Sweden, United Kingdom and Belgium); Southern (Italy, Malta, Israel and Spain) and Eastern (Czech Republic, Lithuania and Croatia).
5	34	McNulty CA, Boyle P, Nichols T, et al. Don't wear me out—the public's knowledge of and attitudes to antibiotic use.	• Great Britain (England, Wales and Scotland); • 2003 (February, March, June and July); • 7120 participants.	• Explore public knowledge about, attitudes to ABs and behavior with respect to AB use.	• Attitudes to ABs and knowledge about AB resistance were high; • No simple relationship was between increased knowledge and more prudent AB use; • Better knowledge of and attitude to ABs was strong associated with finishing a course of ABs as prescribed, but was also associated with higher AB self-medication and obtaining ABs in other countries without prescriptions; • Younger (16- 24) and older (>= 75) people, males, people with greater deprivation and lower education were less knowledgeable about ABs.
6	35	Cals JW, Boumans D, Lardinois RJ, et al. Public beliefs on antibiotics and respiratory tract infections: an internet-based questionnaire study.	• The Netherlands; • 2006 (October, November); • 935 participants (16 years and over).	• Explore public knowledge, beliefs, and experiences of AB use.	• Public misconceptions on the effectiveness of, and indications for, ABs existed; • Disease labeling influenced on the expectations of AB use; • Female sex, use of ABs at any time previously, and recent information on ABs were associated with accurate knowledge of AB effectiveness; • Patients with chronic

					pulmonary disease did not have better knowledge about ABs; • Doctors were the main source of information about ABs.
7	16	Napolitano F, Izzo MT, Di Giuseppe G, et al. Public knowledge, attitudes, and experience regarding the use of antibiotics in Italy.	• Italy; • December 2011; • 419 participants.	• Explore influence of socio-demographic characteristics the on AB use; • Estimate knowledge about AB use and AB resistance; • Estimate the level of self-medication with ABs; • Estimate sources of information regarding AB use.	• Low level of knowledge about AB resistance; • Respondents with higher education, employed, with a family member working in the health care sector had more knowledge about AB resistance; • Users of self-medication with ABs had lower self-rated health status, were under 40 years old, did not use the physician as source of information on ABs, and didn't attend a physician in the last year; • Sore throat was the most frequent reason for self-medication with ABs; • Physicians were the main source of information about ABs.
8	17	Skliros E, Merkouris P, Papazafiropoulou A, et al. Self-medication with antibiotics in rural population in Greece: a cross-sectional multicenter study.	• Greece; • November 2009-January 2010; • 1139 participants.	• Estimate the use of ABs without medical prescriptions.	• Prevalence of self-medication with ABs was high; • The main reasons for self- medication with ABs were fever and common cold; • The main source of self-medication was pharmacy.
9	18	Deschepper R, Grigoryan L, Lundborg CS, et al. Are cultural dimensions relevant for explaining cross-national differences in	• Data from three European studies were used (1997-2003): Self-medicatio	• Explore whether cross-national differences in use of ABs (prescribed and non-	• PDI and UAI- positive significant correlations; • MAS- not significantly correlated. But correlation values for Masculinity become stronger; • IDV and LTO- no significant correlations;

		antibiotic use in Europe?	n with Antibiotics and Resistance in Europe (SAR), European Surveillance on Antimicrobial Consumption, Eurobarometer study; • 27 European countries.	prescribed) are associated with differences between national cultures as described in Hofstede's model of cultural dimensions.	❖ Countries: Sweden, Netherlands, Austria, Denmark, Poland, UK, Belgium (Fl.), Czech Rep., Lithuania, Luxemburg, Slovenia, Romania, Ireland, Malta, Croatia, Italy, Slovakia, Bulgaria, Estonia, Finland, France, Germany, Greece, Hungary, Norway, Portugal, Spain. ❖ 5 cultural dimensions: Power Distance (PDI), Individualism (IDV), Masculinity (MAS), Long- Term Orientation (LTO) and Uncertainty Avoidance (UAI).
10	36	Muras M, Krajewski J, Nocun M, et al. A survey of patient behaviours and beliefs regarding antibiotic self-medication for respiratory tract infections in Poland.	• Poland; • 1March-15 May 2010; • 891 participants (69.1% from urban, 30.9% from rural area).	• Describe the prevalence of AB self-medication for RTIs; • Explore patients' behavior and beliefs regarding AB self-medication; • Determine the available sources of such ABs.	• 41.4% of patients had self-medication with ABs for RTIs: in rural area- 62.2%, urban- 32.1%; • In both groups, the main sources of ABs were home medical kits: 62.1% and 83.1% respectively; • Respondents' knowledge about AB use was incomplete.
11	37	Godycki-Cwirko M, Cals J, Francis N, et al. Public Beliefs on Antibiotics and Symptoms of Respiratory Tract Infections among Rural and Urban Population in Poland: A Questionnaire Study.	• Poland; • 6- 11 May 2011; • 1210 participants.	• Explore differences between the rural and urban population about knowledge, attitudes and beliefs about AB use for RTIs.	• Antimicrobial awareness, education and number of children were associated with knowledge about AB effectiveness; • Despite significant differences between rural and urban levels of education, there were no significant differences in knowledge about the effectiveness of ABs; • Rural- more use of ABs

					for RTIs, less confidence in their knowledge about ABs, greater belief in their effectiveness; • The main source of info about ABs was physicians.
12	38	Alili-Idrizi E, Dauti M, Malaj L. Validation of the parental knowledge and attitude towards antibiotic usage and resistance among children in Tetovo, the Republic of Macedonia.	• Republic of Macedonia; • October 2013-January 2014; • 500 participants.	• Explore the knowledge and attitudes of parents on the use of ABs among children.	• Education and age influenced on the AB use; • Insufficient knowledge about ABs and AB resistance existed; • There was enough knowledge about allergic reaction due to ABs; • It was found an important role of doctors in the appropriate use of ABs among children.
13	31	Jorgji K, Bebeci E, Apostoli P, et al. Evaluation of use of antibiotics without prescription among young adults in Albania case study: Tirana and Fier District.	• Albania; • December 2012-March 2013; • 350 participants.	• Investigate the prevalence of purchase of ABs without prescription and appropriateness of use among adults; • Determine the impact of the education level on the level of AB use.	• 78.14% of young adult population used ABs without medical prescription; • The most common reasons for self-medication: fever, sore throat; • The major source of self-medication was the pharmacy without prescription; • There were a link between lower education and higher level of self-medication.
14	19	Belkina T, Al Warafi A, Hussein Eltom E, et al. Antibiotic use and knowledge in the community of Yemen, Saudi Arabia, and	• Yemen, Saudi Arabia and **Uzbekistan**; • November 2012; • 1200 participan	• Knowledge, attitudes and practices of AB use among secondary schools teachers.	**About Uzbekistan:** • The prevalence of self-medication and inappropriate use of ABs in the educated adult population was alarmingly high (78%); • The main source of non-prescribed ABs and info was pharmacy;

		Uzbekistan.	ts (including 400 from Uzbekistan).		• The main reason for AB use was respiratory inflammation; • Age, gender did not affect self- medication; • There were a link between irrational AB use and lower educational level.
15	5	Papakosta M, Zavras D, Niakas D. Investigating factors of self-care orientation and self-medication use in a Greek rural area.	• Greece; • January-February 2011; • 150 participants.	• Detect factors that influence on self-medication.	• 54.7% used prescription medications without a doctor's prescriptions; • The absence of permanent doctors in rural Greece, previous experience of drug effectiveness encouraged self-medication practices; • Factors of self-medication: female gender, absence of chronic disease and higher educational level; • Accumulation of previously prescribed medicines and high exchange prevalence between residents may lead individuals to self-medication practices.
16	45	Azevedo MM, Pinheiro C, Yaphe J, et al. Assessing the impact of a school intervention to promote students' knowledge and practices on correct antibiotic use.	• Portugal; • 2013; • 82 participants (9th grade students).	• Evaluate knowledge on the use of ABs of middle-school students; • Evaluate the efficacy of the school intervention in improving students' knowledge on correct AB use.	• Pre- test: ✓ Lack of knowledge among students regarding AB spectra and indications and incorrect attitudes to ABs. • Post- test: Significant increases of knowledge: ✓ ABs against bacterial diseases rather than viral diseases 43% -> 76%; ✓ Knowledge of the risk of bacterial resistance to ABs from their incorrect use 48% -> 74%; ✓ In respect to the obligation to comply with the schedule set 73% -> 82.2%.

17	32	Mangrio E, Wremp A, Moghaddassi M, at al. Antibiotic use among 8-month-old children in Malmö, Sweden--in relation to child characteristics and parental sociodemographic, psychosocial and lifestyle factors.	• Sweden; • 2003–2006; • 7266 participants.	• Investigate the associations between AB use among 8-month-old children and characteristics of the child as well as parental socio-demographic characteristics, lifestyle factors, and psychosocial support.	• Parental characteristics associated with higher AB use: low educational level, being born outside Sweden, economic stress, and having low emotional support; • The child-related characteristics associated with higher AB use: male gender, low birth weight, having siblings, having an allergy, not being breastfed at all; • No statistically significant associations between AB use and parental age, paternal, employment status, maternal employment status, or maternal smoking during pregnancy.
18	20	Grigoryan L, Burgerhof JG, Haaijer-Ruskamp FM, et al. Is self-medication with antibiotics in Europe driven by prescribed use?	• 19 European countries: Austria, The Netherlands, Sweden, the UK, Ireland, Denmark, Italy, Malta, Luxembourg, Belgium, Spain, Israel, Romania, Czech Republic, Slovakia, Lithuania, Slovenia, Croatia and Poland; • 2006;	• Association between prescribed use and self-medication in general (with ABs, for URTIs); ❖ URTIs: cough, sneezing/nasal congestion, throat symptom, sinus symptom, sinusitis, upper respiratory infection, acute tonsillitis, influenza and strep throat.	• The association between prescribed use and self-medication was modified by source of self-medication, region in Europe and education; • Prescribed use for URTIs increased the likelihood of self-medication with leftover ABs for these symptoms/diseases in all European regions; • The most common reasons for AB self-medication: URTIs, teeth or gum symptoms; • The association between prescribed use and self-medication in general implies that ABs prescribed for one symptom/disease may be used both as self-medication for (repeated) episodes of the same

			• 15 548 participants.		symptom/disease and for another symptom/disease.
19	21	Raz R, Edelstein H, Grigoryan L, et al. Self-medication with antibiotics by a population in northern Israel.	• Northern Israel; • October 2002-December 2003; • 467 participants: Jewish-90.6%, Arab-9.4%.	• Estimate the level of AB self-medication among population in northern Israel.	• In Israel ABs were available by prescription only. OTC acquisition of ABs was rare. However, the storage of leftover ABs at home was 24.4%; • 26.3% of whose who had ABs stored at home also intended to use them without a prescription. However, only 4.3% would give ABs to their children without seeking medical advice; • URTIs and cystitis were the most frequent reasons for the use of ABs; • Amoxicillin was the most commonly used AB.
20	22	Stratchounski LS, Andreeva IV, Ratchina SA, et al. The inventory of antibiotics in Russian home medicine cabinets.	• 9 large Russian cities: Kaliningrad, Smolensk ,Moscow, Volgograd, Nizjni Novgorod , Ekaterinburg, Tyumen, Novosibirsk, Yakutsk; • 1999–2001; • 900 families.	• Evaluate the stock of ABs in the home medicine cabinets (HMCs) of the "non-medical" general population in Russia and to find out for which indications people report that they would use ABs without a physician's recommendation.	• 83.6% of families had ABs for systemic use in HMCs; • 62 different ABs were found in the HMCs. The maximum found in a single HMC was 9; • The major indications for self- medication with ABs: acute viral RTIs, cough, intestinal disorders; • 25% of respondents kept ABs that had passed the expiration dates in their HMCs; • 3 main factors influencing the presence of ABs in the HMCs: ✓ Excessive administration of ABs by physicians in outpatient clinics; ✓ Availability ABs OTC in drug stores;

					✓ Low-quality info about ABs in the mass media, popular print, the Internet.
21	30	Ramalhinho I, Cordeiro C, Cavaco A, et al. Assessing determinants of self-medication with antibiotics among Portuguese people in the Algarve Region.	• Algarve region, Portugal; • Questionnaires were distributed February-April, 2011; • 1192 participants.	• Estimate the prevalence of self-medication with ABs and evaluate the predictive factors associated with such self-medication.	• Self-medication with ABs was more common among males and adults 18- 34 and 50-64 years old, and less frequent among those who believed it was not easy to buy ABs without a medical prescription; • The dispensation of ABs in Portugal was only legal when they were prescribed by doctors; • A higher level of education could mean greater knowledge about ABs and more ease with self-medication.
22	23	André M, Vernby A, Berg J, et al. A survey of public knowledge and awareness related to antibiotic use and resistance in Sweden.	• Sweden; • January-March 2006; • 1000 participants (21–80 years).	• Examine the level of knowledge about AB treatment and awareness of AB resistance among the general public in Sweden.	• The high level of awareness about AB resistance was in Sweden; • People with higher education less trust in the high antibiotic prescribing doctor; • Sex, higher education and reported previous use of ABs were associated with accurate knowledge of the effectiveness of ABs; • 'Pharmacy personnel often provide information on AB use' more than 'doctors often take the time to provide information on AB use'.
23	24	Panagakou SG, Spyridis N, Papaevangelou V, et al. Antibiotic use for upper respiratory tract infections in children: a	• Greece; • January-July, 2007; • 5264 participants: parents with children	• Analyze parental knowledge, attitudes and practices (KAP) on AB use for children with URTIs.	• 80% of parents knew that UTRIs were mostly self-limited, although 74% of them expected to receive ABs when such a diagnosis was given; • Earache was the most common reason for which parents expected

		cross-sectional survey of knowledge, attitudes, and practices (KAP) of parents in Greece.	5- 6 years old.		ABs; • Almost 70% of parents confused ABs with other medicines; • Greek parents had a trusted relationship with their pediatrician --> rarely gave ABs without medical advice; • 90% of parents obtained information on judicious AB use from pediatricians.
24	14	Grosso G, Marventano S, Ferranti R, et al. Pattern of antibiotic use in the community: non-adherence and self-prescription rates in an Italian urban population.	• Catania, Italy; • October 2009-October 2010; • 1269 participants.	• Assess the pattern of AB use in a community setting of an urban area of Italy; • Identify factors that affect adherence to AB use.	• About 45% of patients were non- compliant with AB therapy; • Low educational and socioeconomic status were associated with a higher risk of non-adherence; • No relation was found between non-adherence and gender, age; • Main predictors of AB self- prescription: younger age (22- 44), female gender, higher socioeconomic and educational status.
25	4	Azevedo MM, Pinheiro C, Yaphe J, et al. Portuguese students' knowledge of antibiotics: a cross-sectional study of secondary school and university students in Braga.	• Braga, Portugal; • February-April 2007; • 349 participants: 9th and 12th grades of secondary school and in the first year of university	• Assess the student's knowledge about ABs and the correct use of them.	• Lack of general knowledge on correct AB use; • 70% knew that inappropriate use of ABs can contribute to resistance to these drugs; • There was an increase of knowledge about ABs by grade level up to university; however there was significant heterogeneity among university study areas.
26	25	Berzanskyte A, Valinteliene R, Haaijer-Ruskamp FM, et al. Self-	• Lithuania; • October 2002-Decembe	• Estimate the prevalence of AB use in the general population	• 53.2% of respondents took non-prescribed ABs at least once a year; • More often used self-medication people with

		medication with antibiotics in Lithuania.	r 2003; • 746 participants.	of Lithuania with special interest in self-medication with ABs and sources of their acquisition.	higher work positions, healthy ones, in rural areas; • Age, gender, education level- didn't have influence on frequency of AB use; • The main reasons for AB self-medication were tonsillitis, sore throat; • Lack of correct information about appropriate use of ABs, their side effects, easy access to ABs without prescription influenced on self- medication; • The main source of ABs for self-medication: OTC acquisition in community pharmacies.
27	26	Cagri Buke A, Ermertcan S, Hosgor-Limoncu M, et al. Rational antibiotic use and academic staff.	• Ege University, Turkey; • 2002 year; • 602 participants.	• Determine the knowledge, attitude and behavior of a highly educated group of people towards AB use and self-medication with ABs.	• Knowledge about ABs was higher in Gr.A than in Gr.B; • Better knowledge didn't correlate with appropriate use of ABs; • Gr.A (64.5%) more preferred self-medication than the Gr.B (40.0%). ❖ Gr. A- staff from the Faculties of Dentistry and Pharmacy; ❖ Gr. B- staff from the Faculties of Letters, Education, Science, Communication, Economic and Administrative Sciences, Fisheries, Agriculture and Engineering; ❖ Faculty of Medicine was excluded.
28	33	Buke C, Hosgor-Limoncu M, Ermertcan S, et al. Irrational use of	• Ege University, Turkey; • 2004 year;	• Evaluate the knowledge, attitude and behavior of AB use in the student	• There was inappropriate use of ABs among university students; • Specific education regarding ABs can increase the knowledge

		antibiotics among university students.	• 678/672 participants: Group A/ Group B.	groups of a University in a country where the ABs are taken without prescriptions.	about ABs but it did not always correlate with appropriate behavior; • The main reason for AB use in both groups was common cold; • The knowledge in Gr.A was statistically high, but it was surprising that they approved ABs against common cold; • Pharmacology lessons may have contributed to the differences between the groups. ❖ Gr. A- Faculty of Dentistry and Pharmacy; ❖ Gr. B- Faculties of Letters, Education, Science, Communication, Economic and Administrative Sciences, Fisheries, Agriculture and Engineering; ❖ Faculty of Medicine was excluded.
29	27	Emslie MJ, Bond CM. Public knowledge, attitudes and behaviour regarding antibiotics- a survey of patients in general practice.	• Grampian, North-East Scotland; • February-March 2000; • 351 participants.	• Assess public knowledge, attitudes and behavior regarding ABs.	• ABs were available in the UK only on prescriptions; • There was a link between awareness of AB resistance and AB use; • 53.5% agreed that most infections clear up by themselves without the need for ABs; • 75% indicated they would ask a pharmacist for advice about the treatment of RTIs.
30	28	Ilhan MN, Durukan E, Ilhan SO, et al. Self-medication with antibiotics: questionnaire survey among primary care	• Ankara, Turkey; • 30 January 2006- 9 February 2006; • 2696 participan	• Determine the frequency and reasons for self-medication with ABs among primary	• The frequency of self-medication with ABs was 54.1%; • The patients can buy any ABs from the pharmacy without a prescription; • The most common reasons for AB self-medication: sore throat,

		center attendants.	ts.	healthcare center attendants aged 18 or over in Ankara.	fever; • Self-medication was associated with male sex, being single, being at age 30–59, high level of education, being employed and not having social security; • Patients who self-medicated with ABs had made a habit of this and they self- medicated often.
31	39	Väänänen MH, Pietilä K, Airaksinen M. Self-medication with antibiotics--does it really happen in Europe?	• Costa del Sol region, Spain; • 2002 year; • 530 participants (Finns immigrants).	• Determine whether ABs are used for self-medication in southern Spain; • Study whether the AB usage patterns change when people move to a country where it is a common practice for pharmacists to dispense ABs without a prescription.	• Self- medication with ABs was common among Finnish immigrants; • AB use habits of the Finns totally changed when they moved from strictly regulated country to another, where buying the non-prescription ABs was common; • The most common reason for AB use: common cold; • No link between AB use and gender, age, marital status, working situation, self-reported health or smoking.
32	40	Rousounidis A, Papaevangelou V, Hadjipanayis A, et al. Descriptive study on parents' knowledge, attitudes and practices on antibiotic use and misuse in children with upper respiratory tract infections in	• 2 districts in Cyprus; • 1 February-13 May 2006; • 1462 participants.	• Explore the parental knowledge, attitudes and practices (KAP) regarding AB use for children 4–7 years old.	• Knowledge: ✓ Pediatrician was the main sources of info about ABs; ✓ High level of knowledge. • Attitudes: ✓ Asked ABs for earache, fever; ✓ Changed the doctor if she/he prescribed easily ABs. • Practices: ✓ Majority followed pediatricians' instructions.

		Cyprus.			• Demographic factors: ✓ Educational level, residence area, ethnicity, parental age, sex were associated with KAP.
33	29	Pavydė E, Veikutis V, Mačiulienė A, et al. Public Knowledge, Beliefs and Behavior on Antibiotic Use and Self-Medication in Lithuania.	• Lithuania; • 2015 year; • 1005 participants.	• Assess public knowledge, beliefs, and behavior concerning AB use and self-medication in Lithuania.	• Poor knowledge of ABs was associated with the overestimation of self-knowledge of ABs, which was associated with higher prevalence of self-medication with ABs; • The level of self-medication with ABs had increased by 10% since 2006 (it made 31.0%); • Self- medication was associated with male gender, rural place of residence, absence of children, age > 40; • No associations between self-medication and education level and knowledge of AB; • The main sources of AB information: physicians, pharmacists, family members or friends and the Internet; • 58% of parents followed the physicians' advice on AB use, 23.1%- pharmacists'; • The main source of ABs without prescription: pharmacies.
34	41	Panagakou SG, Papaevangelou V, Chadjipanayis A, et al. Risk factors of antibiotic misuse for upper respiratory tract infections in children: results from a cross-	• Greece; • January-July 2007; • 5312 participants.	• Identify possible risk factors associated with AB misuse in Greece.	• Being father, low education and immigrant status were associated for all the sections KAP. In the knowledge section additional RFs: parents living in the islands, having low income, <2or >3 children, no experience in recurrent URTIs. In attitude section

		sectional knowledge-attitude-practice study in Greece.			additional RFs: being a single parent, having no experience in recurrent URTIs; • Drug legislation forbided purchasing ABs without prescriptions.
35	42	Fernandes M, Leite A, Basto M, et al. Non-adherence to antibiotic therapy in patients visiting community pharmacies.	• Lisbon, Portugal; • February-April 2009; • 243 participants.	• Measure prevalence and reasons for non-adherence to AB treatment and to identify factors associated with it.	• The prevalence of non-adherence was 57.7 % (in 2000 it made 40.7 %); • Factors associated with non-adherence: duration of treatment, formulation characteristics, younger age, difficulty in buying the ABs, satisfaction with the info given by physicians; • No association: having read the package leaflet or receiving info regarding the ABs at the pharmacies.
36	43	Ivanovska V, Zdravkovska M, Bosevska G, et al. Antibiotics for upper respiratory infections: public knowledge, beliefs and self-medication in the Republic of Macedonia.	• Macedonia; • April 2012; • 402 participants.	• Assess public knowledge, beliefs and behavior regarding AB use in adults for URTIs; • Identify demographic factors associated with non-prescription AB use.	• Low level of public knowledge about ABs; • 43.3% purchased ABs OTC, despite drug legislation; • No significant association between OTC purchase of ABs and demographic factors: age, gender, education, employment status, residence, marital status, insurance, financial situation.
37	44	Mira JJ, Navarro I, Huttner B, et al. What do Spaniards read about the prudent use of anti-microbial agents and what do they really	• Printed media (1 January 2007–31 May 2009); • Institutional and news	• Influence of the media and institutional campaigns on AB use.	• The info from the press and institutional websites was correct; • Less knowledge was among men, patients discharged from hospital, in rural areas and among elderly; • Passive role (more in

		do?	media websites (March–May 2009); • Telephone survey (1- 30 September 2009); • Spain; • 1526 participants.		rural area) in doctor-patient communication increased self-medication; • Correct information about inappropriate AB use and resistance didn't reduce self-medication; • There was no association between self- medication and age, sex or type of healthcare service used previously.