



ANTIMICROBIAL RESISTANCE and causes of non-prudent use of antibiotics in human medicine in the EU



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Country codes

The following country codes are used in this report:

AT: Austria	IE: Ireland	SR: Slovakia
FR: France	PT: Portugal	EL: Greece
NL: Netherlands	DE: Germany	LU: Luxembourg
BE: Belgium	IS: Iceland	SE: Sweden
HR: Croatia	RO: Romania	ES: Spain
NO: Norway	DK: Denmark	LV: Latvia
CY: Cyprus	IT: Italy	UK: United Kingdom
HU: Hungary	SI: Slovenia	FI: Finland
PL: Poland	EE: Estonia	MT: Malta
CZ: Czech Republic	LT: Lithuania	



Executive summary

1. Antimicrobial resistance: a public health problem

Antimicrobial resistance (AMR) is an increasing worldwide public health problem with important implications for the European Union (EU). When antibiotics become ineffective, bacterial infections lead to increased morbidity, use of healthcare, mortality and cost.^{1 2 3 4} Globally, estimates suggest that AMR leads to 700 000 deaths per annum.⁴ For the EU, the European Centre for Disease Prevention and Control (ECDC) has estimated that AMR currently causes 25 000 deaths annually and losses of at least EUR 1.5 billion per annum in extra healthcare costs and productivity.⁵

An important driving force behind AMR is the non-prudent use of antimicrobial agents in both humans and animals.^{2 3} Reducing the unnecessary consumption of antibiotics can therefore have a powerful impact upon resistance.⁴ Several reports have been published in recent years that outline measures to reduce the consumption of antibiotics, for example by the Organisation for Economic Cooperation and Development (OECD)² and the AMR review group.⁴ A variety of actions have been proposed, including global awareness campaigns, increasing financial resources for infectious diseases in the healthcare sector, the development of new antibiotics and policies aimed at the reduction of antibiotic use.

Worldwide, the focus of research and policy actions has been on prescribed antibiotics, with much less attention being paid to the human use of antibiotics without a prescription. This while the use of antibiotics without a prescription represents a non-prudent use of antibiotics because of its lack of medical guidance.⁶ Reducing the use of antibiotics without a prescription will contribute to controlling bacterial resistance.⁷ Strategies, therefore, to improve the prudent use of antibiotics in the EU and its Member States should include action to address antibiotic use without a prescription.

2. Aims of the ARNA project

This report describes the results of the ARNA ('Antimicrobial resistance and the causes of non-prudent use of antibiotics') project, which was carried out under a contract with the European Commission (Directorate-General for Health and Food Safety). Most of the data collection and work on the project took place from July 2014 to June 2016.

The ARNA project aimed to:

1. identify key factors that drive the sales and non-prudent use of antibiotics in human medicine obtained without a prescription;
2. assess the level of enforcement of the legislation regarding 'prescription-only' use of antimicrobial agents in the EU;
3. document good practices aimed at strengthening more prudent use of antibiotics;
4. develop policy options for more prudent use of antibiotics.

To achieve these goals, a wide range of activities were performed within the ARNA project. These activities are listed in Box 1.



Box 1. Activities within the ARNA project.

The frequency of antibiotic use without a prescription (Chapter 2)

- A summary of existing data on antibiotic use in the EU Member States from the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) and the 2013 and 2016 Eurobarometer surveys on the use of antibiotics.
- A systematic literature review of the prevalence of the use of antibiotics without a prescription.

Explaining differences in non-prescription use across the EU (Chapter 3)

- A literature review of the determinants of antibiotic use without a prescription on the population, healthcare-professional (HCP) and healthcare-system levels.
- An analysis of the 2013 Eurobarometer survey data. These data are used to study determinants of antibiotic use for all 28 EU Member States.
- An online survey among ministries of health and national experts to describe policy measures that EU Member States have taken on a healthcare-system level to enhance the prudent use of antibiotics.

Use of antibiotics without a prescription in seven EU Member States (Chapter 4)

- Interview surveys among patients who used antibiotics without a prescription, general practitioners (GPs) and pharmacists in seven Member States (Cyprus, Estonia, Greece, Hungary, Italy, Romania and Spain).

Good practices in the EU (Chapter 5)

- A literature review of good practices such as policy measures or interventions.
- An online survey among ministries of health and national experts to collect information on measures and interventions not described in the literature.

Expert opinions and a consensus statement on policy options to reduce the use of antibiotics without a prescription in the EU (Chapter 6)

- An expert meeting with a group of 20 experts from nine EU Member States and two non-EU Member States. The experts reviewed and discussed interventions that EU Member States could use to reduce the non-prudent use of antibiotics.

Policy measures to enhance more prudent use of antibiotics in six EU Member States (Chapter 7)

- Country-dialogue meetings were held in six EU Member States (Cyprus, Greece, Hungary, Italy, Romania and Spain). Each Member State had a local organiser and all the relevant stakeholders were represented by the participants in the meetings.

Consensus statement on the prudent use of antibiotics (Chapter 8)

- An international conference was held on 17 June 2016 to discuss the results of the project, as well as to conclude the ARNA project with an overview of actions. Sixty participants, from 21 EU Member States, attended the conference. The main conclusions and recommendations were summarised in the ARNA Utrecht conference statement on the prudent use of antibiotics.

3. The use of antibiotics without a prescription

The first part of the ARNA project focused on the frequency of antibiotic use without a prescription. Data from the 2013 and 2016 Eurobarometer surveys suggest that the proportion of antibiotics that were used without a prescription increased from 5 % of all antibiotics used in 2013 to 7 % in 2016.⁸ However, rates varied across EU Member States. The highest rates were found in Greece, Romania and Cyprus, both in 2013 and in 2016.

The two prevailing sources of antibiotics without a prescription are over-the-counter (OTC) selling in pharmacies and the use of leftover antibiotics. In Member States such as Greece, Cyprus and Romania, antibiotic use without a prescription is mainly driven by OTC selling in pharmacies. Between 80 % and 100 % of all the most recently used courses of antibiotics without a prescription had been bought in a pharmacy. In other Member States, such as Italy, Hungary and Spain, the use of leftover antibiotics is also an important source of non-prescription use. The Eurobarometer data suggest that the internet does not seem to be an important source for obtaining antibiotics without a prescription. Finally, the analysis revealed a positive, but moderate, association between prescription use and non-prescription use of antibiotics.

The selection of Member States for the ARNA project

Surveys regarding the use of antibiotics without a prescription were performed in seven Member States, among patients, pharmacists and GPs. The seven Member States were chosen on the basis of the 2013 Eurobarometer survey^(a) as this is the only source that both includes all EU Member States and measures antibiotic use in exactly the same way. The main criterion for selecting the seven ARNA countries was the level of antibiotic use without a prescription. The Member States with high rates of non-prescription antibiotic use measured as a percentage of total use were: Cyprus (10 %), Estonia (6 %), Greece (16 %), Hungary (8 %), Romania (20 %) and Spain (8 %). Italy (4 %) was not on the list of top Member States, but was chosen, in agreement with the European Commission, due to regional differences in use. There was higher use in southern Italy and lower use in the north.

4. Key factors that drive the non-prudent use of antibiotics obtained without a prescription

The assessment of determinants of antibiotic use without a prescription shows that it is a complex phenomenon that can be partly explained by various determinants on different levels, such as the patient, the healthcare professional (HCP) and the healthcare system. An extensive literature review showed that the scientific literature has mainly focused on patient-level factors that might drive the use of antibiotics without a prescription. The literature results were inconclusive for sociodemographic factors such as for the patient's gender, age and educational level, and for the location of the pharmacy. Despite this, some determinants were consistently found to be associated with the use of antibiotics without a prescription. These are discussed below.

Patient level

On the patient level, a lack of knowledge of antibiotics is associated with higher use of antibiotics without a prescription. This result was confirmed in a secondary data analysis of the 2013 Eurobarometer data. Here, differences between EU Member States in the rates of non-prescription use — relative to the use of prescription antibiotics — can be explained in part by differences in the level of knowledge and

(^a) The choice for the ARNA countries was made in 2014.

attitudes towards antibiotics. The patient interviews in the seven ARNA countries further supported the importance of a lack of knowledge as a determinant for non-prudent use. Knowledge about antibiotics among patients who use antibiotics without a prescription was found to be lower compared to the general population in the Eurobarometer surveys.

A lack of knowledge is also reflected in the main reasons why patients use an antibiotic without a prescription in the seven ARNA countries. Influenza, common cold, sore throat, cough, fever and headache are all common reasons given for using antibiotics without a prescription. Finally, a previously prescribed antibiotic treatment is the main motivation for patients to use antibiotics without a prescription in all seven Member States. This determinant was also found in some of the studies included in the literature review.

Healthcare professional (HCP) level

The knowledge and attitudes of pharmacists regarding antibiotics is also important. The better the knowledge, and the more reluctant the attitude of the pharmacist, then the less likely he or she will be to dispense antibiotics without a prescription. Other pharmacist- and pharmacy-related characteristics, such as the location of the pharmacy and the age and gender of the pharmacist, did not have an association with the use of antibiotics without a prescription. However, pharmacists in smaller pharmacies seem to be more likely to dispense antibiotics without a prescription.

Patient requests for an antibiotic are a driving factor for non-prudent use that was mentioned by both pharmacists and GPs who were interviewed in the seven ARNA countries. GPs and pharmacists do not always fulfil the requests from these patients, however some of them sometimes do prescribe or dispense an antibiotic when there is patient pressure or there is shared decision-making with the patient. Pharmacists also report that they fear that customers will otherwise go to another pharmacy. In the ARNA countries ^(b), cooperation between pharmacists and GPs on the issue of antibiotic use is limited and could be strengthened.

Health-system level

On the healthcare-system level, a literature review found that dispensing the exact number of tablets instead of whole packages reduces the use of antibiotics without a prescription. Moreover, a survey among ministries of health (MoHs) and experts in all EU Member States revealed that OTC sales of antibiotics are illegal in some countries for most, but not all, antibiotics. The main exceptions concern topical antibiotics. From this survey, we also conclude that actions are being taken by all Member States to reduce the non-prudent use of antibiotics, but the type and intensity of actions differ by Member State. The most common measures were 'surveillance of resistance and antibiotic use', 'educational interventions' and 'media campaigns'. Antibiotic stewardship programmes were reported by eight Member States. The different measures are aimed at reducing the non-prudent use of antibiotics but their effect on the use of antibiotics without a prescription has not been measured.

Conclusions: the key factors

Based on the analysis of determinants, we conclude that interventions and policies that simultaneously target patients and HCPs will be more effective than approaches targeting just one of them. An increasing amount of awareness and knowledge is needed from both groups — patients and professionals — in order to induce

^(b) The ARNA countries are the seven Member States selected for the in depth study: Cyprus, Estonia, Greece, Hungary, Italy, Romania and Spain.



behavioural change. Moreover, the enforcement of laws and regulations is necessary to ensure the sustainability of behavioural change.

5. Enforcement of legislation regarding the ‘prescription-only’ use of antimicrobial agents in the EU

In the EU, all Member States have legislation requiring that antibiotics are only dispensed with a medical prescription. OTC sales of antibiotics are illegal in all Member States, although there are some exceptions in a number of them — for example creams or eye drops that contain antibiotics.

Despite this legal framework, we found that significant amounts of OTC sales occur in several Member States (see Section 3 above). These findings highlight the need for Member States to enforce existing laws better in order to ensure antibiotics are only available with a prescription.

6. Documenting good practices aimed at strengthening more prudent use of antibiotics

In May 2015, the WHO urged all countries to have multisector national action plans to address AMR in place by 2017. The EU ministers of health have also called upon Member States to have such a plan. The ARNA study showed that 14 EU Member States had such a national antibiotic plan or plan to combat AMR. Nevertheless, 26 EU Member States had activities to enhance the prudent use of antibiotics, with surveillance systems looking at both AMR and antibiotic use. This is the most important national policy, but others include educational interventions, found in 20 Member States, and media campaigns, found in 19.

Evidence from the literature shows that education and information, provided for the public and for HCPs, are effective interventions in enhancing the prudent use of antibiotics. This is in line with the finding that a lack of knowledge of antibiotics, both among patients and HCPs, is a key driving force for the non-prudent use of antibiotics. For HCPs, other effective interventions exist such as providing assistance via technological support tools or guidelines. On the policy level, cooperation between different stakeholders such as HCP organisations, patient organisations and policymakers is important. So too is the creation of national committees that stimulate information promoting research and monitoring such as the Strama programme in Sweden.

Overall, the most effective way to stimulate the prudent use of antibiotics is the implementation of a combination of interventions on different levels simultaneously, repeated over a number of years. In many other Member States, a variety of initiatives were found. Examples include the setting of targets for a reduction in the number of antibiotic prescriptions and the measurement of adherence to treatment recommendations ^(c). Providing the infrastructure for monitoring the use of antibiotics, both nationally and regionally, is another example ^(d). Moreover, policymakers can encourage professional associations to identify and monitor indicators of rational prescribing and the control of sales of antibiotics ^(e). However, given that many of the interventions have not been properly evaluated, especially those on a healthcare-system level, it is difficult to be sure whether all of the interventions are effective. This is an area that requires further attention. However, we found that many initiatives

^(c) E.g. <http://strama.se/about-strama/?lang=en>; <https://guidelines.nhg.org/>

^(d) E.g. <http://www.eurosurveillance.org/viewArticle.aspx?ArticleId=19036>

^(e) E.g. <http://fingertips.phe.org.uk/profile/amr-local-indicators>

exist. Member States across the EU can learn from each other how to develop activities better in order to promote the prudent use of antibiotics.

7. Developing policy options for more prudent use of antibiotics

Expert opinion: proposed interventions

Within the context of the ARNA project, a group of experts discussed and agreed a set of interventions that EU Member States can use in order to reduce the non-prudent use of antibiotics.

Public health/patient-level interventions

Public health campaigns should be integrated into multifaceted interventions which are tailored to both the profile of a specific Member State and to important target groups, including patients with low health literacy. Patients should be educated, for example, on when to consult their doctor or pharmacist and when an antibiotic is appropriate. Mass-media messages should also be supported by pharmacists and GPs.

CPHCP-level interventions

The communication skills of HCPs towards their patients should be improved, taking into account the health literacy of patients. These skills should be supported by patient information. Collaboration between HCPs, and especially between GPs and pharmacists, should be strengthened. HCPs should also be made familiar with guidelines for the prudent use of antibiotics. Finally, point-of-care tests may be of additional value but there is still no clear evidence of this.

Policy option interventions

National plans to combat AMR should be further encouraged and the laws banning OTC sales need to be enforced more stringently in some Member States. To promote this enforcement, incentives — preferably positive, but negative ones too — should be used to promote the prudent use of antibiotics. The experts also found that antibiotic packaging should be tailored to the course of treatment and that the length of time that antibiotic prescriptions should be limited and maybe the period that they are valid, i.e. the period during which the patient can fill the prescription, should be harmonised across all EU Member States. These currently vary from 2 weeks to 1 year. In addition, delayed prescribing should be encouraged. Surveillance is, however, according to the expert group, only useful if it includes quality indicators meaning indicators that are tailored to a certain diagnosis.

EU-level interventions

The experts agreed that the EU's European Antibiotic Awareness Day is an excellent initiative but needs to be complemented with activities and/or interventions on a national level in order to produce sustainable behavioural change. Another issue discussed was benchmarking, which was considered a powerful approach as Member States in the EU want to do their best, and this stimulates action. Moreover, it helps to improve transparency, which is important for governance. Benchmarking should be encouraged on both a national and a regional level.

ARNA countries: plans for action

The ARNA project organised country-dialogue meetings in cooperation with national authorities in six Member States (Cyprus, Greece, Hungary, Italy, Romania and Spain) to which all relevant stakeholders were invited. These events aimed to generate action plans to combat the non-prudent use of antibiotics. We found that each Member State has its own problems and, therefore, different approaches were discussed and



included in each of the action plans. The action plans also demonstrated some similarities. Common actions included: the need for large-scale educational campaigns with clear messages and focused on health literacy; increasing the use and availability of rapid tests; and stimulating vaccination programmes, such as against influenza, in order to reduce bacterial infections. Other actions that were frequently cited included: educational programmes for HCPs; the use of electronic medical records to monitor treatments more effectively; and the development of simple treatment guidelines that are easy to disseminate. Common actions also included the involvement of all stakeholders, in particular patient groups and stimulating collaboration between primary and secondary care.

ARNA Utrecht conference statement, 17 June 2016

A final conference was held to conclude the ARNA project and to discuss further actions to reduce the non-prudent use of antibiotics. A conference statement was discussed and agreed which summarises the final conclusions of the ARNA project. It was agreed that there is a need for clear leadership in all EU Member States as the development and implementation of national plans to combat AMR, such as the national antibiotic resistance plan in Spain, should be in place before mid 2017 according to the WHO. Better collaboration is also needed on the local, national, European and global levels. The establishment of multidisciplinary professional networks, such as Strama in Sweden, Bapcoc in Belgium and SWAB in the Netherlands, create important structures that support, coordinate and stimulate interventions in EU Member States. Regarding the prudent use of antimicrobials in human medicine, multifaceted approaches are needed that target prescribers, the general public and healthcare as a whole.

There is a need to combine interventions, such as measures to restrict antibiotic prescribing, patient education to improve health literacy, and multi- or inter-professional collaboration. It is important to recognise that the prudent use of antimicrobials is the responsibility of all stakeholders. A variety of interventions can be taken on different levels including, among others, the general public, healthcare workers, the health system and the EU. This was also discussed with the experts and in the six country-dialogue meetings.

Importantly, there were many similarities between the conclusions of the conference statement, the expert meeting and the six country-dialogue meetings. As such, the conference statement can be used by EU Member States, as well as stakeholders within each Member State, to establish their own programmes to enhance more prudent use of antibiotics.

More information on the ARNA project can be found on the ARNA website: <https://www.nivel.nl/en/arna>



1. Introduction

This report describes the results of the ARNA ('Antimicrobial resistance and causes of non-prudent use of antibiotics') project. The ARNA project was aimed at enhancing the prudent use of antibiotics in the European Union (EU), with an emphasis on the use of antibiotics without a prescription. The ARNA project was carried out under a contract with the European Commission's Directorate-General for Health and Food Safety.

1.1. Background

Antimicrobial resistance

Antimicrobials can be divided into groups based on the organisms that they target, for example antibacterials which act on bacteria (commonly known as antibiotics), antivirals which act on viruses and antifungals which act on fungi. Although resistance to antifungals is increasing, the number of infections with drug-resistant fungi is far smaller than those caused by antimicrobial-resistant bacteria^(f). Antibiotics are the focus of the ARNA project and this report.

Antimicrobial resistance (AMR) is defined as the ability of an organism to grow or survive in the presence of high levels of antimicrobials (antibiotics). The existence of AMR in humans is gained either through gene mutation or by the acquisition of genetic information from other bacteria through horizontal gene transfer^(g). The development of AMR is a natural phenomenon in microorganisms, and is accelerated by the selection pressure exerted by the use or misuse of antibiotics in humans and animals^(h). The misuse of antibiotics includes the use of dosages that are either too high or too low or the use of the wrong type of antibiotics (including the use of antibiotics to treat conditions that are not caused by a bacterial infection). The development of resistance is a normal evolutionary process for microorganisms, but it is accelerated by the selective pressure exerted by widespread use of antibiotics.¹ Indeed, the development of each new antibiotic has been followed by the detection of resistance. Until the 1970s, many new antibiotics were developed to which most common pathogens were initially fully susceptible, but the last complete new classes of antibiotics were discovered during the 1980s (Monobactam and Daptomycin), and efforts to combat AMR are therefore highly important.¹

Antimicrobial resistance: a public health problem

Antibiotics are considered to be one of the greatest discoveries of the 20th century, as they save millions of lives from once deadly diseases. AMR is an increasing worldwide public health problem and the WHO currently considers it to be one of the three greatest threats to human health for the next decades⁽ⁱ⁾.

Established and newly emerging infectious diseases are increasingly threatening people's health as AMR makes it more difficult to treat bacterial infections effectively.¹²³⁴ If antibiotics become ineffective, these infections will lead to increased morbidity, an increased burden on healthcare and, eventually, premature deaths.⁴⁵ The economic consequences include loss of productivity and increased costs of diagnostics

^(f) <http://www.jpiamr.eu/document-library/strategicresearchagenda>

^(g) <http://www.jpiamr.eu/document-library/strategicresearchagenda>

^(h) <http://www.jpiamr.eu/document-library/strategicresearchagenda>

⁽ⁱ⁾ <http://www.jpiamr.eu/document-library/strategicresearchagenda>



and treatment.^{2 9} Estimates suggest that, globally, AMR currently leads to the deaths of 700 000 people per year.⁴ This is more than the number of people that currently die from cancer.⁴ In the United States, the yearly cost of AMR to the health system alone has been estimated at USD 21-34 billion, accompanied by more than 8 million additional days in hospital.¹⁰ For the EU, the European Centre for Disease Prevention and Control (ECDC) has estimated that AMR causes 25 000 deaths annually and results in extra healthcare costs and productivity losses of at least EUR 1.5 billion.⁵

The impact on particularly vulnerable patients is most obvious. In Europe, an ageing population and the increasing prevalence of conditions such as obesity and diabetes will contribute to an increase in the number of vulnerable members of society who are at a higher risk of mortality and morbidity from infections which are resistant to antibiotics.

Antimicrobial resistance: public health action

AMR is a complex public health challenge, and no single strategy or intervention will be sufficient to fully counter the emergence and spread of infectious organisms that become resistant to the available antimicrobial drugs.¹¹ Antibiotics have been misused both in humans and animals because of several factors, such as their low cost, easy availability (OTC in some countries), poor understanding of their curative limits and economic factors (the use of antibiotics as animal growth promoters). Coordinated public health actions need to be taken in these diverse sectors of society to address and control AMR.

The WHO is leading efforts to address AMR on a global level. In Europe, public health action is being carried out by the Commission, ECDC, EU Member States (e.g. the Joint Programming Initiative on Antimicrobial Resistance, WHO and various professional bodies (e.g. the European Society for Clinical Microbiology and Infectious Diseases and the Pharmaceutical Group of the European Union). The European Union has put in place an action plan against AMR for the period 2011-2016. This action plan is intended to prevent the spread of microbial infections, ensure the appropriate use of antimicrobials and undertake research into effective ways to combat resistance (^j).

Action to combat AMR needs to recognise that the use of antimicrobials and the resulting patterns of AMR in human and animal health are linked by interactions through direct physical contact, the food chain and the environment. Therefore, measures to combat the spread of AMR for human health also need to include corresponding actions in the animal health field and require multidisciplinary collaboration. This is the basis for the One Health approach to action on AMR recommended by WHO and followed by the EU. For instance, there has been an EU-wide ban on the use of antibiotics as growth promoters since 2006, with veterinarians only allowed to use antibiotics to prevent and fight bacterial infections (^k).

The use of antibiotics: a driving force for AMR

The global demand for antibiotics is rapidly increasing, and a major driving force for AMR is the non-prudent use of antimicrobial agents both in humans and animals.^{e.g. 2 3} This is partly as a result of improved access to life-saving medicines because of economic development around the world (e.g. Asia), but also because antibiotics are used unnecessarily rather than because there is a genuine medical need.⁴

(^j) Communication from the Commission to the European Parliament and the Council — Action plan against the rising threats from antimicrobial resistance, COM(2011) 748, 15 November 2011.

(^k) <http://www.jpiaamr.eu/document-library/strategicresearchagenda>

Within the EU, ESAC-Net monitors the use of antibiotics in humans. Figures from this surveillance network show large differences in the human consumption of antibiotics.³ In 2014, the outpatient consumption of antibiotics for systemic use ranged from 10.6 defined daily doses (DDD) per 1 000 inhabitants per day in the Netherlands to 34.1 DDD per 1 000 inhabitants per day in Greece (^l). Other Member States with high levels of antibiotic use in humans include, for example, Romania, France, Belgium and Italy. In EU Member States, higher levels of AMR are generally observed where there is a higher level of antibiotic use³, suggesting that a reduction in unnecessary consumption of antibiotics can have a powerful impact on resistance.⁴

Over the last few years, several reports have been published which address measures to reduce the consumption of antibiotics, for example by the OECD² and the AMR review group.⁴ The reports call for a variety of policies, including global awareness campaigns, increasing financial resources for the infectious diseases healthcare sector, the development of new antibiotics and policies aimed at the reduction of antibiotic use.

AMR has been an important public health issue in Europe and was one of the priorities of the Dutch Council Presidency during the first half of 2016. Indeed the EU Member States reached an agreement in June 2016 on how to combat AMR (^m), which included the requirement for each Member State to have a One Health action plan to address AMR in both the human and the veterinary sectors and the need to take measures to ensure the prudent use of antibiotics in humans and animals. The Commission-funded ARNA project focuses on this last group of measures as it aims to support policies to decrease the non-prudent use of antibiotics, with a specific focus on antibiotics without a medical prescription.

The use of antibiotics without a prescription

Within the EU, a considerable proportion of all antibiotics are obtained without a prescription.⁸ Both in 2009 and 2013, data from the Eurobarometer surveys, commissioned by the Commission,^{12 13} showed that 5 % of all antibiotics that were used in the EU were obtained without a prescription. In 2016, this percentage increased slightly to 7 % (Eurobarometer data, 2016). Antibiotic use without a prescription is more substantial in some Member States, such as Greece, Romania and Cyprus, where over 10 % of all antibiotics that are consumed are not issued by a doctor.^{12 13}

The use of antibiotics without a prescription has different forms. One is OTC sales by pharmacists without a prescription. Although, throughout the whole EU, antibiotics for human use are legally available only with a prescription issued by a healthcare professional (Directive 2001/83/EC), OTC selling still exists in some Member States (see Chapters 2 to 4 for more information). Other forms of non-prescription use are the use of leftover antibiotics or buying through the internet.⁸ The reason why it is important to pay attention to the use of antibiotics without a prescription is that it represents a non-prudent form of antibiotic use due to a lack of medical guidance accompanying the use.⁶ Eventually, this can lead to adverse effects and to increasing numbers of drug-resistant microorganisms.¹⁴ Reducing the use of antibiotics without a prescription to a minimal level will contribute to the control of bacterial resistance.⁷ Therefore, strategies to improve the prudent use of antibiotics in the EU and its

(^l) <http://ecdc.europa.eu/en/eaad/antibiotics-get-informed/antibiotics-resistance-consumption/Documents/antibiotics-consumption-EU-data-2015.pdf>

(^m) <https://www.rijksoverheid.nl/ministeries/ministerie-van-volksgesondheid-welzijn-en-sport/nieuws/2016/06/17/nauwere-europese-samenwerking-tegen-dure-geneesmiddelen-en-antibioticaresistentie> (lastly read June 21 2016)

Member States should include antibiotic use without a prescription. The ARNA project, therefore, focuses on this use.

1.2. The need to integrate measures

There is a large amount of variation between EU Member States in the use of antibiotics, both with and without a prescription. These differences cannot be explained by differences in morbidity rates alone. Previous studies showed that the differences between countries in the use of antibiotics and other medicines are determined by a complex mix of factors on different levels.^{6 15-17 18 19} The use of medicines, including antibiotics, occurs within the context of healthcare systems that vary widely in how they provide for the health needs of individuals, groups, communities and wider society due to differences in political, historical, cultural and socioeconomic traditions. As a result, the organisational arrangements for healthcare differ considerably between EU Member States. Therefore, policymakers across the Member States may make distinctly different decisions regarding their own population's access to medicines. Moreover, doctors make decisions specific to their individual patients with regard to their choices between treatment options. At the same time, patients' behaviour varies in relation to how they seek treatment. As a result, variation in the use of medicines is largely determined by each Member State's healthcare system.

Variation in the use of prescribed antibiotics was reviewed in an article in *The Lancet* by Cars et al. in 2001.²⁰ They argued that the large variation they observed in the use of antibiotics is unlikely to be caused by differences in the frequency of bacterial infections. The authors concluded that the attitudes of physicians and patients to antibiotics, their historical backgrounds, cultural and social factors and disparities in healthcare systems were also important factors in determining the antibiotic-prescribing patterns observed. The importance of cultural diversity in antibiotic prescribing was also stressed in a study by Deschepper et al. (2008), who identified several cultural aspects associated with antibiotic use, such as the relationships between HCPs and patients and those between professionals.¹⁷ As such, it has been shown that single causes of variation in the use of antibiotics with a prescription are often difficult to identify, as various elements may play a particular role.

In order to understand the causes of certain patterns of antibiotic use, an integrated approach that includes all relevant processes and regulations within a healthcare system is needed. This integrated approach includes all the relevant levels and all the actors within those levels. This helps both to understand the use of antibiotics in the context of the healthcare system and to assist in the development of good practices and optimal pharmaceutical policies. This probably holds true for the use of antibiotics both with and without a prescription. The ARNA project therefore used an integrated approach in order to attempt to distinguish the levels where factors influence the use of antibiotics. These factors can be found on different levels.

1. The **healthcare-system level**, including the cultural background and regulations that focus on relevant processes and regulations within the healthcare setting. Examples of factors on this level include regulations that apply to the dispensing of antibiotics, the enforcement of the law not to dispense antibiotics without a prescription, the existence of national guidelines for the use of antibiotics and the culture within a country regarding the use of antibiotics.
2. The **healthcare-professional level**, where the focus is on the behaviour of prescribers and pharmacists with regard to prescribing and the OTC dispensing of antibiotics. Factors that may have an impact upon the dispensing of antibiotics



without a prescription may, for example, include the knowledge and attitudes of pharmacists towards antibiotics, the willingness of GPs to prescribe antibiotics, patient pressure and competition with other pharmacies.

3. The **patient** level, with a focus on the behaviour of patients with regard to the use of antibiotics. Factors that may play a role here include, for example, the knowledge and attitudes of the patient, the costs of the doctor's consultation and the cost of the antibiotics.

The ultimate use of antibiotics without a prescription is determined by the interplay between different factors on these three different levels. All these levels, therefore, need to be taken into account, not only when studying the use of antibiotics but also when attempting to improve the prudent use of antibiotics. The ARNA project uses these three levels within all its activities aimed at enhancing the prudent use of antibiotics.

1.3. Aims of the ARNA project

Notwithstanding the studies previously quoted, relatively little attention has been paid to explaining the differences in the level of use of antibiotics without a prescription, nor to policies and measures that specifically target the reduction of antibiotic use without a prescription. The ARNA project aimed to fill this gap.

More specifically, the ARNA project aimed to:

1. identify the key factors that drive the sales and non-prudent use of antibiotics in human medicine obtained without prescription;
2. assess how far the level of enforcement of the legislation regarding the 'prescription-only' use of antimicrobial agents within the EU is enforced;
3. document good practices aimed at strengthening more prudent use of antibiotics;
4. develop policy options for more prudent use of antibiotics.

To achieve these goals, a wide range of activities were performed within the ARNA project. These activities are listed in the next sections in the report.

1.4. The structure and content of the report

The structure of the report is described below. After the title of each chapter, we state to which of the four objectives in Section 1.3 it contributes. Each chapter starts with an introduction, followed by a section in which the methods are described in detail.

Chapter 2: The use of antibiotics without a prescription (*objective 1*)

A major aim of the ARNA project was to identify factors that drive the sales and non-prudent use of antibiotics obtained without a prescription. In order to understand the factors that influence different types of non-prudent use in EU Member States it was important to have an overview of the use of antibiotics in general, and the use of antibiotics without a prescription in particular. Chapter 2 provides this overview. It consists of the following elements:

- a summary of existing data on antibiotic use in the EU Member States from the European Antimicrobial Resistance Surveillance Network and the last two Eurobarometer surveys on the use of antibiotics^{8 13};
- a literature review of the prevalence of the use of antibiotics without a prescription.

Based upon the results in this chapter, seven Member States were selected for further in-depth analyses (Chapter 4) and country-dialogue meetings. Here, policy options these Member States could use to reduce the non-prudent use of antibiotics were discussed with policymakers and other relevant stakeholders (Chapter 6) ^(ⁿ).

Chapter 3: Explaining differences in the non-prescription use of antibiotics across the EU (*objectives 1/2*)

Chapter 3 provides insight into the factors that drive the use of antibiotics without a prescription. The following methods were used:

- a literature review of the determinants on the population, HCP and healthcare-system levels of the use of antibiotics without a prescription;
- an analysis of the 2013 Eurobarometer survey — these data enabled us to study the determinants for all 28 EU Member States in one analysis;
- an online survey among ministries of health/national experts to describe the differences in policies taken by Member States on a healthcare-system level to enhance the prudent use of antibiotics.

Chapter 4: The use of antibiotics without a prescription in seven EU Member States (*objective 1*)

In some Member States the level of antibiotic use without a prescription is higher than in others. In Chapter 2, seven Member States were selected that have a relatively high level of non-prescription use of antibiotics (Cyprus, Estonia, Greece, Hungary, Italy, Romania and Spain). For these seven Member States, more detailed insight into the nature of their antibiotic use was obtained through surveys where patients who used antibiotics without a prescription were interviewed, along with GPs and pharmacists.

Chapter 5: Good practices in the EU (*objective 3*)

Documenting good practices aimed at reducing the non-prudent use of antibiotics was another major aim of the ARNA project. The following methods were used to collect information on good practices:

- a literature review of good practices such as policy measures or interventions;

^(ⁿ) For the country-dialogue meetings six out of these seven Member States were selected.



- an online survey among ministries of health/national experts (see also Chapter 3) to collect information on measures and interventions not described in the literature.

Chapter 6: Expert opinions and a consensus statement on policy options to reduce the use in the EU of antibiotics without a prescription*(objective 4)*

Chapter 6 is the first of three chapters that focus on the development of policy options for more prudent use of antibiotics. It describes the results of a meeting with a group of 20 experts from nine EU Member States and two non-EU countries. The experts reviewed and discussed interventions that Member States could potentially use to reduce the non-prudent use of antibiotics. The results from this expert meeting were used as important input for meetings in the seven selected Member States, showing a relatively high level of antibiotic use without a prescription (see chapter 2).

Chapter 7: Towards approaches to enhance more prudent use in six EU Member States *(objective 4)*

As a part of the ARNA project, country-dialogue meetings were held in six of the seven Member States on which an in-depth analysis was performed — see Chapter 4 (Cyprus, Greece, Hungary, Italy, Romania and Spain)^(°). These meetings were organised using local people participating in decision-making about the strategy and taking a lead in the selection of the priorities to be pursued in their respective Member States. The participants were representatives of all relevant stakeholders who were invited by the local organiser, thus ensuring a bottom-up approach. The ARNA team supported the local organisers by providing data, part of which were specific to their Member State, from the ARNA study (Chapters 2 to 4) and also suggestions for policies that resulted from the literature review (Chapter 5) and the expert meeting (Chapter 6).

Chapter 8: Consensus statement on the prudent use of antibiotics *(objective 4)*

An international conference was held to discuss the results of the project and to conclude the ARNA project with an overview of actions. Sixty participants representing 21 Member States attended. The main conclusions and recommendations were summarised in the ARNA Utrecht conference statement on the prudent use of antibiotics, which is included in Chapter 8.

Chapter 9: Conclusion and discussion on the use of antibiotics without a prescription

The final chapter draws the overall conclusions of the ARNA project regarding the use of antibiotics without a prescription and discusses the findings.

^(°) There was no country-dialogue meeting held in Estonia as there were far fewer problems with the use of non-prescribed antibiotics than was anticipated.



2. The use of antibiotics in the EU

Main findings

- Large variations in antibiotic use are observed within the EU, in use both with and without a prescription. There is a positive, but moderate, association between the amount of prescription use and the amount of non-prescription use of antibiotics at the country level.
- The Netherlands is the Member State with lowest antibiotic use with a prescription (in 2014); Greece has the highest use.
- In the Eurobarometer surveys (2013, 2016), Greece, Romania and Cyprus are the three Member States where patients most frequently report the use of antibiotics without a prescription. Other Member States with high levels of antibiotic use without a prescription include Italy, Lithuania, Malta and Spain (results from the literature).
- Buying OTC from a pharmacy is the prevailing source of obtaining an antibiotic without a prescription, followed by the use of pills left over when a course was not completed.
- Greek and Spanish studies show that the majority of pharmacists are willing to sell antibiotics OTC.
- Non-prescription use of antibiotics most frequently occurs when treating upper or lower respiratory tract infections.
- Although OTC selling through the internet is a much debated topic, no EU studies were found that addressed this topic.

2.1. Introduction

A major aim of the ARNA project was to assess the non-prudent use of antibiotics in the EU and to identify factors that drive the sales and the non-prudent use of antibiotics obtained without a prescription. Non-prescription use of antibiotics occurs in various ways, such as OTC sales without a prescription, the use of pills left over when a course was not completed or antibiotics obtained through the internet.⁶ In order to understand the factors that influence different types of non-prudent use in EU Member States (see Chapters 3 and 4), it is important to have an overview of the use of antibiotics in general and the use of non-prescription antibiotics in particular.

In recent years, numerous data have repeatedly been collected on antibiotic use in the EU, for example through the ECDC's ESAC-Net (outpatient consumption data) and the Eurobarometer survey. The Eurobarometer data include information on self-reported non-prescription use of antibiotics. The scientific literature is another source for information on non-prescription use of antibiotics. Thus, two different data sources were used to analyse and describe the use of antibiotics:

1. existing data on prescription and non-prescription use (Section 2.2);
2. scientific literature (Section 2.3).

The selection of Member States for the in-depth analysis in Chapter 4 was made based upon the figures in this chapter. This chapter thus sets the scene with regard to the frequency of antibiotic use across the EU as a basis for the chapters that follow.



2.2. Antibiotic consumption rates in the EU

2.2.1. Methods

The following databases were used to describe antibiotic consumption across the EU.

1. European Surveillance of Antimicrobial Consumption Network (ESAC-Net).
Data on the use of antibiotics in the community within the EU have been collected by the ECDC's ESAC-Net. These data are publicly available through the ECDC website ^(p). The data sources for ESAC-Net are national sales and reimbursement data, including information from national drug registries. It should be noted that Romania and Cyprus provided data including both the outpatient and the hospital sector. Spanish data included reimbursement data rather than whole sales data. This means that the use without a prescription and of other non-reimbursed courses of antibiotics in Spain was not included.

2. Eurobarometer survey data ^(q).
Eurobarometer data available to the public were retrieved through Gesis.² These included self-reported data collected by a questionnaire. The retained variables included those relating to 'reported actual self-medication with antibiotics during the last year'. The Eurobarometer survey has run since the 1970s. The mission of Eurobarometer is to monitor public opinion in the EU. Each year a survey is made of citizens of EU Member States, and as such the Eurobarometer constitutes a repeated cross-sectional design. Each year a multistage, random sample is taken. Firstly, a random selection of sampling points or areas is taken after stratification for the type of area (metropolitan, urban and rural areas) ^(r). Next, a cluster of addresses is selected from an area chosen using standard random route procedures, beginning with an initial randomly selected address. Finally, one member from each of the households living at these addresses is selected by a random procedure (e.g. the first-birthday method). Only one person is interviewed in each household. Questionnaires are developed in English and French and translated into the other relevant languages using the principle of back-translation by independent translators. Interviews take place at the respondents' homes. The Eurobarometer studies are run and coordinated by TNS opinion[®].

There are special topics in addition to the standard questionnaire modules in the Eurobarometer. One of these special topics is AMR. Data about AMR were collected in 2009, 2013 and 2016. In this report, data from 2013 and 2016 are used. Data were collected through interviews in all 28 Member States. Table 2.1 shows the number of respondents per Member State in 2013 and 2016. In this chapter, data are included from questions on whether or not the respondent used antibiotics, and if so whether this was on prescription or not. In case a respondent used an antibiotic without a prescription, the source from which this antibiotic was obtained was asked for.

^(p) <http://ecdc.europa.eu/en/eaad/antibiotics-get-informed/antibiotics-resistance-consumption/Pages/data-reports.aspx>

^(q) <https://dbk.gesis.org/dbksearch/SDesc2.asp?ll=10¬abs=&af=&nf=&search=&search2=&db=E&no=5852>

^(r) <http://www.gesis.org/eurobarometer-data-service/survey-series/standard-special-eb/sampling-and-fieldwork/>



Table 2.1. Number of respondents participating in the Eurobarometer survey on AMR in 2013 and 2016 by EU Member State (absolute numbers).
(Source: Eurobarometer surveys.^{8 13})

Country	Total number of respondents in 2013	Total number of respondents in 2016
Austria	1 034	1 011
Belgium	1 006	1 007
Bulgaria	1 025	1 040
Croatia	1 000	1 057
Cyprus	506	500
Czech Republic	1 026	1 047
Denmark	1 010	1 010
Estonia	1 008	1 004
Finland	1 003	1 008
France	1 053	1 045
Germany	1 505	1 563
Greece	1 002	1 008
Hungary	1 033	1 058
Ireland	1 001	1 016
Italy	1 025	1 033
Latvia	1 018	1 032
Lithuania	1 023	998
Luxembourg	502	501
Malta	500	501
Netherlands	1 013	1 041
Poland	1 000	1 015
Portugal	1 007	1 010
Romania	1 053	1 014
Slovakia	1 000	1 038
Slovenia	1 005	994
Spain	1 008	1 053
Sweden	1 000	1 035
United Kingdom	1 314	1 330

Data analyses

ESAC-Net data

The data on antibiotic consumption in the community are presented for 2014 ⁽⁵⁾. Two indicators are presented.

- The number of DDD per 1 000 inhabitants per day based on the anatomical therapeutic chemical (ATC) classification and the DDD measurement unit ^(t) (Figure 2.1). This indicator takes into account the number of antibiotic doses consumed and its potential ecological effect on the development of AMR.
- The number of packages per 1 000 inhabitants dispensed per day according to the ATC classification (Figure 2.2). This indicator does not take into account dosage information. It is a good proxy for the number of antibiotic treatment courses.

Eurobarometer data

Descriptive analyses as reported in the 2013 and 2016 Eurobarometer reports on AMR are presented.^{8 21} These include:

- the percentage of respondents using an antibiotic in 2013 and 2016;
- the percentage of respondents using the antibiotic with or without a prescription in 2013 and 2016;
- the percentage of respondents using non-prescription oral antibiotics in 2013 and 2016, divided by the source from which the antibiotic was obtained.

Combined analysis of ESAC-net and Eurobarometer data

Outpatient antibiotic consumption data, expressed in DDD per 1 000 inhabitants per day, for 2013 were linked to the 2013 Eurobarometer data. The average proportion (percentage) of respondents taking an antibiotic without a prescription (Eurobarometer data) was calculated as the sum of the number of respondents who reported having obtained antibiotics as follows: (1) without a prescription from a pharmacy; (2) without a prescription from elsewhere; (3) left over from a previous course; or (4) do not remember spontaneously. This is then divided by the total number of respondents who have taken an oral antibiotic during the last 12 months. This ratio is expressed as a percentage (per 100 respondents) by country.

2.2.2. Antibiotic consumption

Antibiotic consumption in the community: ESAC-Net data

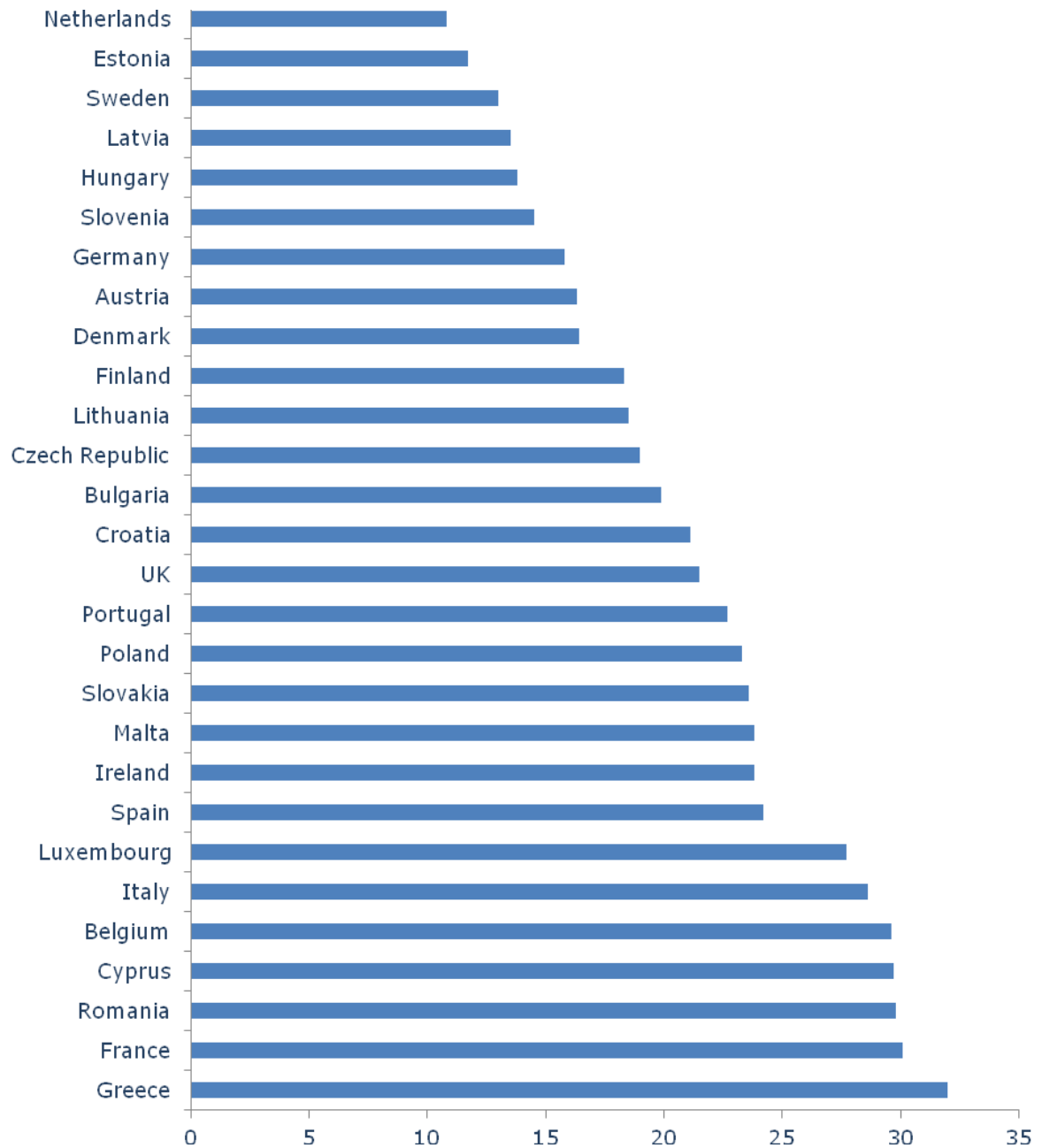
DDD/1 000 inhabitants/day

The ESAC data include antibiotic consumption in the community. Figure 2.1 shows that the Netherlands had the lowest consumption in 2014 (10.6 DDD/1 000 inhabitants/day) and Greece the highest (34.1 DDD/1 000 inhabitants/day). This indicates a 3.2-fold difference between the Netherlands and Greece. The five Member States with the highest levels of outpatient antibiotic consumption includes Greece, Romania, France, Belgium and Italy.

⁽⁵⁾ <http://ecdc.europa.eu/en/eaad/antibiotics-get-informed/antibiotics-resistance-consumption/Pages/data-reports.aspx>

^(t) ATC classification system: Guidelines for ATC classification and DDD assignment. <http://www.whocc.no/>

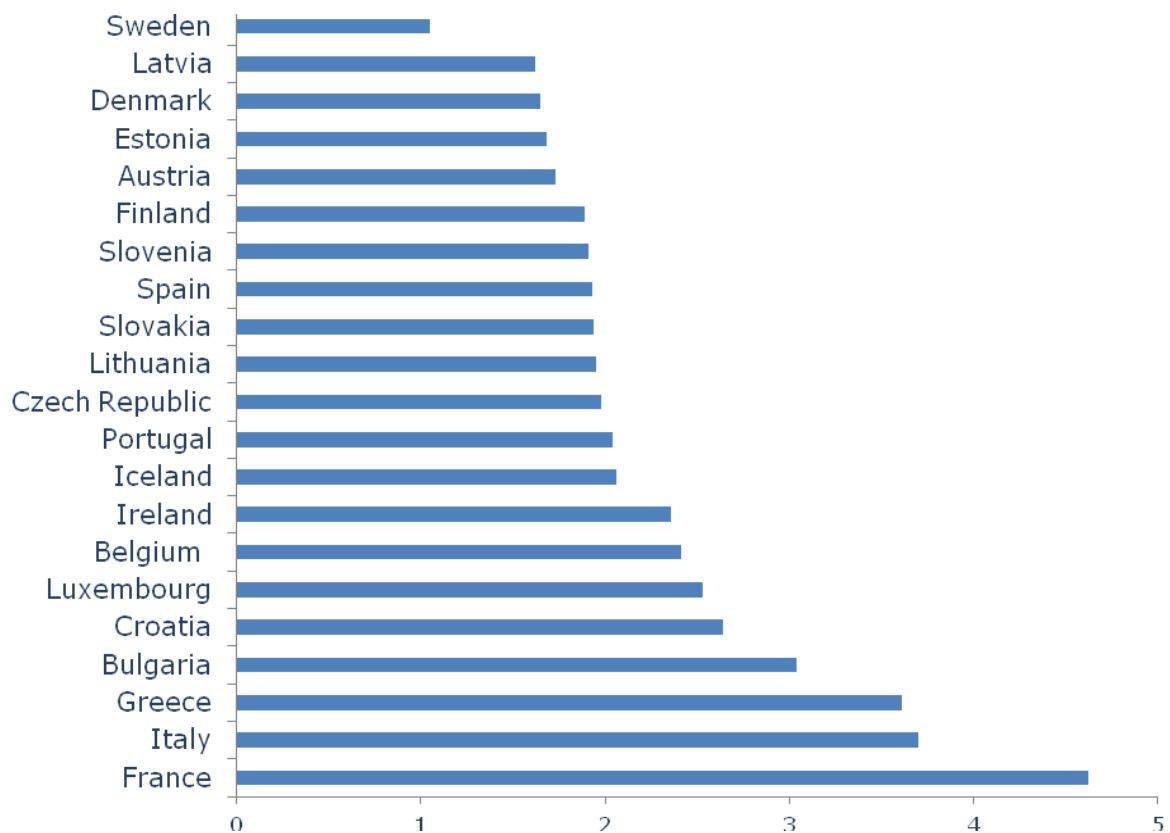
Figure 2.1. Consumption of antibiotics for systemic use in the community by antibiotic group in EU Member States, 2014 (expressed in DDD per 1 000 inhabitants per day). (Source: ESAC-Net.)



Packages per 1 000 inhabitants per day

The EU mean of the number of packages dispensed per day amounts to 3.0 packages per 1 000 inhabitants (⁴). The median (2.0 packages/1 000 inhabitants/day) is much lower than the mean, indicating that there are a few countries where the use is substantially above the arithmetic mean of the European Union. Figure 2.2 shows that the three Member States where the most packages are dispensed include France (4.6 packages/1 000 inhabitants/day), Italy (3.7 packages/1 000 inhabitants/day) and Greece (3.6 packages/1 000 inhabitants/day).

Figure 2.2. Antibiotic consumption in the community for systemic use in 21 EU Member States, 2014 (expressed in *packages per 1 000 inhabitants per day*). (Source: ESAC-Net.)



⁽⁴⁾ Romania and Cyprus reported data for the total care sector and could, therefore, not report data on the package level (in the hospital sector consumption is often reported by units because of its parenteral use (e.g. vials). Nor could other EU Member States provide data on this indicator.

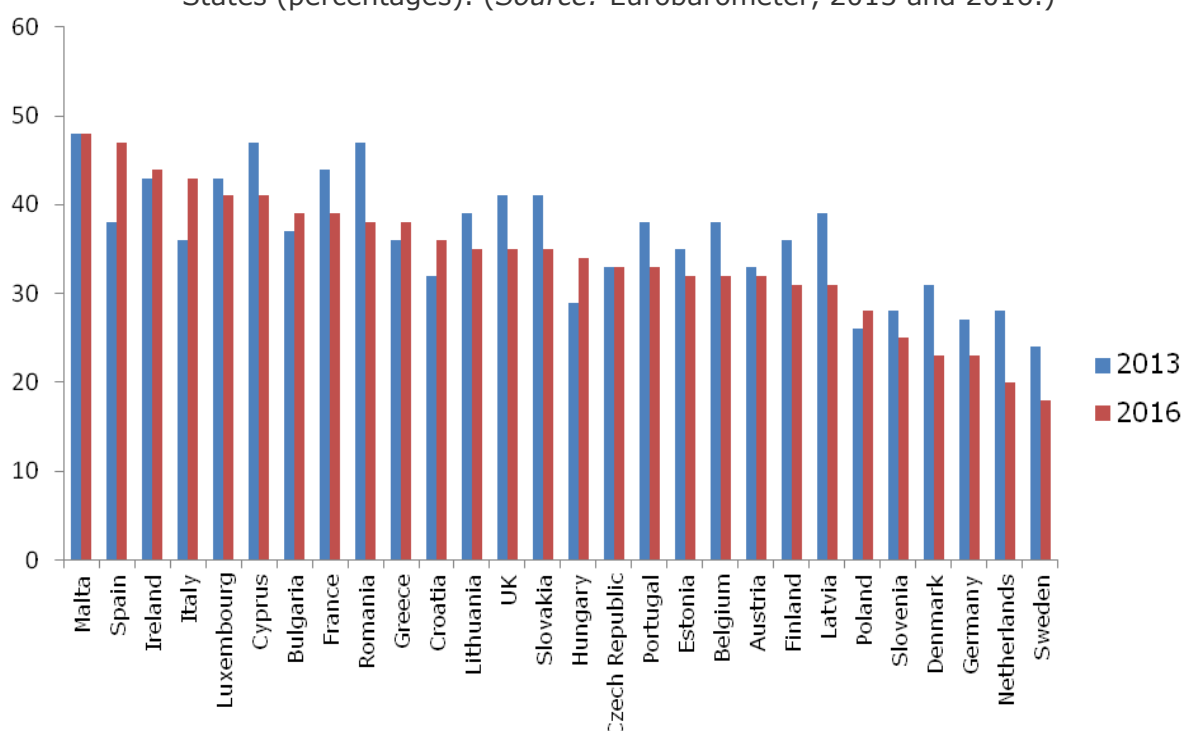
Eurobarometer data

Respondents who used an antibiotic

Both in 2013 and 2016, about 35 % of EU inhabitants who were interviewed reported using at least one oral antibiotic during the last 12 months.⁸ The observed variation between EU Member States is considerable, reflecting the same variation as shown with the outpatient antibiotic consumption data from ESAC-Net. In 2016, a 2.7-fold difference in use was found between Sweden, the Member State with the lowest proportion of people who reported taking at least one antibiotic (18 %), and Malta, with the highest proportion of people (48 %) (Figure 2.3). This difference is higher than in 2013 when a twofold difference between Malta (highest use, 48 %) and Sweden (lowest use, 24 %) was observed.

The percentage of respondents who reported using an antibiotic in 2016 was lower compared to 2013 in 15 Member States: Belgium, Cyprus, Denmark, Finland, France, Germany, Latvia, Lithuania, Luxembourg, the Netherlands, Portugal, Romania, Slovenia, Sweden and the United Kingdom. However, there are also six Member States for which an increase of at least 2 % in the number of respondents who reported having used an antibiotic was observed: Bulgaria, Greece, Hungary, Italy, Poland and Spain. The largest increase was observed for Spain (+ 9 %), Italy (+ 7 %) and Hungary (+ 5 %). Decreases in the number of respondents who reported having used an antibiotic were, for example, found for Romania (– 9 %) and Cyprus (– 6 %).

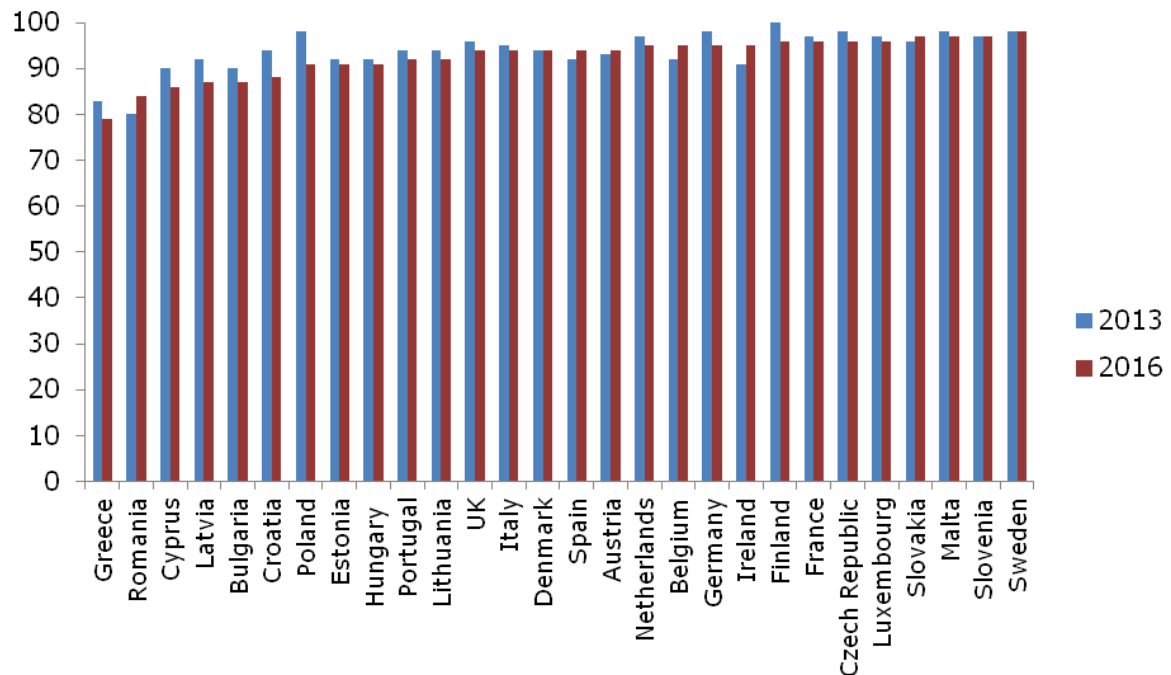
Figure 2.3. Percentage of respondents who reported having taken at least one antibiotic over the last 12 months in 2013 and 2016 for the EU Member States (percentages). (Source: Eurobarometer, 2013 and 2016.)



Respondents who used prescribed antibiotics

The Eurobarometer data also include self-reported information on patients' sources of antibiotics. Figure 2.4 shows the percentage of patients who reported that the antibiotics that they took were prescribed, expressed as a percentage of all those who used an antibiotic (^v). In all EU Member States, the vast majority of antibiotics were obtained with a prescription. And yet, differences between Member States can still be observed. In Greece, 79 % of respondents reported that the antibiotics used in 2016 were prescribed, while in Sweden this figure was 98 % in both 2013 and 2016. Member States other than Greece with relatively low levels of prescribed antibiotics included Romania, Cyprus and Latvia. There was a slight decrease in the percentage of respondents who had obtained antibiotics without a prescription. In the 2016 Eurobarometer report it was stated that these changes were likely caused by a slight change in the way the question was asked (^w).

Figure 2.4. Percentage of users of an antibiotic over the last 12 months who reported having obtained their medication with a prescription in 2013 and 2016 for the 28 EU Member States (percentages). (Source: Eurobarometer, 2013 and 2016.)



(^v) Figures on non-prescription use can be found in the next section.

(^w) Literal text from report: 'In the 2016 survey, the order of the first four response options was rotated, whereas in 2013 the order was kept constant. This is likely to have affected the proportions giving individual answers. When examining changes since 2013, the analysis therefore focuses on change for combined responses, based on two groupings: "from a medical practitioner" (either "from a medical prescription" or "administered by a medical practitioner") and "not from a medical practitioner" (all other sources).'



2.2.3. Use of antibiotics without a prescription

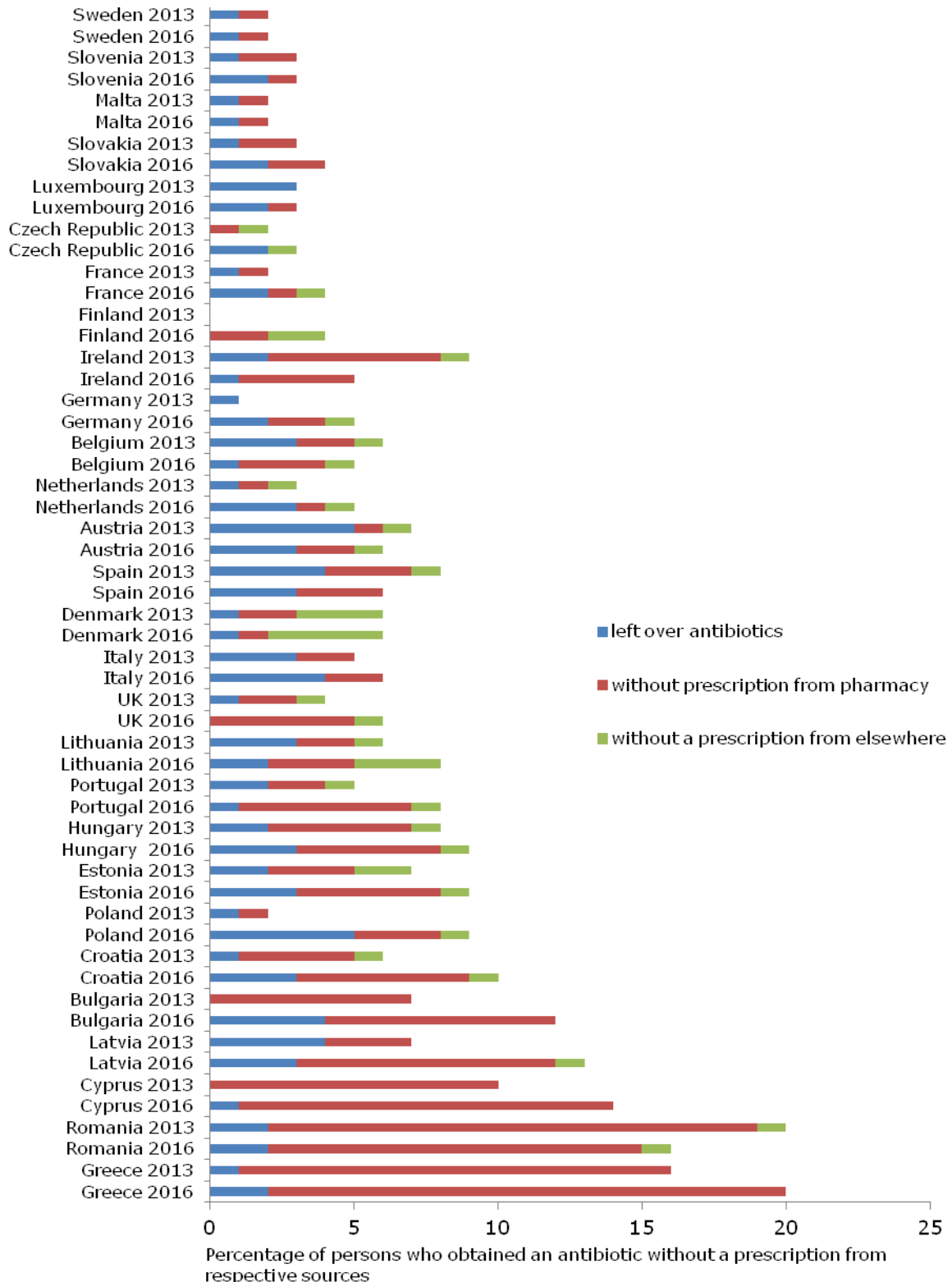
The Eurobarometer provides additional information on the use of antibiotics without a medical prescription (*). There is a wide variation between Member States in the self-reported use of non-prescription antibiotics. The highest use can be found in Romania (in 2013, 20 % of all users of an antibiotic in the last 12 months used non-prescription antibiotics; in 2016, 16 %) and Greece (in 2013, 16 %; in 2016, 20 %). For the following Member States an increase in the use of antibiotics without a prescription between 2013 and 2016 was observed: Bulgaria, Cyprus, Croatia, Finland, Germany, Latvia, Lithuania, and Poland.⁸

Both the 2013 and 2016 Eurobarometer surveys also contain self-reported information about how non-prescription oral antibiotics were obtained, firstly from a pharmacy, secondly from elsewhere or thirdly where the respondent had some pills left over from a previous course (see Figure 2.5). In most Member States with a relatively high level of use of antibiotics without a prescription, the prevailing source for obtaining antibiotics was the pharmacy. This group of Member States includes Bulgaria, Croatia, Cyprus, Estonia, Greece, Hungary, Ireland (2013), Latvia (2016), Portugal (2016) and Romania. This implies that allowing OTC sales or not enforcing the law on OTC sales of antibiotics is a major driver for the use of antibiotics without a prescription. Also, in the United Kingdom, although it has a lower use of antibiotics without a prescription, OTC sales are the main source. Although the Eurobarometer asks for oral antibiotics, respondents who used, for example, eye drops, which are freely available in a number of Member States, such as the United Kingdom, may have answered they used an antibiotic without a prescription. It is not clear to what extent respondents could have included topical use of antibiotics, which could have distorted the results obtained. This may apply to the results from Denmark, where a high proportion of non-prescription use obtained without a prescription is classified as 'from elsewhere'. Also, in Lithuania the proportion of antibiotics obtained without a prescription from elsewhere is higher than in other Member States. As the Eurobarometer reports do not specify what these other sources are, it is hard to elaborate on the reasons why Denmark and Lithuania have higher percentages than other Member States.

There are also Member States where the use of leftover antibiotics contribute to the use of antibiotics without a prescription. A Member State with a relatively high use in 2013 where leftover antibiotics contributed more to the non-prescription of antibiotics is Spain. This is in line with data suggesting that fewer antibiotic treatments or prescriptions have been issued but at higher doses (see ESAC-Net results; the difference in the two indicators: number of DDD/1 000 inhabitants/day and the number of packages/1 000 inhabitants/day). These figures are also consistent with the possibility that Spanish patients often do not finish their antibiotic courses, resulting in antibiotic medication remaining that can be consumed at a later time. A similar pattern, where the use of leftover antibiotics is the prevailing source of non-prescription use, is also seen in Italy and several other Member States (e.g. Austria, Slovakia, the Netherlands).

(*) 2013 Eurobarometer data: <https://dbk.gesis.org>; http://ec.europa.eu/dgs/health_food-safety/amr/docs/eb445_amr_generalreport_en.pdf

Figure 2.5. Percentage of non-prescription oral antibiotics broken down by the means by which respondents obtained the antibiotic for the 28 EU Member States in 2013 and 2016 (percentage of all respondents who reported having used an oral antibiotic during the last 12 months). (Source: 2013 and 2016 Eurobarometer surveys.)



2.3. Comparison of prescription and non-prescription use

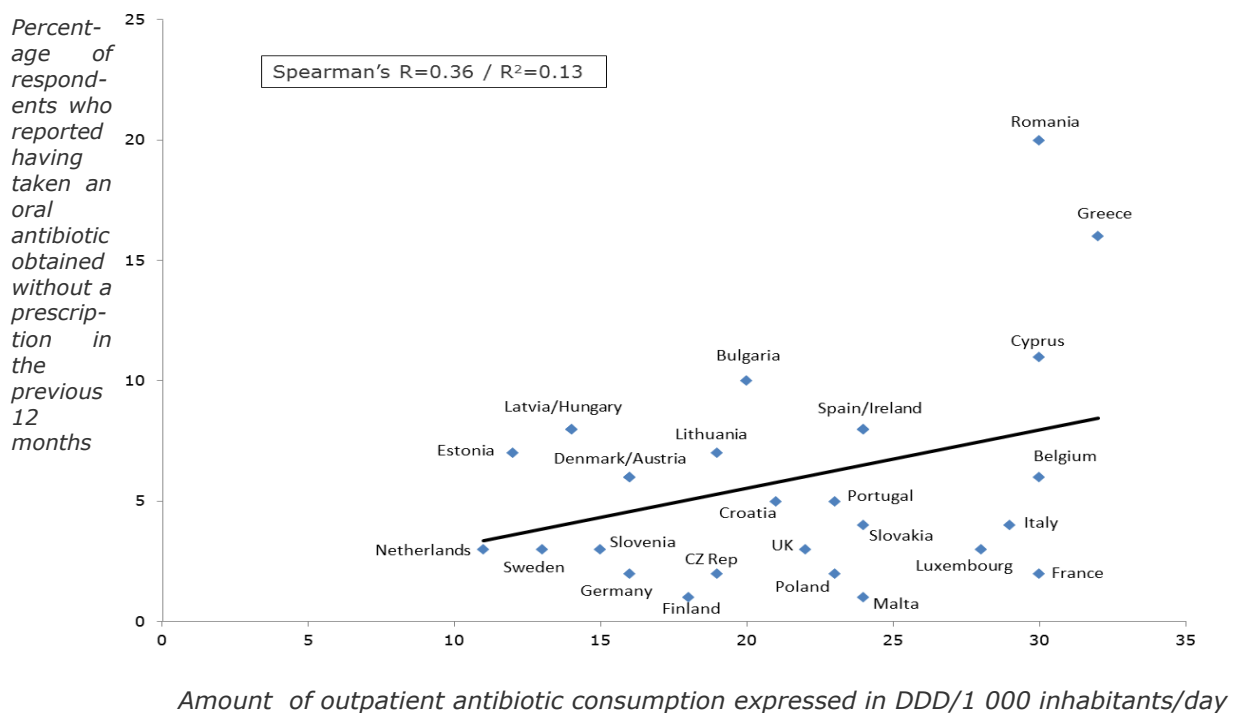
A comparison of the outpatient antibiotic consumption (ESAC-Net data) and the self-reported use of antibiotics without a prescription (Eurobarometer data)

A pertinent question concerns what relationships there may be between prescription use and non-prescription use of antibiotics. One possible assumption is that the use of non-prescription antibiotics might be higher in Member States with a low use of prescribed antibiotics because citizens might turn to other sources than a prescription. However, another assumption might be that in Member States where many antibiotics are prescribed there is a more positive attitude towards antibiotic use in general. This would then result in a high level of both prescription and non-prescription use. Knowledge of the patterns of antibiotic use in a country may therefore be relevant to developing policies to combat non-prudent use.

Figure 2.6 reports overall volumes of outpatient antibiotic consumption expressed in DDD/1 000 inhabitants/day for the year 2013 next to the percentage of respondents who reported the use of an antibiotic without a prescription for the same year (Eurobarometer data). The highest percentages of respondents who reported having used an antibiotic without a prescription during the last 12 months in relation to overall outpatient antibiotic consumption were observed for Greece (16 %) and Romania (20 %). Greece and Romania also belong to the group of Member States with higher volumes of outpatient antibiotic consumption (expressed in DDD/1 000 inhabitants/day; see Figures 2.1 and 2.6).

However, both in Member States with low volumes of outpatient antibiotic consumption (the Netherlands, Sweden, Slovenia) and in those with high volumes of outpatient antibiotic consumption (France, Luxembourg), there are fewer than 5 % of all antibiotic users who reported having used an antibiotic without a prescription in the previous 12 months. Further statistical analyses showed a positive linear relationship between the number of respondents who reported using an antibiotic without a prescription during the last 12 months (2013 Eurobarometer data) and the 2013 volumes of outpatient antibiotic consumption (ESAC-Net data, 2013). These analyses showed a correlation coefficient of $r = 0.36$ (Spearman's correlation: significant at $p < 0.05$) and an r -squared of 0.13 (Figure 2.6). This means that there is a positive association between the amount of prescription use and non-prescription use of antibiotics at the Member State level. However, the association is moderate.

Figure 2.6. Amount of outpatient antibiotic consumption expressed in DDD/1 000 inhabitants/day (source: 2013 ESAC-Net data) in relation to the percentage of respondents who reported having taken an oral antibiotic obtained without a prescription in the previous 12 months. (Source: 2013 Eurobarometer data.)



2.4. A literature survey of antibiotic use without a prescription

A literature survey was conducted to explore further the volume and nature of the use of antibiotics without a prescription both within the EU and in other Western countries. While the Eurobarometer data only include information on the use by patients, in the literature review other perspectives, such as that of the pharmacist, were explored as well.

2.4.1. Methods

Search strategy

A comprehensive literature search was conducted in the scientific electronic databases PubMed, Scopus and Embase for studies published from January 2000 to September 2014. There was no limitation on the language. In addition, the electronic searches were supplemented by manual searches of the reference lists and citation tracking of articles that were selected on the basis of their relevance (see below).

The search string included the following search terms and their equivalents: antibacterial agents, drug resistance or antibiotic; non-prescription, over-the-counter or self-medication; and Europe, Anglo-Saxon countries or other Western or European countries. Suitable search strategies were developed for Scopus and Embase, using adaptations of the PubMed search string. The following search terms were used for

exclusion of publications: animal use, plant and agricultural use, hospital use and other countries.

Relevant websites were searched in order to cover relevant grey literature including those of the ministries of health of EU Member States, national regulatory offices, public health institutes and EU websites. Search terms that were used included the following: self-medication, over-the-counter use, antibiotics and antimicrobial agents. Documents were searched for the 2000-2014 period. The search terms were translated into each Member State's national official language or languages.

Selection criteria

A publication was selected if it met all of the following criteria: (1) the publication has as one of its main subjects use of antibiotics without a prescription; (2) the publication addresses the volume and nature of use and/or determinants of OTC use of antibiotics (^y); (3) the publication addresses OTC use of antibiotics within the geographical context of at least one EU Member State or other Western, European or Anglo-Saxon country; (4) the publication is robust, in either a professional or scholarly manner, in that it is a scientifically peer-reviewed study or a publication from a government or professional association; and (5) the publication was published between 2000 and 2014. The following types of articles were excluded: any paper that focused on antibiotics in animals, antibiotics used for plant agriculture or antibiotics used in hospital settings; and papers about studies in other countries.

Data synthesis and analysis

The titles of the hits retrieved through the search were each screened by two authors (a combination of either DL, JP and LvD). This was followed by a screening of the remaining abstracts by the same authors. Disagreements were resolved by discussion between the two reviewers. Full texts were judged by one author (DL), who consulted one of the other authors (LvD) if there were doubts about whether or not to include a publication. One author (DL) then extracted data from the publications included and one other author (LvD) checked the data that were extracted. For each study included in the review (n= 59), the following general items of information were extracted from the papers: first author, year of publication, country, focus of the publication, population, sample size, antibiotics consumed, source of antibiotics, symptoms for which the drugs were used and volume of use.

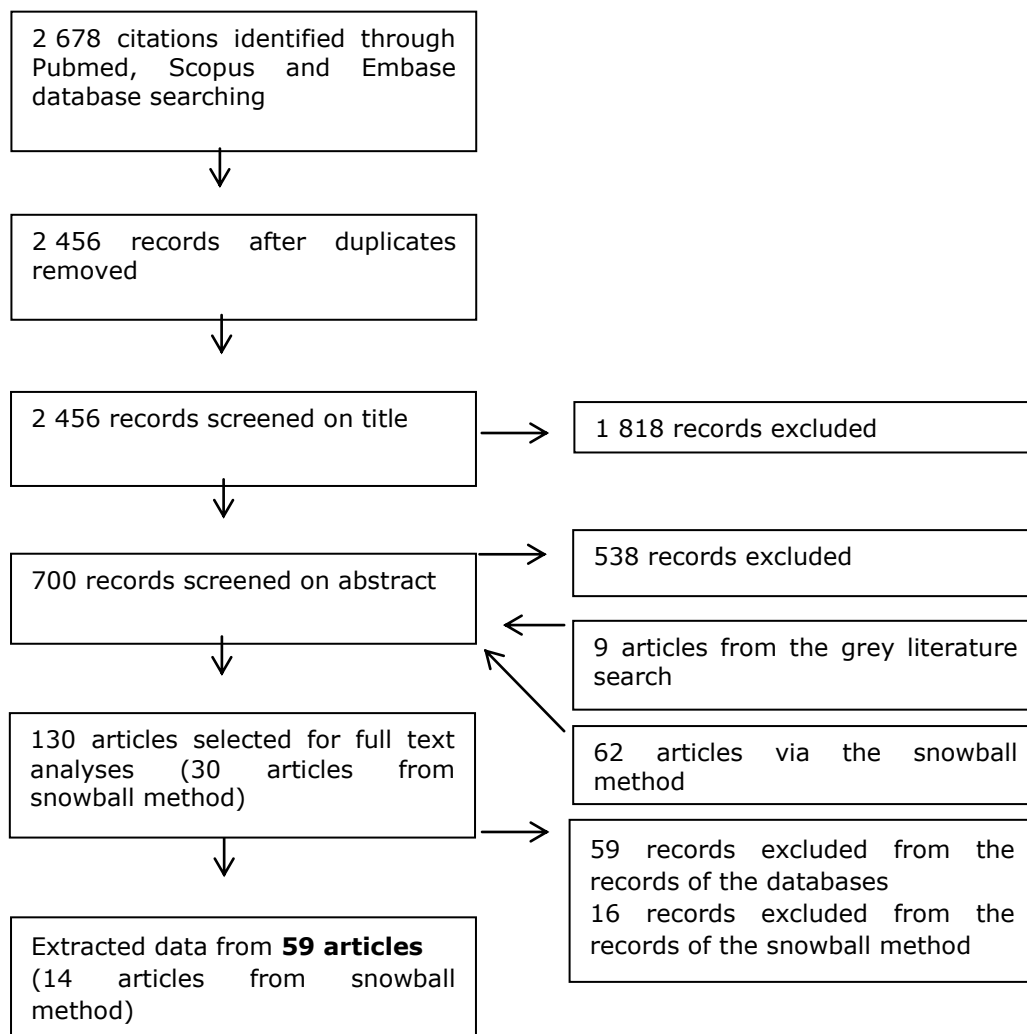
2.4.2. Search results and study characteristics

The search in the electronic databases resulted in 2 678 hits (1 624 hits in PubMed, 806 in Scopus, 248 in Embase). Of these, 2 456 hits were unique. Screening of titles resulted in a total of 638 potentially relevant articles. Subsequent screening of the corresponding abstracts yielded 100 abstracts that were potentially relevant for this study. From these 100 publications, the full texts were obtained. Finally, after reading the full text, 45 articles were included in the review. By using the snowball method, 30 additional articles were included for full-text analyses. Of these, 14 were included in this review, which resulted in a total of 59 articles (Figure 2.7). These publications were published in 42 different journals.

(^y) A combined search was performed for the literature review on the volume and nature of non-prescription use (this chapter) and for the literature review on determinants of off-label use (Chapter 3).

The grey literature search resulted in nine possibly relevant documents. The documents were from: Germany (<http://www.rki.de>), Italy (<http://www.agenziafarmaco.it>), Spain (<http://www.msc.es>), Sweden (<http://www.folkhalsomyndigheten.se/about-folkhalsomyndigheten-the-public-health-agency-of-sweden>), the United Kingdom (<http://dh.gov.uk>) and the United States (<http://www.cdc.gov>). However, after translating and reading the texts, none of the articles were included in the literature review as they did not provide any usable information about self-medication with antibiotics.

Figure 2.7. Flow diagram of the study selection process.



Countries and perspective

Table 2.2 shows in which countries the studies included were performed. Within the EU, most studies were performed in Spain ($n = 12$), followed by Greece ($n = 6$). Nine studies included multiple countries, mostly spread across Europe. Outside of the EU, most studies were found from the United States ($n = 13$). Most studies used the patient perspective, meaning that data were collected on patient behaviour and perceptions on the use of antibiotics without a prescription, followed by studies from the pharmacist's perspective.

Table 2.2. Countries in which studies were performed and the perspectives which were used; literature review regarding the volume and nature of antibiotic use without a prescription (n = 59 publications).

Country	Patient's perspective (n = 47)	Pharmacist's perspective (n = 10)	Other (n = 2)	Total
Croatia	1			1
Czech Republic	1			1
Greece	4	2		6
Denmark	1			1
Hungary		1	1	2
Italy	2			2
Lithuania	1			1
Malta	1			1
Poland	2			2
Romania	2			2
Spain	7	5		12
Sweden	1			1
United Kingdom	2			2
Multiple Western countries	8			8
<i>Other countries</i>				
Former Yugoslav Republic of Macedonia	2			1
United States of America	11	1	1	13
Russia	1			1
New Zealand		1		1
Serbia		1		1

Design

The vast majority of the 47 articles that analysed data from the patient's perspective used a quantitative cross-sectional design. Three articles used a qualitative design. The 10 studies from a pharmacist's/pharmacy's perspective used a variety of methods: cross-sectional studies, semi-structured interviews and prospective studies to examine how easy it is to obtain antibiotics at a pharmacy ⁽²⁾.

Study population

Table 2.3 describes the patient populations in the included studies. It shows that most studies focused on adults (43 out of 47 studies). Most studies focused on the general adult population. However, a substantial number of studies included a specific group, such as immigrants (n = 9). These were mainly studies on immigrants to the United States from Latin American countries. Other studies focused on visitors to the pharmacy or female heads of households. Three studies included children and another seven chose parents of children — in different age categories — as their study population. The studies from the pharmacist perspective all included community pharmacists (data not in table). The studies clearly included a wide variety of study populations, making it hard to compare results as they refer to different populations in different contexts.

⁽²⁾ Two studies used a different perspective (the internet).

Table 2.3. Study populations' characteristics in 47 studies with a patient perspective included in the literature review regarding the volume and nature of antibiotic use without a prescription.

Adults	Number of studies*
Total,	43**
including the following specific groups:	
migrants	9
visitors of pharmacies who wanted an antibiotic	3
housewives/female heads of family	2
students	2
other specific groups	8
Children and their parents	Number of studies
Total children themselves,	3
including the following categories:	
10-17 years	1
visiting emergency department	1
unknown	1
Total parents of children,	7
including the following age categories:	
0-4 years	1
0-12 years	2
0-16 years	1
0-18 years	1
5-18 years	1
15-17 years	1

* Some studies included both adults and children.

** Some studies were on adults in general, other studies included specific patient groups.

Outcome measures

The use of antibiotics without a prescription can be measured in different ways. Table 2.4 shows that, out of the 47 studies that used a patient perspective, 36 studies measured the use of antibiotics without a prescription. Nine studies had the intended use of antibiotics as one of the outcome measures. Eight studies measured the storage of medication left over after a course of treatment. The period of time used in measuring the use of antibiotics without a prescription varied across studies (see Table 2.5, next section). Reports over the past 12 months are most often used, but some studies have asked patients to report whether they have ever used an antibiotic without a prescription.

Six studies from the pharmacist's perspective looked at the estimated dispensing of antibiotics, while one focused on intended dispensing. Three studies had the response of the pharmacist to the request of an actor for an antibiotic without a prescription as an outcome measure.

Table 2.4. Outcome measures in studies included in the literature review on the volume and nature of antibiotic use without a prescription (n = 59 studies).

Patient perspective	Number of studies*
Use without a prescription, general	36
Intended self-medication	9
Storage of antibiotics	8
Pharmacist perspective	Number of studies
Estimated dispensing of antibiotics without a prescription	6
Response to request from an actor for an antibiotic without a prescription	3
Intention to dispense an antibiotic without a prescription	1

* Some studies included more than one outcome measure.

There should be caveats about the interpretation of the results due to the different ways of measuring and defining non-prescription use across the studies included. Any interpretation should keep in mind that they are dependent on the study design and the number of respondents that participated in the study.

2.4.3. Patient perspective

Use of antibiotics without a prescription

Table 2.5 summarises the findings from studies that used a patient perspective. Results from qualitative studies and studies where requests for antibiotics in a pharmacy were measured, rather than actual use, were excluded from the table. Where studies included more countries and reported information on the country level, data for individual countries are included in Table 2.5.

Studies in which patients were asked to report whether they have ever used antibiotics without a prescription generally show a higher prevalence of non-prescription use compared to studies in which patients reported over a certain period of time, usually the past 12 months^(aa). The highest percentage of patients who had ever used antibiotics without a prescription was found in a study in Greece (75 % of adults),²² followed by Lithuania (62.4 % of adults).¹⁶ Austria and Belgium are the countries in western Europe where the highest percentages of patients who had ever used an antibiotic without a prescription were reported, 18.8 % and 18.1 % respectively. This is lower than in other countries that were included in the same study such as Croatia, Czech Republic, Italy and Malta.¹⁶

Lower percentages were found in studies that report use of antibiotics without a prescription over the last 12 months. The study that found the highest prevalence is from Greece (44.6 % of adults),²³ followed by Italy (32.7 % of parents of children aged 5-18 years)²⁴ and Lithuania.²⁵ Here again, studies in western and northern Europe reported lower percentages of patients who used antibiotics without a prescription. The highest percentage was found for the United Kingdom (12 %).¹⁷ This might be explained by the fact that in the United Kingdom, some topical antibiotics are available OTC.

(^{aa}) For sentences that introduce paragraphs, references can be found in the text that follows and in tables.



Intention to self-medicate with an antibiotic

In addition to studies on the actual use of antibiotics without a prescription, there are also studies that measured patients' intention to self-medicate with an antibiotic in the future. The findings are in line with the results for actual use. The highest percentages of patients who have the intention to self-medicate are found in studies in Lithuania (45 %),²⁵ Romania (43.1 %),⁶ Slovakia (32.4 %)⁶ and Spain (31.4 %).⁶ Compared to other countries in the western part of Europe, studies in Ireland and the United Kingdom reported a relatively high percentage of patients who intend to self-medicate.⁶

Storage of antibiotics

Several studies made an inventory of the number of households that stored antibiotics obtained without a prescription. Although the percentages varied across studies, a considerable number of households do store antibiotics. A study in Italy, for example, found that 57 % of all respondents stored antibiotics. In two studies in Spain, 37 % and 50 % of respondents indicated that they have stored antibiotics.^{6 26} High levels of storage of antibiotics were also found in Croatia (46 %)²⁷, Greece (40 %)²⁸, Malta (35 %)²⁹ and Romania (32.1 %).⁶ A few studies compared the use of antibiotics without a prescription among patients who stored antibiotics at home with those who did not. As can be expected, use is higher among patients who have stored antibiotics at home.

Requesting antibiotics in pharmacies

Three studies looked at the number of requests made for antibiotics without a prescription in community pharmacies in Spain. One study found that 23.8 % of all requests for antibiotics were for a course without a prescription.³⁰ The two other studies found higher percentages: 53.5 % and 57.5 % respectively.^{31 32}

**Table 2.5.** Results on use, intention to use and storage of antibiotics gained without a prescription; literature review regarding the volume and nature of antibiotic use without a prescription (n = 59 studies).

Country (1st author)	Year	Participants	Time period	Storage	Intention to use	Use
Austria (Grigoryan) ⁶	2006	442 adults	Past 12 months	5.2	7.3	0.9
Austria (Grigoryan) ¹⁶	2008	101 adults	Ever			18.8
Belgium (Grigoryan)	2006	1 734 adults	Past 12 months	12.3	8.0	0.9
Belgium (Grigoryan) ¹⁶	2008	99 adults	Ever			18.1
Croatia (Aljinović-Vučić) ²⁷	2005	287 medical students	For antibiotics stored in home	46		37
Croatia (Grigoryan) ⁶	2006	615 adults	Last 12 months	21.2	20.5	3.1
Croatia (Grigoryan) ¹⁶	2008	96 adults	Ever			37.5
Czech Republic (Andrajati) ³³	2005	1 169 adults	Last 12 months	7.5	16.9	0.5/1.6*
Czech Republic (Grigoryan) ⁶	2006	1 169 adults	Last 12 months	6.4	17.9	0.7
Czech Republic (Grigoryan) ¹⁶	2008	100 adults	Ever			21
Denmark (Muscat) ³⁴	2006	1 881 adults	Past 12 months	8.0	13	3.5
Denmark (Grigoryan) ⁶	2006	1 881 adults	Past 12 months	8.4	13.2	7
Greece (Mitsi) ²²	2005	173 adults	Ever			75
Greece (Papaioannidou) ²⁸	2009	140 adults		40		25
Greece (Skliros) ²³	2010	1 130 adults	Past 12 months	27		44.6
Greece (Tsiligianni) ³⁵	2012	40 families (85 persons)	Current storage	17		0.7
Ireland (Grigoryan) ⁶	2006	793 adults	Past 12 months	10.0	15.0	1.4
Italy (Di Matteo) ³⁶	2005	213 adults	Past 12 months	57	24.3	6
Italy (Grigoryan) ⁶	2006	213 adults	Past 12 months	56.9	24.3	6.2
Italy (Grigoryan) ¹⁶	2008	80 adults	Ever			21.3
Italy (Napolitano) ³⁷	2013	419 parents of children 5-18 y	Past 12 months	29	22.7**	32.7
Lithuania (Berzanskyte) ²⁵	2006	746 adults	Past 12 months		45	22
Lithuania (Grigoryan) ⁶	2006	747 adults	Past 12 months	33.3	44.9	21
Lithuania (Grigoryan) ¹⁶	2008	101 adults	Ever			62.4
Luxembourg (Grigoryan) ⁶	2006	675 adults	Past 12 months	13.2	8.3	0.9
Malta (Borg) ³⁸	2002	175 adults	Ever	35		19/11*
Malta (Grigoryan) ⁶	2006	541 adults	Past 12 months	26.9	22.8	5.6
Malta (Grigoryan) ¹⁶	2008	99 adults	Ever			29.3
Netherlands (Grigoryan) ⁶	2006	1 634 adults	Past 12 months	3.6	8.5	0.1
Netherlands (Grigoryan) ¹⁶	2008	116 adults	Ever			2.5
Poland (Olczak) ³⁹	2006	938 adults				13
Poland (Grigoryan) ⁶	2006	935 adults	Past 12 months	13.7	11.5	3.3
Poland (Muras) ⁴⁰	2013	891 adults	Ever			41
Romania (Grigoryan) ⁶	2006	430 adults	Past 12 months	32.1	43.1	19.8
Romania (Damian) ⁴¹	2014	281 students	Past 6 months			44
Slovakia (Grigoryan) ⁶	2006	546 adults	Past 12 months	30.2	32.4	4.2
Slovenia (Grigoryan) ⁶	2008	1 134 adults	Past 12 months	18.3	28.0	1.7
Spain (Gonzales) ²⁶	2006	1 000 female head household	Current	37		
Spain (Grigoryan) ⁶	2006	204 adults		50.0	31.4	15.2
Spain (Väänänen) ⁴²	2006	533 adults	Past 6 months			11.5
Spain (Carrasco-Garrido) ⁴³	2008	19 514 adults	2 weeks			< 1 %
Spain (Mira) ⁴⁴	2014	1 526 adults	Not clear			6
Sweden (Svensson) ⁴⁵	2004	690 adults	Past 12 months	4	11	< 1 %
Sweden (Grigoryan) ⁶	2006	704 adults	Past 12 months	4.3	11.8	0.4 %
Sweden (Grigoryan) ¹⁶	2008	103 adults	Ever			12.6
United Kingdom (McNulty) ⁴⁶	2006	6 983 households with children	Past 12 months			4.6
United Kingdom (McNulty) ⁴⁷	2007	7 120 adults	Ever			4.8
United Kingdom (Grigoryan) ⁶	2006	675 adults	Past 12 months	7.4	16.6	12
United Kingdom (Grigoryan) ¹⁶	2008	95 adults	Ever			15.8
Combined results for multiple countries without presenting results for individual countries						
Central, western, northern EU						
19 Member States (Grigoryan) ¹⁵	2007	15 548 adults	Past 12 months			3.1



Non EU-countries						
Macedonia (Bosevska) ⁴⁸	2012	239 persons 10-67 years	-			13.4
Macedonia (Ivanovska) ⁴⁹	2013	402 adults, 122 children	12 months (storage)	72.1		17.8/1.8*
Russia (Stratchounski) ⁵⁰	2003	900 families	6 months (use for URTI)		83.6	
United States (Ceaser) ⁵¹	2000	101 adults	Current		25.7	
United States (Richman) ⁵²	2001	1 363 patients admitted to emergency dept	Ever			17
United States (Edwards) ⁵³	2002	801 parents with children	Past 12 months			8.2
United States (Céspedes) ⁵⁴	2006	Unknown (Latino)	Past 12 months			26
United States (Landers) ⁵⁵	2010	100 female head household	Past 12 months			23.6 % of all antibiotic courses

* Adults/children.

** Of those who never self-medicated.

*** Same figures can be found in Tesar 2008.

Sources of antibiotics without a prescription

Several studies suggested that patients obtain antibiotics without a prescription in different ways (see also Section 2.2.3). Buying antibiotics OTC and the use of leftover medication are the main sources of antibiotics without a prescription. In some studies buying OTC is clearly dominant,^{23 25 29} while in other studies the use of leftover medication is the source that is most frequently mentioned.^{14 24 26 39 56} No clear pattern across countries can be observed. Friends, family members and neighbours are the third important source of antibiotics without a prescription (see table 2.6).

Table 2.6. Sources for obtaining antibiotics without a prescription. (Source: Literature review regarding the volume and nature of antibiotic use without a prescription (n = 59 studies).)

Country (1st author)	Year	Number of users	Pharmacy	Left-over medication	From family, friends, etc.	Other/unknown
Denmark (Muscat) ³⁴	2006	66		64		36
Greece (Mitsi) ²²	2005	129	40.4	30.2	22.3	7.1
Greece (Skliros) ²³	2010	508	76.2	15.3	7.2	1.3
Italy (Napolitano) ³⁷	2013	137	43.2	68.6		
Lithuania (Berzanskyte) ²⁵	2006	298	86.0	23.2	6.1	
Malta (Borg) ³⁸	2002	168	85.7	4.8	4.8	4.8
Poland (Olczak) ³⁹	2006	122	?	56.4	18.2	
Poland (Muras) ⁴⁰	2013	372	13.4	73.1	12.6	0,01
Spain (Gonzales) ²⁶ (storage)	2006	370	14.3	84.9	0.8	
Non EU-countries						
United States (Céspedes) ⁵⁴	2006	192	31	61		

Type of antibiotic

Fewer than half of all studies (n = 25) reported which type of antibiotic, or group of antibiotics, patients used or requested. Both broad-spectrum antibiotics (amoxicillin, ciprofloxacin, cefaclor and norfloxacin) and narrow-spectrum antibiotics (azithromycin or penicillins) were being used or requested by patients to treat their symptoms on their own initiative. The antibiotics most often used or requested were penicillin derivatives.^{6 30-32 34 36 57 58}

Type of symptoms or disease

Thirty-one studies included information on the symptoms for which antibiotics were used or requested. The most common reasons for patients to use non-prescribed antibiotics were upper or lower respiratory tract infections such as sore throat or bronchitis.^{6 14 15 23 25 29-32 34 38 41 56-61} Other reasons stated included fever,^{23 56 57 60} urinary tract infections,^{15 30 38 41 57} dental problems,^{6 15 24 30-32 36 56-58} kidney infections,³⁸ flu,^{31 36 38 57 60} sinusitis⁶¹ and prophylaxis.³⁶

2.4.4. Pharmacist/pharmacy perspective

Ten studies using a pharmacist or pharmacy perspective were included in the literature review: two from Greece, five from Spain, one from Slovakia, one from the United States and one from New Zealand. The eight EU studies included information on dispensing behaviour, either based on pharmacists' self-reports or on pharmacy staffs' reactions to actors posing as patients (see Table 2.7 for references). All studies except one, in Spain, found that in over 40 % of all pharmacies, antibiotics were dispensed even though the patient did not have a prescription (see Table 2.7). The two non-EU studies also indicated a high degree of intention to sell antibiotics OTC (not in table).^{62 63}

Table 2.7. The dispensing of antibiotics without a prescription in pharmacies. (Source: literature review regarding the volume and nature of antibiotic use without a prescription; n = 7 studies.)

Country (1st author)	Year	Number of participants	Way of measuring dispensing	Percentage of pharmacist dispensing antibiotics without a prescription
Greece (Contopoulos) ⁶⁴	2001	98	Mystery guest	77.6
Greece (Plachouras) ⁶⁵	2010	174	Mystery guest	72.4
Spain (Caamano Isorna) ⁶⁶	2004	164	Self-report	65.9
Spain (Llor) ^{67 68}	2009 /2010	197	Mystery guest	45.2
Spain (Simó) ⁶⁹	2013	50	Mystery guest	8
Spain (Zapata) ⁷⁰	2014	286	Self-report	64.7
Slovakia (Markovic-Pekovic) ⁷¹	2012	131	Mystery guest	58

The most frequently offered antibiotics were penicillins, macrolides and fluoroquinolones. Pharmacists dispensed different types of broad-spectrum antibiotics such as amoxicillin, cephalosporin or norfloxacin.^{64 66 67 69} The studies that involved an actor posing as a patient presented one or more cases to the pharmacists in order to see whether they would sell an antibiotic without a prescription for that particular case. A study in Greece, for example, distinguished between a case where the patient had a low fever versus a patient with a high fever. Pharmacists, who were confronted with cases of high fever sold antibiotics OTC more often (86 %) compared to pharmacists who were confronted with low-fever cases. However, even when presented with patients with low fever, still over two thirds of the pharmacists sold an antibiotic OTC (69 %).⁶⁴ A study in Spain, described in two articles, showed that pharmacy staff were most inclined to dispense antibiotics when the actor presented with a urinary tract infection.^{67 68} Here 79.7 % of pharmacy staff sold an antibiotic without a prescription. These percentages were considerably lower for sore throat (34.8 %) and acute bronchitis (16.9 %).^{67 68}

2.4.5. Internet

The use of antibiotics obtained via the internet is considered to be a growing problem. However, only a single US study was found that explicitly focused on the use of an antibiotic acquired through the internet without a prescription.⁷² Of 138 unique online vendors of medicines, 36.2 % sold antibiotics without a prescription. They were also likely to sell antibiotics in courses that exceed the number of days an antibiotic is needed.

2.5. Discussion and selection of Member States for the ARNA project

Main findings

There is a large variation in outpatient antibiotic consumption in the EU as is shown by data from ESAC-Net and Eurobarometer surveys, and by an extensive literature review of 59 studies. This large variation is found for the use of antibiotics both with and without a prescription. The ESAC-Net data and Eurobarometer surveys show that there is a positive but moderate association between the levels of consumption of prescribed and non-prescribed antibiotics at the country level. However different patterns of use exist. Some Member States, such as Greece, Romania and Cyprus, show high levels of both prescription and non-prescription use, while Member States such as the Netherlands and Sweden have low levels of both prescription and non-prescription use. Estonia is a Member State with a low level of use of antibiotics with a prescription, but a relatively high level of use without a prescription. For a Member State such as France the opposite holds true. Buying OTC from a pharmacy is the prevailing source of an antibiotic without a prescription, followed by the use of medication left over from a previous treatment by the patient or another household member.^{8 13} This is the case in most EU Member States, but in some (Luxembourg, Austria, Belgium and Spain) leftover medication is the main source of antibiotics without a prescription.^{8 13}

Strengths and limitations

There is large variation in the methods used between studies included in the literature survey, for example the way in which outcome variables are measured, the size and nature of the populations that are included and the period for which use is measured. Data cannot, therefore, be compared easily. Moreover, studies from the patient's perspective are based on self-reported data. Self-reporting can induce socially desirable responding, and as such the use of antibiotics without a prescription may be underestimated.⁷³ This not only holds true for the studies in the literature review, but also for the Eurobarometer surveys. A strength of the Eurobarometer surveys^{8 13} is that they include all EU Member States and measure use of antibiotics in exactly the same way in all Member States, making it possible to compare between them. Overall, despite the variety in methods used, the results in this chapter show that the use of antibiotics without a prescription is still occurring across the EU and needs attention.

Selection of Member States for the ARNA project

The ARNA study pays particular attention to the use of antibiotics without a prescription. Based on the results from previous studies, seven Member States were selected to perform surveys into the use of antibiotics without a prescription among citizens, pharmacists and GPs (see Chapter 4). As the Eurobarometer surveys are the only data source that include all EU Member States and measure use in exactly the same way, it was decided to select Member States on the basis of the 2013



Eurobarometer survey ^(bb). The European Commission requested that the ARNA team include five large and two small Member States in the project. The main criterion for selecting a Member State was the level of antibiotic use without a prescription. Two small Member States with high percentages of such use were Cyprus (10 % of all antibiotic use was without a prescription) and Estonia (6 %).¹³ The four large Member States with the highest use included Romania (20 %), Greece (16 %), Hungary (8 %) and Spain (8 %). Italy (4 %) was not in the top-five large Member States with a high use of non-prescription antibiotics, but was chosen, in agreement with the Commission, because of its regional differences in use.^{74 75}

^(bb) The choice for the ARNA countries was made in 2014.

3. Explaining differences in antibiotic use across the EU

Main findings

Literature review

A literature review, including 41 studies, found that the use of antibiotics without a prescription is a complex phenomenon that can only be explained by looking at a variety of determinants on different levels. The results for sociodemographic factors such as gender, the age and educational level of the patient and the location of the pharmacy (rural versus urban) in this regard were inconclusive. Examples of determinants found in the literature that were associated with a higher use of antibiotics without a prescription include:

- on the patient level, a lack of knowledge about antibiotics and a previous successful experience with the use of antibiotics;
- on the HCP level, insufficient knowledge on the part of the pharmacist;
- on the healthcare-system and country level, the dispensing of whole packages of antibiotics rather than the exact amount of pills needed.

Eurobarometer data

- In Chapter 2, differences were noted between EU Member States in the level of use of antibiotics without a prescription. Further analyses of the Eurobarometer in this chapter suggest that differences between Member States can partly be explained by differences in the level of knowledge, information use and attitudes towards antibiotics among the general population.
- Countries with high levels of antibiotic use without a prescription, after correcting for the level of knowledge, information use and attitudes towards antibiotics, include the ARNA countries Hungary, Cyprus, Greece, Italy and Estonia.

Ministries of health survey

- All 28 EU Member States have a legal framework that either promotes the prudent use of antibiotics or prohibits the sale of antibiotics without a prescription.
- A number of EU Member States report that OTC sales are illegal but that there are exceptions for topical antibiotics such as creams and eye drops. One Member State reported that fuzaridin can be obtained without a prescription.
- Despite the legal framework, a number of EU Member States reported that patients can obtain antibiotics OTC from pharmacies in their country.
- The survey indicated that antibiotics are frequently available over the internet without a prescription.
- Actions are being taken by all EU Member States to reduce the non-prudent use of antibiotics, but the type and intensity of actions differs by country. Only one Member State reported that there were no national measures.
- The main policy differences between the ARNA countries and the other EU Member States were the existence of, firstly, national antibiotic plans, of which there were fewer among the ARNA countries, and, secondly, national surveillance systems in outpatient care. Here too there were fewer among the ARNA countries.

3.1. Introduction

Chapter 2 noted large variations between EU Member States in antibiotic use both with and without a prescription. These differences can have several causes. The current chapter aims to identify determinants of the use of antibiotics without a prescription. The use of antibiotics without a prescription is a complex phenomenon that appears in different forms and can have negative public health effects. Therefore, it is important to identify the determinants that drive patients to use antibiotics without a prescription. These determinants can be found on different levels. These

are: in the general population, such as the behaviour of individuals; among HCPs, such as the services they provide; and in the healthcare system, for example legislation. Knowledge about determinants on these different levels is necessary to stimulate targeted interventions aimed at achieving more prudent use of antibiotics. However, little information currently exists about the factors on these different levels. Therefore, the ARNA team performed a literature review in order to gain an overview of the determinants of antibiotic use without a prescription on three levels: the population, the HCP and healthcare-system levels. Moreover, an additional analysis was performed using the 2013 Eurobarometer to study determinants of non-prescription use within the EU. Finally, we also collected information on regulations and policy measures taken to improve rational antibiotic use in EU Member States.

3.2. Determinants: a literature review

3.2.1. Methods

Search strategy

A comprehensive and systematic literature search was conducted in PubMed, Scopus and Embase. We searched for studies published between January 2000 and September 2014 without a limitation on language or type of study. The following search terms were used: (antibacterial agents OR drug resistance OR antibiotic) AND (non-prescription OR over-the-counter OR self-medication) AND (Europe OR Anglo-Saxon countries OR other western or European countries). Studies on both actual use and the intention to use were included. The electronic searches were supplemented by manual searches of reference lists and citation tracking of selected articles. This search was combined with the one in Chapter 2 (see Section 2.3). After checking the data it appeared that the studies of determinants in non-European countries seemed less relevant for the European situation as all of them, except one, focused on the Latino population in the United States and not on the general population ^(cc).

Selection criteria

Publications were selected if the two following criteria were met: (1) the focus of the study is on the determinants of use of antibiotics without a prescription within the geographical context of at least one EU Member State or other European country; (2) the publication describes a quantitative empirical study. Articles were excluded if they focused on antibiotics in hospital settings, or animal or plant agriculture.

Data synthesis and analysis

Firstly, the titles were each screened by two authors (a combination of DL, JP and LvD). Then the same authors screened the abstracts. Next, the first author (DL) extracted data from the selected publications. Another author (LvD) checked the extracted data. Disagreements were resolved by discussion between the two authors. The determinants were categorised according to three levels.

1. Population level: individual characteristics and behaviours such as gender, knowledge or preferences.
2. HCP level: characteristics and behaviour of HCPs, their services and the organisation they work in, such as professional knowledge or providing patients with information about their medicines.
3. Healthcare-system level: the characteristics of healthcare systems such as access, payment, quality or organisation

^(cc) Readers who are interested in receiving to receive information on these studies can contact the authors of the report.

Finally, for each determinant, the effect upon self-medication was extracted ('positive', 'negative' or 'no effect').

3.2.2. Search results

The search resulted in a total of 2 678 records (1 624 records in PubMed, 806 in Scopus, 248 in Embase), of which 2 456 hits were unique. The screening of titles resulted in a total of 638 potentially relevant publications. The subsequent screening of the corresponding abstracts yielded 100 publications that were potentially relevant. By using the snowball method, 30 additional publications were regarded as potentially of interest. After screening, 41 articles appeared to be of interest for part of the review. For more details on the studies, see Chapter 2 (Table 2.2).

3.2.3. Population perspective

Table 3.1 shows an overview of the determinants that were studied using a patient perspective^(dd). Numerous determinants have been researched in relation to the use of antibiotics without a prescription. Sociodemographic characteristics are the most frequently studied determinants, followed by characteristics related to treatment. Other determinants focus on the patient's health condition, the relationship of the patient with the HCP and the patient's view of how the healthcare system influences patients' choices. In the text below we discuss determinants that were addressed in three or more studies.

Sociodemographic characteristics

The association between age and the use of antibiotics without a prescription has been researched in 15 studies and published in 16 articles in countries across Europe. Two studies that collected data in 19 European countries report on the same population and are counted as one study^{6 58}. Seven studies did not find an association between age and the use of antibiotics without a prescription.^{14 16 25 42 46 49 76} One study found that younger citizens were more likely to use antibiotics without a prescription,^{6 58} while two other studies found that older citizens were more likely to.^{22 33} The remaining studies used different categorisations for age but a general picture arises from these studies.^{32 43 56 77 78} Citizens between the ages of 16 and 50 years, the age at which people study or work, are more likely to use antibiotics without a prescription. This is in line with the findings of a study that suggested that employed people in higher managerial positions use antibiotics without a prescription more often compared to people who are retired — the reference category in that study.²⁵ However, three other studies did not find an effect for employment status.^{42 43 49}

Fifteen studies, published in 16 articles, studied differences between men and women in the use of antibiotics without a prescription. Seven studies did not find any differences.^{6 16 25 42 44 46 56 58} Of the remaining studies, five found that women used antibiotics without a prescription more often,^{22 25 35 43 77} while three studies found that men did so.^{30 31 78} The findings were not clustered within certain countries or related to the population under study. As such, no conclusions for gender can be drawn from the literature. The same holds for marital status. Two Spanish studies found no association between marital status and the use of antibiotics without a prescription.^{42 43} One study, which included three countries in Europe (Italy, the Netherlands, Russia), found that single people use antibiotics without a prescription more often compared to people who are married.⁷⁸

Educational level was included as a determinant in eight studies and published in nine articles. Half of the studies found that higher-educated people used antibiotics without

^(dd) For sentences that introduce paragraphs, references can be found in the text that follows and in tables.

a prescription more often.^{6 22 43 46 58} The other half of the studies did not find differences in relation to the level of education.^{16 25 29 49} As such, a low level of education does not seem to be associated with the use of antibiotics without a prescription. Finally, patients who have less time to visit a doctor more often use of antibiotics without a prescription.^{28 56}

Another determinant that attracted much attention, being covered in nine studies, published in 10 articles, is where people live or, more specifically, whether this is in a rural or an urban area. It can be hypothesised that access to doctors is better in urban areas compared to rural areas, especially in countries with a low population density. This means that in urban areas it is easier to obtain a prescription. However, there are also more pharmacies in urban areas and as such, theoretically, better access to antibiotics without a prescription. The literature is inconclusive. In six studies, no differences were found between people from urban and rural areas.^{6 16 26 39 49 57 58} Two studies, those from Poland and Lithuania, reported higher use of antibiotics without a prescription in rural areas,^{14 25} while one other study, among Romanian students, reported higher use in urban areas.⁴¹

Characteristics related to treatment

The association between the knowledge of antibiotics and beliefs about antibiotics, on the one hand, and the use of antibiotics without a prescription, on the other, has been regularly studied. Eight studies addressed different aspects of knowledge and beliefs. Three studies showed that better knowledge of several aspects of antibiotic use is associated with less use of antibiotics without a prescription.^{16 44 56} These aspects include, for example, knowledge of resistance, adverse effects and appropriate reasons for antibiotic treatment. Two studies from the United Kingdom, however, found the opposite, that better knowledge of antibiotics was associated with greater use of medication that has been left over.^{46 47} A Greek study found that the belief that the doctor would prescribe them an antibiotic anyway was a reason for 18 % of the participants to buy an antibiotic OTC²⁸. Another Greek study showed that the belief that antibiotics are safe because they are easily available was associated with a higher level of antibiotic use without a prescription.³⁵ An international study in 11 countries demonstrated that the belief that antibiotics can be stored and used again was related to an increased use of antibiotics without a prescription.⁷⁸ Storage of antibiotics in itself is a determinant of future use,^{6 29 46 57} as is the use of medication left over from previously prescribed courses.^{15 46 78} A successful previous use of antibiotics, either with or without a prescription, induces the use of, or intention to use, antibiotics without a prescription.^{28 29 31 34 44}

Characteristics related to health and disease

Four studies included general, self-reported, health status as a determinant of antibiotic use without a prescription. Two studies found that poor health status was associated with more use of antibiotics without a prescription.^{56 78} However, one other study found that better, self-reported, health was associated with more use of antibiotics without a prescription,⁴³ and another study found no association at all.⁴² Other studies looked at the association between having a chronic disease and the use of antibiotics without a prescription. Three studies, published in four articles, found that patients with a chronic disease are less likely to use an antibiotic without a prescription compared to people who are healthy.^{6 25 43 58} Two studies found no differences in this regard.^{16 42}

Characteristics related to HCPs and the health system

HCPs can influence the patient's choice to use antibiotics without a prescription. This was shown in two studies that found that patients used antibiotics without a prescription following the advice of a pharmacist to do so. Over a quarter (27 %) of all



respondents in an Italian study of parents of adolescents and parents of students, stated that they had received such advice from a pharmacist.⁵⁶ A Greek study among a general sample of adults found a comparable proportion (25 %).²⁸ In a Spanish study, 6.5 % of all respondents were advised to use antibiotics without a prescription, but the authors did not specify by whom this advice was provided.³¹

The patient's choice to use antibiotics without a prescription cannot only be influenced by HCPs, but also by factors related to the healthcare system itself. A lack of reimbursement for prescribed antibiotics was found to be a reason to use antibiotics without a prescription in a study among adults in 19 European countries,⁶ but not in a smaller follow-up study in 11 of those countries.¹⁶ In a Greek study, it was found that a lack of healthcare insurance coverage was associated with higher use of antibiotics without a prescription²⁸, but a study in the nearby former Yugoslavian Republic of Macedonia did not find such an association.⁴⁹

Table 3.1. Determinants of the use of antibiotics without a prescription studied from the population perspective; systematic literature review (n = 30 publications).

Determinant	Association with determinant (No of articles)		
	Positive Association	Negative association	No association
<i>Sociodemographic characteristics</i>			
▪ Age ^{6 14 16 22 25 32 42-44 46 49 56-58 77 78}		See text	
▪ Gender: women ^{16 22 25 31 35 42-44 49 56 58 77 78}	5	3	8
▪ Education: higher education ^{6 16 22 25 29 34 43 46 49 58}	4		4
▪ Location: rural area ^{6 14 16 25 26 33 39 41 49 58}	2	1	6
▪ Occupational and employment status ^{25 42 43 49}	1*		3
▪ Marital status: single ^{78 42 43}			
▪ Financial situation ⁴⁹			1
▪ Socioeconomic status ⁴⁶			
▪ Parents (versus other adults) ²²		1	
<i>Treatment-related determinants</i>			
▪ Lack of knowledge and incorrect beliefs on antibiotics ^{16 35 44 46 47 56 60 78}	6	2	
▪ Storage for future needs ^{6 29 46 57}	4		
▪ Successful treatment in past ^{28 29 31 34 44}	4		1
▪ Use of prescribed antibiotics ^{15 46 78}	3		
▪ Self-medication with medicines other than antibiotics ²⁷	1		
▪ Need for antibiotics (e.g. during holiday/sudden illness) ²⁸	1		
▪ Perceived availability of antibiotics ¹⁶	1		
<i>Health- and disease-related</i>			
▪ Having a chronic disease ^{6 16 25 42 43 58}		3	2
▪ Health status: good ^{42 43 56 78}	2	1	1
▪ Lifestyle ⁴³	1**	1	1**
<i>Healthcare professional-related</i>			
▪ Advice from a pharmacist or from lay persons ^{28 31 56}	3		
▪ Lack of information provision ⁷⁸	1		
▪ Attending a physician ^{43 56}	1		1
▪ Healthcare professional as household member ²⁷	1		
<i>Healthcare system-related</i>			
▪ No complete reimbursement/insurance issues ^{6 16 28 49}	2		2
▪ Lack of time or money to visit a doctor ^{28 29}	2		

* Higher management/unemployed more compared to retired.

** Different associations for different lifestyle behaviours in one study.

3.2.4. The pharmacist's perspective

This section reports on the potential determinants of the use of antibiotics without a prescription taken from studies that used a pharmacist perspective. The literature search was directed to other HCPs as well, but only studies with a pharmacist perspective were found. Table 3.2 shows a summary of the results of these eight studies. Most studies were from Spain (n = 5),⁶⁶⁻⁷⁰ with two studies from Greece^{64 65} and one study from the Republika Srpska (part of Bosnia and Herzegovina).⁷¹

Pharmacy and pharmacist characteristics

The age and gender of the pharmacist were, in most studies, not associated with the dispensing of antibiotics without a prescription.⁶⁷⁻⁷⁰ Only one Spanish study, from 2004, found that younger pharmacists were more inclined to dispense antibiotics without a prescription.⁶⁶ As age does not seem to be associated with OTC selling, it is not surprising that no associations were found with the number of years of practical experience as a pharmacist.^{66 70} Nor were there any differences found in the level of dispensing of antibiotics without a prescription between pharmacies in rural and in urban areas.^{65 67 68 70} This was also the case between different cities.⁶⁹ The results for the association between pharmacy ownership and the dispensing of antibiotics without a prescription are inconclusive. One Spanish study found that pharmacy owners are more likely to dispense antibiotics without a prescription,⁶⁶ while a more recent Spanish study and the study from Republika Srpska found no association with pharmacy ownership.^{70 71} The size of the pharmacy does, however, seem to matter, at least in Spain. Two Spanish studies found that in smaller pharmacies more antibiotics were dispensed without a prescription than in larger pharmacies.^{68 69} The study by Llor et al. (2010), for example, found that 63 % of the small pharmacies dispensed antibiotics without a prescription, whereas this was only 12 % of the largest pharmacies.⁶⁸ The authors concluded: 'Large pharmacies, that probably have a greater income, more closely followed the prevailing legislation of not selling antibiotics to patients without a prescription.'⁶⁸

Factors related to health and treatment

Zapata-Cachafeiro et al. (2014) studied the impact of knowledge and attitudes of pharmacists on their dispensing behaviour.⁷⁰ They concluded that insufficient knowledge was associated with dispensing of antibiotics without a prescription. They measured knowledge with statements such as 'antibiotic resistance is an important health issue', 'the fact that an antibiotic is prescribed to a patient will not influence the appearance of resistance' and 'when dispensing antibiotics, I warn the patient about the importance of correct therapeutic compliance'. They also found that pharmacists who were more complacent were more likely to dispense antibiotics without a prescription.⁷⁰ This was measured by the statement: 'antibiotics are sometimes dispensed without a prescription because the patient is known to have difficulty in gaining access to a doctor'. External responsibility was another factor that was related to the dispensing of antibiotics without a prescription. This is true in the sense that pharmacists who seek causes for AMR outside themselves, such as society, regulation and their patients, were more likely to dispense antibiotics without a prescription. Finally, Zapata-Cachafeiro et al. found that an indifferent attitude towards AMR was associated with a higher level of dispensing of antibiotics without a prescription.⁷⁰

Another study found that arguments related to patient safety, such as concerns for allergies or complications, were a reason for pharmacists not to dispense antibiotics without a prescription.⁶⁴ This study also found that pharmacists were more likely to dispense an antibiotic without a prescription in cases where they were confronted with a patient with a high temperature — either simulated or not — than when the patient had a low temperature.⁶⁴ Arguments related to health were also found to be a reason for not dispensing antibiotics without a prescription in a Spanish study, but these arguments were not further specified in the publication.⁶⁷ A wait-and-see principle is also sometimes used, as was shown in a study by Markovic-Pekovic.⁷¹

Factors related to the patient

Only a few studies from the pharmacist perspective included patient characteristics as a determinant. The age, gender and socioeconomic status of the patient do not seem to influence the decision of the pharmacist to dispense antibiotics without a prescription.^{67 68} However, it was reported in one study that pharmacists with a patient

population with high socioeconomic status received more requests to dispense antibiotics without a prescription.⁶⁶ A study by Camaano-Isorma et al. (2004) showed that a higher proportion of pharmacists dispense antibiotics without a prescription in cases where they know the patient (59 %) than in cases where they do not know the patient (34 %).⁶⁶

Regulation

Regulations in Greece for dispensing certain antibiotics have become stricter. Since 2003 the regulations state that: 'a separate specific prescription form needs to be filled in by the prescriber, justifying the choice of any fluoroquinolone or third generation cephalosporin prescribed orally, before the drug is dispensed'.⁶⁵ The reason for implementing this measure was to preserve the efficacy of these antibiotics. However, according to Plachouras et al. there is no reinforcement of the regulation.⁶⁵ They studied whether the regulation had an impact on the dispensing of antibiotics without a prescription and found that it appears that the implementation of this regulation was 'effective in reducing, although not eliminating, inappropriate dispensing'.

3.2.5. The healthcare-system and country perspective

There are fewer studies of the determinants of the use of antibiotics without a prescription on the healthcare-system level. Three studies on this level were included in the review, two of which were also included in Section 3.2.5 (population perspective).^{16 17 78}

Dispensing regulation

Both Grigoryan et al. (2008) and Kardas et al. (2007) studied whether the dispensing regulation in a country was associated with the use of antibiotics without a prescription.^{16 78} Grigoryan's study included 10 European countries and Israel, four of which had a regulation that allowed for the dispensing of the exact amount of tablets instead of the whole package (the Czech Republic, Israel, the Netherlands and the United Kingdom). It was found that the likelihood in these countries of using antibiotics without a prescription was lower compared to the seven countries where whole packages were dispensed.¹⁶ Kardas et al, who included 11 countries, worldwide, in their study, came to the same conclusion.⁷⁸

Wealth

The Grigoryan 2008 study also looked at the association between a country's wealth and the use of antibiotics without a prescription, expressed as the gross domestic product. They concluded that the higher the gross domestic product of a country, the less likely it is that its citizens use antibiotics without a prescription.¹⁶

Cultural impact

Cultural factors are known to play an important role in the use of antibiotics.^{e.g.79} Deschepper et al(2008) looked at the impact of cultural dimensions on both prescribed and non-prescribed antibiotics.¹⁷ They used Hofstede's model of cultural dimensions. Hofstede distinguished six dimensions along which cultural values can be compared with other cultures: individualism, collectivism, uncertainty avoidance, power distance (strength of social hierarchy), masculinity–femininity (task orientation versus person orientation); long-term–short-term orientation and indulgence–restraint.⁸⁰ Deschepper et al. included 27 EU Member States in their study. They only found one significant association between these cultural dimensions and the use of antibiotics without a prescription, namely for power distance. Power distance refers to the degree of hierarchy in a country. Deschepper et al. hypothesised and found that, in countries with a hierarchical system, the use of antibiotics would be more favoured because of

the 'doctor-knows-best attitude'. This might hold for prescribed antibiotics, but less so for antibiotics used without a prescription. Yet, it becomes unclear how Deschepper et al. interpret the finding that more power distance leads to more use of non-prescribed antibiotics.⁸⁰

3.2.6. Discussion

This review of the literature shows that the use of antibiotics without a prescription is a complex phenomenon that is driven by a variety of determinants that act on different levels. On the population level, the use of antibiotics without a prescription is, for example, associated with the storage of antibiotics at home, previous experiences with antibiotic treatment and a lack of knowledge^(ee). The association between the sociodemographic characteristics of patients and the use of antibiotics without a prescription is, however, not consistent as contradictory results were found (see Table 3.1). For example, it was found that non-prescription use is not associated with education level in highly educated persons, while better knowledge of several aspects of antibiotic use is associated with less use of antibiotics without a prescription. This implies that highly educated people do not necessarily have a better knowledge of antibiotic usage. On the pharmacy level, the knowledge and attitudes of the pharmacist towards antibiotics seem important.^{64 67 70 71} Other pharmacist- and pharmacy-related characteristics, such as location and the age and gender of the pharmacist, do not seem to have an association with the use of antibiotics without a prescription.^{65 67 68 70} However, pharmacists in smaller pharmacies seem to be more likely to dispense antibiotics without a prescription.^{68 69} Dispensing the exact amount of antibiotics prescribed instead of whole packages seems to reduce the use of non-prescription antibiotics.^{16 78}

This review provides an overview of the determinants that are associated with self-medication and could therefore be used to frame interventions. Based upon the results, it can be concluded that interventions and policies that simultaneously target patients and HCPs might be more effective than single-factor approaches. For both groups — patients and professionals — increased awareness and knowledge is needed in order to bring about behavioural change. Moreover, the enforcement of laws and regulations is necessary to ensure the sustainability of behavioural change. The studies included in this review paid little attention to the enforcement of laws, while in many European and western countries obtaining antibiotics without a prescription is illegal. These insights were used in the expert meeting that was organised within the context of the ARNA project (see Chapter 6).

The review had some limitations. Despite our comprehensive search, it is possible that we did not find all the information about the non-prescription use of antibiotics due to publication bias. Still, we found a large variety of studies that did focus on this use. Another limitation is how far the studies we included can be compared. This is because of the different outcome measures they presented and the variety of study designs. Moreover, little information was found on the determinants on the healthcare-system level. On the pharmacy level, the majority of studies included, five out of the eight, were from Spain. Moreover, there was a limited number of studies focusing on the pharmacist, and no studies were found that took into account the prescriber's perspective. And yet, HCPs are key players in educating their patients about the proper use of medicines. As such, more research is needed on the perspective of HCPs. We will look at this again in Chapter 4 of this report. The same is true for the healthcare-system level. There is still much to be explored in the role of governments and other institutions in the prudent use of antibiotics, including the use of antibiotics

^(ee) For exact references, see Table 3.1.



without a prescription. Section 3.4 provides more insight into the efforts of EU Member States in this respect.

Table 3.2. Determinants of the use of antibiotics without a prescription studied from the pharmacist's perspective; systematic literature review (n = 8 studies).

Determinant	Results
<i>Pharmacy and pharmacist characteristics</i>	
<ul style="list-style-type: none"> ▪ Gender ▪ Age 	No difference ⁶⁷⁻⁷⁰ One study: younger pharmacists more often dispense antibiotics without a prescription ⁶⁶ Other studies: no association ^{67 69 70}
<ul style="list-style-type: none"> ▪ Years of experience as a pharmacist ▪ Ownership of the pharmacy 	No association ^{66 70} One study: owners dispense antibiotics without a prescription more often than other pharmacists ⁶⁶ Other studies: no association ^{70 71}
<ul style="list-style-type: none"> ▪ Location of the pharmacy 	No differences between rural and urban areas ^{65 67-70}
<ul style="list-style-type: none"> ▪ Size of the pharmacy 	Small pharmacies more often dispense antibiotics without a prescription than large pharmacies ^{68 69}
<i>Treatment- and health-related characteristics</i>	
<ul style="list-style-type: none"> ▪ Knowledge and beliefs/attitudes towards antibiotics 	Insufficient knowledge, an indifferent attitude towards antibiotics, complacency and external responsibility associated with more dispensing of antibiotics without a prescription ⁷⁰
<ul style="list-style-type: none"> ▪ Patient safety 	Concerns about patient drug allergies and complications were a reason for not dispensing antibiotics ⁶⁴
<ul style="list-style-type: none"> ▪ Health/diagnoses 	One study found that in 57 out of 108 pharmacies, where no antibiotics were sold without a prescription, health-related arguments were used to justify this decision (no more specific information) ⁶⁷ Another study found that for a more severe diagnosis more antibiotics were dispensed without a prescription ⁶⁴
<ul style="list-style-type: none"> ▪ Wait-and-see advice 	One study found that patients were told to come back if the patient's situation did not improve ⁷¹
<i>Patient-related characteristics</i>	
<ul style="list-style-type: none"> ▪ Age of patient ▪ Gender of patient ▪ Socioeconomic status of patient 	No association ⁶⁸ No difference ⁶⁸ One study: higher-socioeconomic-status population, fewer requests for antibiotics without a prescription ⁶⁶ Other studies: no association ^{67 68}
<ul style="list-style-type: none"> ▪ Patient known by pharmacist 	Pharmacists are more likely to dispense an antibiotic to patients they know ⁶⁶
<i>Regulation</i>	
<ul style="list-style-type: none"> ▪ Restrictions on the prescribing of certain antibiotics 	Restriction in regulation for certain antibiotics led to fewer of those antibiotics being dispensed without a prescription ⁶⁵

3.3. Eurobarometer data

3.3.1. Methods

The Eurobarometer data enable the determinants for all 28 EU Member States to be studied simultaneously. In the Eurobarometer, respondents were asked whether they had used an antibiotic during the last 12 months, and if so they were asked for the source (see next section).

Data source

Eurobarometer 2013 data were used to study the determinants of non-prescription use of antibiotics in the 28 EU Member States. These Eurobarometer data are publicly available and were retrieved through Gesis^(ff).² Eurobarometer data include self-reported data collected by a questionnaire which included questions related to 'reported actual self-medication with antibiotics during the last year'. For a more detailed description of sampling methods and data collection, see Section 2.2.1. Patients who used an antibiotic were selected for the analysis in this section. The characteristics of patients who used an antibiotic without a prescription were compared to those who had a prescription.

Variables

Antibiotic use

Respondents were asked whether they had used an oral antibiotic during the last 12 months, and if so they were asked for the source (see also Chapter 2). Patients were divided into two groups:

- those who took antibiotics with a prescription (value = 0);
- those who took antibiotics without a prescription (value = 1).

Determinants

The following variables were included as, based on the literature review, they were expected to have an impact^(gg) on the choice to use antibiotics without a prescription instead of with a prescription (see Section 3.2).

- Sociodemographic variables: gender, age (six levels), professional status (eight levels), socioeconomic status (three levels), marital status (four categories), degree of urbanisation of location (three categories), educational level (five categories);
- Antibiotic-related variables: knowledge of antibiotics (number of correctly answered questions out of four questions), source for obtaining information on antibiotics, attitude towards antibiotics and reason or indication for the use of antibiotics.
- Country: dummy variables for all EU Member States were created.
- Other: satisfaction with own life (four categories).

^(ff) 2013 Eurobarometer data: <https://dbk.gesis.org>; http://ec.europa.eu/dgs/health_food-safety/amr/docs/eb445_amr_generalreport_en.pdf

^(gg) Although the results for sociodemographic variables were inconclusive in the review, they are still taken into account in the analyses as some studies in the review showed an association.

Analyses

The characteristics of users of antibiotics without a prescription (value 1) versus those who used an antibiotic with a prescription (value 0) were analysed with a logistic regression analysis. Firstly, a model was estimated including dummy variables for all Member States except Finland, which had the lowest use of antibiotics without a prescription and therefore served as the reference. As we were interested in fixed effects we included Member States as dummy variables and did not use a multilevel model. However, we also estimated a multilevel model where Member State was included as a random effect. This provides insight in the extent to which variation in self-medication can be explained by differences between Member States. Next, sociodemographic variables were added to the model, and finally variables on knowledge and attitude towards antibiotics were included (full model). As the full model was not stable due to the fact that it included many variables, a model was estimated that only included variables that were significant ($p < 0.05$) in the full model.

Variables included in the **final model** were as follows.

- Gender (reference: male).
- Age in six categories (< 25 years (ref), 25-34 years, 35-44 years, 45-54 years, 55-64 years, 65 years and older).
- Knowledge of antibiotics: a respondent received a score of '1' if all four items were answered correctly and '0' if one or more items were answered incorrectly^(hh).
- The source from which information was obtained: HCP (reference category), family/friends, media/communication campaigns or no information at all.
- Attitude towards antibiotics ('Everyone has a role to play to ensure that antibiotics remain effective') 1 = totally agree; 4 = totally disagree.

The health symptoms the antibiotics treated were used as control variables as it can be expected that antibiotics used for more severe health conditions are more likely to be prescribed by a doctor. Models for a single EU Member State could not be estimated, as for most the number of patients who used an antibiotic without a prescription was too low.

3.3.2. Results

Table 3.3 shows, for the all of the EU Member States, the characteristics of all antibiotic users both with or without a prescription. Patients who used antibiotics without a prescription were younger and more often male compared to patients who had a prescription. They were also less often informed and fewer patients had good knowledge of antibiotics.

^(hh) A same variable was constructed in which there were at least three correct as opposed to two or fewer answered correctly. This variable was a weaker predictor of non-prescription use than the one ultimately used, which contained four correct answers.

Table 3.3. The characteristics of users of antibiotics divided between users who had a prescription and those who had not. (Source: Eurobarometer 2013.)*

Sociodemographic variable	Users of prescription antibiotics (n = 9 341)		Users of non-prescription antibiotics (n = 562)	
	n	%	n	%
Male	3 709	39.7	278	49.5
Age:				
< 25 years	1 084	11.6	102	18.2
25-34 years	1 308	14.0	94	16.7
35-44 years	1 498	16.0	106	18.9
45-54 years	1 507	16.1	110	19.6
55-64 years	1 589	17.0	80	14.2
65 years and older	2 355	25.2	70	12.5
Antibiotic-related variable				
Knowledge (percentage of persons with four correct answers from four statements on knowledge)**	2 022	28.5	40	10.2
Attitude ('Everyone has a role to play to ensure that antibiotics remain effective' 1 = totally agree; 4 = totally disagree)	8 662	1.7 (average)	512	1.9 (average)
Source of information:				
HCP	1 723	18.9	61	11.0
family/friends	187	2.0	20	3.6
media/communication campaigns	1 773	19.4	92	16.6
no information at all	5 463	59.7	383	68.9

* Only variables included in the final model.

** Statements:

- 1: Antibiotics kill viruses.
- 2: Antibiotics are effective against colds and flu.
- 3: The unnecessary use of antibiotics makes them become ineffective.
- 4: Taking antibiotics often has side effects such as diarrhoea.

*** There is a significant difference between users of prescription antibiotics and users of non-prescription antibiotics on all variables (gender, age, knowledge, attitude and source of information, for all variables: $P < 0.000$).

Analyses

Logistic regression analyses were then performed in the next step. Finland was the Member State with the lowest level of antibiotic use without a prescription and served as the reference. Table 3.4 shows that, if not corrected for patient characteristics, 18 Member States are found to have a significantly higher proportion of users of antibiotics without a prescription among all antibiotic users than Finland — the Member State with the lowest level of non-prescription use in 2013. These Member States logically include all seven Member States selected for undergoing in-depth surveys within the context of the ARNA project: Cyprus, Estonia, Greece, Hungary, Italy, Romania and Spain. It should be noted that confidence intervals for the Member State estimates are wide, meaning that the estimates are less accurate.

When including sociodemographic variables (gender, age), knowledge and source of information and health symptoms for which antibiotics were used in the analysis, the following, additional, Member States do not differ significantly from Finland: Bulgaria, Croatia, Latvia, Portugal, Slovakia, Spain and Sweden. Moreover, the differences for all the Member States are smaller in the final model. This means that the differences between countries can partly be explained by factors such as, knowledge, attitude and information received.

Table 3.4 shows that, compared to people who had a prescription for their last antibiotic course, people who used an antibiotic without a prescription:

- are more often male;
- are younger;
- have less knowledge of antibiotics;
- less often think that everyone has a role in keeping antibiotics effective; and
- more often obtain information about antibiotics from sources other than healthcare professionals or no information at all.

Despite this finding, differences between Member States still remain. This means not all variation is explained by the model. The Member States that still differ significantly from Finland in the final model are a mixed group. They include the following: Austria, Belgium, Cyprus, Denmark, Greece, Hungary, Ireland, Lithuania and Romania. Belgium, Cyprus, Greece, Italy and Romania all fall in the highest quartile (Q1) of countries with a high overall outpatient consumption of antibiotics according to the ESAC-Net data (see Chapter 2). This might imply that these Member States generally have a culture where the use of antibiotics is more generally accepted than in others.¹⁷ Also, the high level of use of prescribed antibiotics might provide persons with opportunities to keep antibiotics in stock (see literature review, Section 3.2). This seems to be true for Belgium and Italy, two Member States with a relatively high share of the use of leftover antibiotics (see Figure 2.5). In Cyprus, Greece, and Romania, non-prescription use of antibiotics is mainly driven by OTC selling. The level of reinforcement of the laws not to sell OTC may be lower than in other Member States in the EU (see Chapter 7). The other Member States with high levels of antibiotic use without a prescription are spread across all the other quartiles in the ESAC-Net data (Q2: Ireland; Q3: Austria, Lithuania, Denmark; Q4: Estonia, Hungary). It should be noted that in Denmark, Italy and Austria some antibiotics for topical use can be sold OTC, which may explain the level of non-prescription use in these countries (see results of the Member State survey, Section 3.4). In Estonia and Hungary, the level of reinforcement of the laws not to sell OTC may be lower than in other Member States.

Table 3.4. Determinants of the use of antibiotics without a prescription versus those with; logistic regression analysis. (Source: Eurobarometer 2013.)*

	Country model (n = 9 903)			Final model (country model plus extra variables) (n = 7 015)		
	Odds ratio	95 % CI	P-value	Odds ratio	95 % CI	P-value
EU Member State						
Austria	10.6	2.5-45.6	< 0.01	6.3	1.3-26.2	0.02
Belgium	9.9	2.3-42.6	< 0.01	6.3	1.4-27.6	0.02
Bulgaria	13.7	3.2-58.0	< 0.01	3.3	0.7-15.7	0.16
Croatia	9.6	2.2-41.9	< 0.01	4.5	1.0-20.3	0.05
Czech Republic	2.0	0.4-10.9	0.43	1.7	0.3-9.4	0.56
Denmark	9.3	2.1-40.7	< 0.01	6.6	1.4-30.8	0.02
Finland	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
France	3.0	0.6-14.1	0.17	1.6	0.3-7.9	0.59
Germany	2.6	0.5-12.8	0.25	1.8	0.4-9.3	0.50
Ireland	14.3	3.4-60.0	< 0.01	6.9	1.6-30.4	0.01
Latvia	12.8	3.0-54.3	< 0.01	4.4	1.0-19.5	0.05
Lithuania	12.1	2.8-51.1	< 0.01	5.2	1.2-23.1	0.03
Luxembourg	4.9	1.0-23.4	0.05	4.0	0.8-20.7	0.10
Malta	2.1	0.4-12.9	0.41	1.0	0.1-7.3	0.99
Netherlands	4.6	1.0-22.0	0.05	2.8	0.5-14.6	0.23
Poland	3.8	0.8-19.1	0.10	1.2	0.2-7.2	0.87
Portugal	7.7	1.8-33.5	0.01	4.1	0.9-18.5	0.07
Slovakia	6.7	1.5-29.2	0.01	3.0	0.7-13.9	0.16
Slovenia	4.2	0.9-20.5	0.08	2.0	.4-11.3	0.42
Sweden	5.1	1.1-24.4	0.04	5.0	1.0-24.7	0.05
United Kingdom	4.0	0.9-17.9	0.07	2.5	0.6-11.6	0.24
Cyprus	18.9	4.4-80.7	< 0.01	5.6	1.2-25.6	0.03
Estonia	10.8	2.5-46.2	< 0.01	5.5	1.2-24.6	0.02
Greece	31.5	7.6-130.2	< 0.01	13.1	3.1-55.0	< 0.01
Hungary	14.0	3.3-59.8	< 0.01	5.2	1.2-23.3	0.03
Italy	7.5	1.7-33.0	< 0.01	5.0	1.1-23.2	0.04
Romania	40.3	9.9-164.7	< 0.01	18.5	4.4-78.4	< 0.01
Spain	13.4	3.2-56.7	< 0.01	2.3	0.5-11.3	0.29
Sociodemographic variable						
Sex (ref = male)				0.6	0.5-0.7	< 0.01
Age						
< 25 yrs				Ref.	Ref.	Ref.
25-34 yrs				0.9	0.6-1.2	0.42
35-44 yrs				0.7	0.5-1.1	0.12
45-54 yrs				0.9	0.6-1.3	0.61
55-64 yrs				0.7	0.5-1.0	0.07
65 yrs and older				0.4	0.2-0.6	< 0.01
Antibiotic-related						
Knowledge*				0.5	0.3-0.7	< 0.01
Attitude				1.2	1.1-1.4	< 0.01
Source of information:						
HCP				Ref.	Ref.	Ref.
family/friends				3.1	1.6-6.0	< 0.01
media/communication campaigns				1.8	1.1-2.7	0.01
no information at all				1.9	1.4-2.7	< 0.01

* Figures in bold are significant at P < 0.05, corrected for health symptoms

3.3.3. Discussion

This section provided a secondary analysis of the 2013 Eurobarometer data.¹³ In line with the results in Chapter 2, it showed that there are large differences between EU Member States in the use of antibiotics without a prescription. These differences can be explained in part by differences in the level of knowledge of their inhabitants. This is in line with the findings from the literature review in which knowledge of and attitudes towards antibiotics were also related to non-prescription use. Also with regard to other determinants, the results from the Eurobarometer analyses generally confirmed the results of the literature review as described in Section 3.2.

The analysis of the Eurobarometer data in this section showed that younger people more often use antibiotics without a prescription, which is in line with the studies in the literature review that found that people having attained a working age or an age to pursue further education are more likely to use antibiotics without a prescription. Contrary to the literature, The Eurobarometer data found that men more often use antibiotics without a prescription. Reasons for this may be differences in the sampled population or differences in the formulation of questions.

The analysis using the Eurobarometer data had some limitations. Firstly, the number of people who used an antibiotic without a prescription was very low in some Member States. This number was, on average, 20 people per Member State. However, it was much lower in Member States such as Finland, Sweden and the Netherlands. Therefore, the estimates on the Member State level are less accurate, which was shown by the large confidence intervals and the fact that a model including all potential determinants was not stable. The low number of respondents in some Member States was also the reason that no multilevel analyses were performed. Secondly, the Eurobarometer data only included a limited number of relevant determinants.

3.4. Policies and measures on antibiotic use in EU Member States

3.4.1. Introduction

We investigated policy measures that EU Member States have taken on the level of the healthcare system to enhance the prudent use of antibiotics. This involved using an online survey among representatives of ministries of health and Member State experts. This survey — referred to as the Member State survey — included respondents from all 28 Member States (see Table 3.5). This section summarises the main findings. We first assessed the legal framework regarding antibiotic use in the EU Member States. This included, in particular, the dispensing systems, which were the only factor that was associated with lower levels of antibiotic use without a prescription in the literature review. We then reviewed national policy measures and finally auditing and surveillance activities. The aim of this review was to identify differences in policy measures between the ARNA countries and the rest of the EU.

3.4.2. Methods

Data were collected from ministries of health and other key stakeholders in all EU Member States using an online questionnaire combined with written or telephone reminders.



Questionnaire

The questionnaire was developed in collaboration with the University of Antwerp and DG Health and Food Safety. Various versions from the questionnaire were discussed. The final version included 32 questions.

The survey contained questions on:

1. national antibiotic plans;
2. national measures to enhance the prudent use of antibiotics, including laws and legal regulations, national policy measures, surveillance and auditing;
3. legal provisions for the prescription of antibiotics in each Member State, including laws and regulations regarding outpatient care and the sale of OTC antibiotics.

The use of a structured questionnaire with predefined answers has the advantage that it is easier to complete and less time-consuming for participants. However, in-depth information is harder to gather with the questionnaires. We have, therefore, offered sufficient space in the questionnaire for remarks (see Annex A). The survey was web-based and the data were collected in collaboration with the NIVEL Data Collection Survey Team.

National contact persons

National contact persons were identified in all 28 EU Member States. These were people working at ministries of health, national health-insurance boards, national institutes of public health and, where applicable, institutes for rational use of medicines or other key stakeholders. The list of national contact persons was collected using various methods. These included: referring to attendance lists of scientific meetings; using the support from the University of Antwerp and DG Health and Food Safety; referring to contacts from previous projects (e.g. APRES); using the survey itself (see question 32, Annex A); checking national websites and scientific publications; and telephone calls to national contact persons.

The final list included 93 contact persons, with generally two or more people per Member State, though we only had one for Cyprus and Luxembourg. For some Member States we had six (the Netherlands) or even eight (United Kingdom). The contact persons were mainly contacted by email, but, at the later stage of data collection, we also contacted people by phone.

Multiple responses from the same Member State

For Member States from where there were multiple responses, we assumed the responses from the ministry of health or the national institute of public health were the most complete for the questions related to 'Legal and regulatory regulations' and 'Surveillance and auditing'. For the questions related to 'National policy measures' we also considered the responses from other organisations, such as universities.

Respondents

Table 3.5 presents an overview of the institutes that responded to the survey. We had a range of responses, which included responses from ministries of health (five), national institutes of public health (five), universities (four) and national agencies for medicines (three). We received a group response from Austria's Federal Ministry of Health and Women's Affairs. We had three responses from the Ministry of Health, Social and Family Affairs in Hungary. Four Member States gave just two responses.

**Table 3.5.** Overview of the institute affiliations of the survey respondents. (Source: Member State survey.)

Member State	Respondent's organisation
1. Austria	Federal Ministry of Health
2. Belgium	University of Antwerp
3. Bulgaria	Medical institute of the Ministry of Interior
4. Croatia	Institute of Public Health Croatia
5. Cyprus	Nicosia General Hospital and Ministry of Health
6. Czech Republic	National Public Health Institute
7. Denmark	Statens Serum Institut
8. Estonia	State Agency of Medicines
9. Finland	Ministry of Social Affairs and Health
10. France	Centre de Coordination de la Lutte contre les Infections Nosocomiales Sud-Ouest (University of Bordeaux)
11. Germany	Robert Koch Institute
12. Greece	Hellenic Centre for Disease Control and Prevention
13. Hungary	Ministry of National Resources Szemmelweis University Szeged University
14. Ireland	Health Protection Surveillance Centre
15. Italy	National Institute of Health
16. Latvia	State Agency of Medicines
17. Lithuania	Institute of Hygiene
18. Luxembourg	Ministry of Health
19. Malta	Mater Dei Hospital National Antibiotic Committee
20. Netherlands	University Medical Centre Utrecht
21. Poland	Depart. of Family Medicine, Medical University of Lodz National Medicines Institute
22. Portugal	Ministry of Health
23. Romania	National Institute of Public Health
24. Slovakia	Regional Public Health Authority (Trencin)
25. Slovenia	University Medical Centre Ljubljana
26. Spain	The Spanish Agency of Medicines and Medical Devices
27. Sweden	The Public Health Agency of Sweden (2x) Swedish Strategic Programme for the Rationale Use of Antimicrobial Agents and Surveillance of Resistance
28. United Kingdom	Department of Health



3.4.3. Legal framework

National legislation, or regulations, in EU Member States

Respondents in the Member State survey were asked if there were any national laws or legal regulations for ambulatory (outpatient) care to reduce the non-prudent use of antibiotics in their country concerning the one or more of the following areas: restrictive prescribing, use of delayed medical prescriptions, unused antibiotics, preventive medical strategies, the use of prices and economic incentives and statutory/legal guidelines on antibiotic usage. Laws or regulations to reduce the non-prudent use of antibiotics in outpatient care were reported in all the 20 Member States who responded to this question. The most common laws, or regulations, concern: 'Restrictive prescribing' (nine Member States) and 'Statutory/legal guidelines on antibiotic usage' (five Member States) (see Table 3.6).

Most Member States (19, see Table 3.7) have legislation that is aimed specifically at prohibiting antibiotic use without a prescription ⁽ⁱⁱ⁾, although seven Member States did not indicate that they had specific legislation on antibiotics (Czech Republic, Estonia, France, Latvia, Lithuania, Slovakia and Slovenia). Yet, all 26 Member States who responded to the question about whether the law requires antibiotics to be dispensed with a prescription indicated that this was the case. Denmark and Ireland did not respond. The laws usually cover both systemic and topical antibiotics, but there are exceptions. A prescription is, sometimes, not required for topical antibiotics.

⁽ⁱⁱ⁾ In the questionnaire this was referred to as self-medication.



Table 3.6. EU Member States with laws or regulations to reduce the non-prudent use of antibiotics in outpatient care. (Source: Member State survey.)

Member State	Yes/No	Restrictive prescribing	Delayed prescriptions	Unused antibiotics	Preventive strategies	Price & economic incentives	Legal guidelines on antibiotic usage	Other
1. Austria	Yes							Two laws
2. Belgium	No answer							
3. Bulgaria	Yes	Yes	Yes		Yes		Yes	
4. Croatia	Yes							National Drug Formulary
5. Czech Republic	Yes	Yes						
6. Denmark	Yes					Yes		
7. Finland	No answer							
8. France	Yes							Strict enforcement
9. Germany	No answer							
10. Ireland	No answer							
11. Latvia	Yes	Yes						
12. Lithuania	Yes	Yes						
13. Luxembourg	Yes							Legally non-binding guidelines
14. Malta	Yes							Non-prescribed use of antibiotics
15. Poland	Yes	Yes						
16. Portugal	No answer							
17. Netherlands	Yes						Yes	
18. Slovakia	Yes							Restrictive prescribing primary care
19. Slovenia	Yes	Yes						
20. Sweden	Yes		Yes					
21. United Kingdom	No answer							
22. Cyprus	Yes							OTC is legally forbidden
23. Estonia	Yes	Yes		Yes				
24. Greece	Yes	Yes					Yes	OTC is legally forbidden
25. Hungary	Yes					Yes	Yes	
26. Italy	No answer							
27. Romania	No answer							
28. Spain	Yes	Yes					Yes	

**Table 3.7.** EU Member States with legal regulations regarding the use of antibiotics without a prescription. (*Source:* Member State survey.)

Member State	Use without a prescription in law	
1. Austria	Yes	Prescriptions only by doctors. Antibiotics only available in pharmacies. Prescriptions required for antibiotics*
2. Belgium	Yes	It is not legal for a pharmacist to provide antibiotics without a prescription
3. Bulgaria	Yes	The Health Act (Ministry of Health of Bulgaria)
4. Croatia	Yes	Antibiotic consumption is not allowed
5. Czech Republic	No	
6. Denmark	Yes	Antibiotics are only sold on prescription by a doctor
7. Finland	No answer	
8. France	No	Nothing more than enforcement of legislation on the prescription-only use of antibiotics
9. Germany	Yes	Antibiotics are drugs which require a prescription
10. Ireland	No answer	
11. Latvia	No	There is no legislation aimed specifically at prohibiting self-medication. However, there is a regulation that lists criteria that define whether medicinal products (drugs) should be distributed as prescription-only medicines. All antibiotics are authorised as a prescription-only medicine
12. Lithuania	No	
13. Luxembourg	Yes	Antibiotics are prescription-only medicines in the country
14. Malta	Yes	Anti-infective agents, including topicals, are prescription-only medicines according to the Medicines Act of Malta
15. Poland	Yes	All antibiotics are available only with a prescription (one exception is fuzaridin. There is a soft recommendation to return leftover antibiotics to pharmacies)
16. Portugal	Yes	Selling antibiotics OTC is illegal, both at the pharmacy and online
17. Netherlands	Yes	Pharmacies are not allowed to dispense antibiotics without prescriptions
18. Slovakia	No	
19. Slovenia	No	
20. Sweden	Yes	It is illegal to sell antibiotics OTC
21. United kingdom	Yes	No answer
22. Cyprus	Yes	It is illegal to sell antibiotics OTC and for pharmacies to dispense antibiotics without a prescription
23. Estonia	No	
24. Greece	Yes	Antibiotics belong on a drug list for which a prescription is mandatory for their procurement
25. Hungary	Yes	Antibiotics are prescription-only medicines. Online shopping is prohibited and antibiotics are categorised as prescription-only
26. Italy	Yes	Good pharmaceutical practice and classification rules for releasing human medical products
27. Romania	Yes	Antibiotics cannot be sold without a prescription at the pharmacy
28. Spain	Yes	The law on the rational use of medicines and medical devices regulates the prescription conditions for medicines. There are also three legal categories of restricted prescription medicines covering hospitals, specialists and the community

Legal provisions for the prescribing of antibiotics: dispensing

The literature review (Section 3.1) showed that in countries where antibiotics are dispensed in whole packages, instead of the exact number of pills prescribed, more people are in possession of leftover antibiotics and the frequency of self-medication is higher.^{16 78}

We assessed how antibiotics are dispensed in the EU Member States (Table 3.8) and found that pharmacists dispense whole packages in 16 out of the 23 Member States who responded to this question. Four did not know and one failed to answer.

We also assessed whether GPs are permitted to prescribe so-called delayed prescriptions. We found that this was possible in 13 Member States (out of 27 responses, Table 3.8). When giving a delayed prescription, the doctor advises the patient to collect the prescription only if symptoms persist or become worse and the objective is to reduce overall antibiotic usage.⁸¹

Table 3.8. Laws and regulations regarding outpatient care across the EU: how antibiotics are dispensed. (*Source: Member State survey.*)

Pharmacists have to dispense the exact number of pills/items/flacons	Pharmacists can dispense incomplete packages	GPs are allowed to prescribe a delayed prescription
Austria	Bulgaria	Belgium
Bulgaria	Estonia	Croatia
Cyprus	Netherlands	Cyprus
Hungary	Poland	Denmark
Netherlands	Romania	Germany
Slovakia	Slovakia	Hungary
Slovenia	United Kingdom	Ireland
United Kingdom		Italy
		Luxembourg
		Malta
		Netherlands
		Sweden
		United Kingdom

Legal provisions for the prescription of antibiotics: OTC sales

Table 3.9 shows whether antibiotics can be purchased OTC at a pharmacy without a prescription from a doctor. All EU Member States indicated that this is either illegal or only possible in some cases — for example in Denmark for creams and vaginal antibiotics.



Legal provisions for the prescription of antibiotics: the internet

Twelve Member States indicated that the internet (see Table 3.9) is an illegal way of acquiring antibiotics in their country. Indeed, a number of respondents indicated that antibiotics can be bought on the internet without a prescription in their own country (seven Member States) or from others (five Member States) ^(j).

Despite these findings, figures from the patient surveys carried out in the ARNA countries, including Estonia, suggest that the internet does not play an important role in providing patients with antibiotics on a regular basis (when patients were asked about where they had obtained the last course of antibiotics without a prescription, internet sources (e.g. e-pharmacies) were hardly ever mentioned in the seven ARNA countries — see 4.3.2).

Comparison of the ARNA countries with the other EU Member States

We could not find any clear differences between the ARNA countries and those countries outside of the project with regard to questions about their 'legal framework'. This suggests that the high levels of non-prescription antibiotic use in the ARNA countries does not appear to be explained by their legal frameworks but due to other factors.

^(j) These are answers provided by the respondents; we were not able to validate those answers

**Table 3.9.** Sales of OTC antibiotics at pharmacies without a prescription from a GP and illegal ways of acquiring antibiotics for the 28 EU Member States. (*Source:* Member State survey.)

Member State	Possible to purchase antibiotics OTC?	Estimate of OTC (%)	Illegal ways of getting antibiotics (e.g. internet or through another country)
1. Austria	No, but there are a couple of exceptions	-	No
2. Belgium	No, it is illegal except for creams, eye drops	0-10 %	Yes, internet
3. Bulgaria	It is illegal, but in some pharmacies it is common	8 %	No
4. Croatia	No, it is illegal (but Tyrosur is available as a gel)	5 %	Don't know
5. Czech Republic	No, it is illegal	5 %	No
6. Denmark	Yes, for specific antibiotics (creams / vaginal drugs)	-	Yes, maybe internet (foreign countries)
7. Finland	No, it is illegal	0 %	Yes, may occur via internet
8. France	No, it is illegal	0 %	Don't know
9. Germany	No, it is illegal	-	Don't know
10. Ireland	No, it is illegal	-	Don't know
11. Latvia	No, it is illegal	-	Don't know
12. Lithuania	It is illegal, but in reality it is possible in some cases	5 %	Yes, via internet, markets (Russia and Belarus)
13. Luxembourg	No, it is illegal	-	Don't know
14. Malta	No, it is illegal	1-5 %	Yes, online, through 'telephone prescribing'
15. Poland	No, but there is one exception (nitrofurantoin)	3 %	No
16. Portugal	It is not allowed, but in some pharmacies it is common practice	5 %	Yes, online/internet
17. Netherlands	No, it is illegal, but in some pharmacies may happen	-	No
18. Slovakia	No, it is illegal	-	Don't know
19. Slovenia	No, it is illegal	0 %	No
20. Sweden	No, it is illegal	0 %	Yes, internet
21. United Kingdom	Yes, for specific antibiotics (eye drops)	0 %	Yes, internet
22. Cyprus	No, it is illegal	-	Yes, illegal dispensing by pharmacists and internet
23. Estonia	No, it is illegal	0 %	Yes, from other countries or illegal internet pharmacies
24. Greece	It is illegal, but in some cases it may happen	-	Online shopping
25. Hungary	Some local antibiotics are available OTC	0-1 %	No
26. Italy	No, it is illegal except for creams, eye drops	-	Don't know
27. Romania	It is illegal, but in some pharmacies it is common	-	Online shopping
28. Spain	No, it is illegal	4 %	No

ARNA countries: numbers 22-28.



3.4.4. National policy measures

National policy measures to enhance the prudent use of antibiotics

Twenty-six Member States indicated that they have started, or, in the case of Latvia, will start, national policy measures to enhance the prudent use of antibiotics in their country (see Table 3.10). Only Slovenia indicated that they have no such policies.

The five most common policy measures are:

- surveillance of resistance and antibiotic use (26 Member States);
- educational interventions (20 Member States);
- media campaigns (19 Member States);
- training of HCPs (17 Member States);
- campaigns for healthcare workers (11 Member States).

Training for healthcare professionals

Training for HCPs — doctors and pharmacists — in good practices regarding the prescription of antibiotics was reported in 21 Member States (see Table 3.11). Malta and the United Kingdom indicated that this was not the case and five countries did not know.

The total number of Member States responding to this question was greater than the previous question (21 versus 17 Member States). This may reflect the nature of the two questions, with one question asking about national policy measures and the other asking a more general question about the existence of training for HCPs.

Do professional bodies publish treatment guidelines?

Twenty-three Member States reported that a professional body in their country publishes treatment guidelines regarding the prescription of antibiotics for the management of infectious diseases (see Table 3.11). This was not the case in Italy and the United Kingdom, but in the later the National Institute for Health and Care Excellence publishes treatment guidelines ^(kk). Three Member States did not know if there were professional guidelines.

^(kk) <https://www.nice.org.uk/guidance?unlid=310756116201461222831>



Table 3.10. National policy measures to enhance the prudent use of antibiotics in the 28 EU Member States. (Source: Member State survey.)

Member State		National policy measures to enhance the prudent use of antibiotics						Strengthen pharmacy regulations
		Media campaigns	Surveillance resistance and use	Educational interventions	Alternative products	Restrictive prescribing	Prevent self-medication (e.g. internet)	
1. Austria	Yes, started		Yes				Yes	Yes
2. Belgium	Yes, started	Yes	Yes	Yes				
3. Bulgaria	Yes, started	Yes	Yes	Yes			Yes	
4. Croatia	Yes, started	Yes	Yes	Yes		Yes		Yes
5. Czech Republic	Yes, started		Yes	Yes				
6. Denmark	Yes, started	Yes	Yes	Yes				
7. Finland	Yes, started		Yes	Yes		Yes		
8. France	Yes, started	Yes	Yes		Yes		Yes	
9. Germany	Yes, started		Yes		Yes			
10. Ireland	Yes, started	Yes	Yes	Yes				
11. Latvia	Yes, near future	Yes	Yes					
12. Lithuania	Yes, started	Yes	Yes	Yes				Yes
13. Luxembourg	Yes, started	Yes	Yes			Yes		
14. Malta	Yes, started	Yes	Yes	Yes				Yes
15. Poland	Yes, started	Yes	Yes	Yes			Yes	Yes
16. Portugal	Yes, started	Yes	Yes	Yes		Yes	Yes	
17. Netherlands	Yes, started	Yes	Yes	Yes	Yes	Yes		
18. Slovakia	Yes, started		Yes	Yes				
19. Slovenia	No							
20. Sweden	Yes, started		Yes	Yes	Yes	Yes		
21. United Kingdom	Yes, started	Yes	Yes					
22. Cyprus	Yes, started	Yes	Yes	Yes		Yes	Yes	
23. Estonia	Don't know							
24. Greece	Yes, started	Yes	Yes	Yes		Yes		Yes
25. Hungary	Yes, started		Yes	Yes			Yes	Yes
26. Italy	Yes, started	Yes	Yes	Yes				
27. Romania	Yes, started	Yes	Yes	Yes	Yes	Yes	Yes	Yes
28. Spain	Yes, started	Yes	Yes	Yes	Yes	Yes	Yes	Yes

**Table 3.10. (cont.)** National policy measures to enhance the prudent use of antibiotics in the 28 EU Member States. (Source: Member State survey.)

Member State	Antibiotic waste	Collaboration with healthcare workers	Campaigns healthcare workers	Training HCPs	Antibiotic stewardship
1. Austria					
2. Belgium	Yes	Yes	Yes	Yes	Yes
3. Bulgaria	Yes		Yes	Yes	
4. Croatia			Yes	Yes	
5. Czech Republic				Yes	
6. Denmark					
7. Finland	Yes			Yes	
8. France				Yes	
9. Germany				Yes	
10. Ireland		Yes	Yes	Yes	Yes
11. Latvia					
12. Lithuania					
13. Luxembourg					
14. Malta		Yes			
15. Poland				Yes	
16. Portugal	Yes	Yes	Yes	Yes	Yes
17. Netherlands		Yes		Yes	
18. Slovakia					
19. Slovenia					
20. Sweden*		Yes	Yes	Yes	Yes
21. United Kingdom					Yes
22. Cyprus			Yes		
23. Estonia					
24. Greece	Yes		Yes	Yes	Yes
25. Hungary	Yes			Yes	
26. Italy		Yes	Yes	Yes	Yes
27. Romania		Yes	Yes	Yes	
28. Spain	Yes	Yes	Yes	Yes	Yes

* Sweden also mentioned the Strama program; ARNA countries: numbers 22-28

**Table 3.11.** Training for HCP professionals — doctors and pharmacists — in good practices regarding the prescription of antibiotics in the 28 EU Member States. (*Source:* Member State survey.)

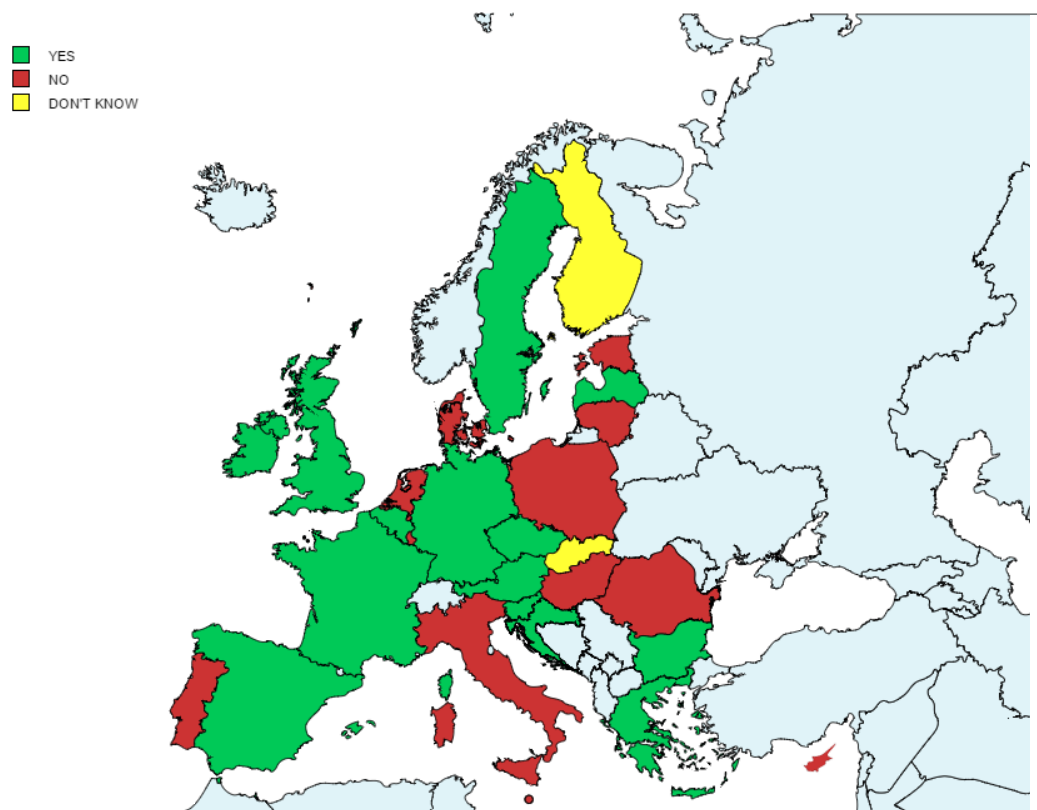
Member State	Training for HCPs	Definition of the training (summary)	Professional body publishing treatment guidelines
1. Austria	Yes	Within education and after education	Yes
2. Belgium	Yes	Reference provided	Yes
3. Bulgaria	Yes	At university and postgraduate education	Yes
4. Croatia	Yes	Croatian symposium on antibiotic resistance	Yes
5. Czech Republic	Yes	Pre- and postgraduate training	Yes
6. Denmark	Don't know	-	Yes
7. Finland	Yes	Prudent use of antibiotics, national treatment guidelines, prescription-only medicines, pharmacists advise patients	Yes
8. France	Yes	Training during their curriculum	Yes
9. Germany	Yes	Courses on antibiotic stewardship	Yes
10. Ireland	Don't know	-	Yes
11. Latvia	Don't know	-	Don't know
12. Lithuania	Yes	There are some training course in universities	Don't know
13. Luxembourg	Don't know	-	Yes
14. Malta	No	-	Yes
15. Poland	Yes	Training for HCPs or recommendations on antibiotic policy and therapy	Yes
16. Portugal	Yes	In-service training provided by local, regional and national AMR structures	Yes
17. Netherlands	Yes	GPs during vocational training and postgraduate courses	Yes
18. Slovakia	Yes	Antibiotic stewardship training, Vienna	Don't know
19. Slovenia	Yes	Postgraduate training since 2010 and different symposia	
20. Sweden	Yes	Educational outreach programmes, antibiotic feedback	Yes
21. United Kingdom	No	-	No
22. Cyprus	Yes	Included in medical and pharmacy curricula	Yes
23. Estonia	Yes	Further education	Yes
24. Greece	Yes	Training for GPs. National public health agency organises mandatory postgraduate seminars	Yes Yes, but for several infections guidelines are lacking and existing guidelines are out of date
25. Hungary	Yes	Postgraduate courses	
26. Italy	Don't know	-	No
27. Romania	Yes	Graduate/postgraduate curricula of medicine and pharmacy students' courses and workshops during national conferences of societies	Yes
28. Spain	Yes	Training is provided by hospitals and healthcare authorities. Education is not well connected and this is being addressed	Yes

ARNA countries: numbers 22-28.

National antibiotic plans

Figure 3.1 presents an overview of whether there is a national antibiotic plan document that sets out activities regarding the promotion of appropriate use of antibiotics, responsibilities, budget and timeline in each Member State. Approximately half of the Member States have a national antibiotic plan (14 out of 28 Member States), but of the seven ARNA countries only two (Greece and Spain) had such a plan in 2015. These figures are lower compared to those in a survey carried out by the European Commission which found that 21 Member States had a national plan (in addition two Member States reported that a plan was under preparation and another two indicated they were carrying out these activities although they have no formal action plans) ⁽¹⁾.

Figure 3.1. National antibiotic plans in the 28 EU Member States. (*Source:* Member State survey.)



A comparison of the ARNA countries with the other EU Member States

Table 3.12 summarises the number of 'national policy measures' for the ARNA and non-ARNA countries. ARNA countries have a national action plan less often than other EU Member States. However, besides that, the ARNA countries have similar policy measures compared to the other Member States.

⁽¹⁾ http://ec.europa.eu/dgs/health_food-safety/amr/docs/amr_projects_3rd-report-councilreprudent.pdf

**Table 3.12.** National policy measures: comparison between ARNA countries and the other EU Member States. (*Source:* Member State survey.)

	Number of countries 'yes' Other 22 MS	Number of countries 'yes' ARNA 6
National antibiotic plan	12	2
Media campaigns	14	5
Surveillance of resistance and use	20	6
Educational interventions	14	6
Restrictive prescribing	6	4
Prevent self-medication	5	4
Strengthening pharmacy regulations	5	4

3.4.5. Surveillance and auditing

The surveillance or audit procedures in outpatient care that target prescribing practices for antibiotics

Twenty Member States reported that they had started, or intended to start, surveillance or audit procedures targeted at antibiotic prescribing practices in outpatient care (see Table 3.13). Five reported they did not have this type of surveillance system (Finland, Germany, Poland, Cyprus and Estonia). In addition, it was not known to exist in Croatia, Romania or the United Kingdom.

Surveillance systems in outpatient care: different HCPs

The Member State survey included questions about the existence of surveillance systems in outpatient care for different HCPs. It found that GPs and paediatricians are the best covered, but systems also exist for pharmacists, dentists and nurses. Sweden stood out as having surveillance systems for all HCPs, but other Member States, such as the Netherlands and Spain, also have extensive surveillance systems.

Surveillance systems in outpatient care: feedback to HCPs

HCPs in 15 Member States receive feedback regarding the results of the surveillance procedures. In two there was no feedback and six did not know. The feedback normally comprises conclusions and recommendations (eight Member States) and a benchmark (five Member States). No feedback was provided from Croatia, Cyprus, Estonia and the United Kingdom.



Table 3.13. Existence of a surveillance or audit procedure among HCPs which targets antibiotic prescribing practices in outpatient care in the 28 EU Member States. (Source: Member State survey.)

Member State	Surveillance or audit procedure
1. Austria	Yes
2. Belgium	Yes
3. Bulgaria	Yes
4. Croatia	Don't know
5. Czech Republic	Intentions to start
6. Denmark	Yes
7. Finland	No
8. France	Yes
9. Germany	No
10. Ireland	Intentions to start
11. Latvia	Intentions to start
12. Lithuania	Intentions to start
13. Luxembourg	Intentions to start
14. Malta	Yes
15. Netherlands	Yes
16. Poland	No
17. Portugal	Yes
18. Slovakia	Yes
19. Slovenia	Yes
20. Sweden	Yes
21. United Kingdom	Don't know
22. Cyprus	No
23. Estonia	No
24. Greece	Intentions to start
25. Hungary	Yes
26. Italy	Yes
27. Romania	Don't know
28. Spain	Yes

ARNA countries: numbers 22-28.

Surveillance systems in outpatient care: other types of surveillance systems

The Member State survey (see Table 3.13) identified many alternative or 'other' surveillance systems investigating factors such as side effects, misuse of antibiotics and OTC sales. They mainly concerned side effects (reported in 17 Member States) and misuse of antibiotics (eight Member States).

Comparison of the ARNA countries with the other EU Member States

The only difference we found between the ARNA and non-ARNA countries with regard to the 'Surveillance and auditing' question was the existence of surveillance or audit procedures in outpatient care. The ARNA countries have less well-developed surveillance systems.

**Table 3.14.** Other national or regional surveillance systems. (*Source:* Member State survey.)

Member State	Other national or regional antibiotic surveillance systems				
	Side effects	Misuse by citizens	Incidents	OTC sales	Other
1. Austria	Yes	Yes	Yes		
2. Belgium	Yes		Yes	Yes	
3. Bulgaria	Yes		Yes	Yes	Yes
4. Croatia	Yes				
5. Czech Republic	Yes				
6. Denmark	-	-	-	-	-
7. Finland	-	-	-	-	-
8. France	Yes				
9. Germany*					
10. Ireland	-	-	-	-	-
11. Latvia	Yes				
12. Lithuania	Yes				
13. Luxembourg					
14. Malta	-	-	-	-	-
15. Netherlands			Yes		
16. Poland*					
17. Portugal	Yes		Yes		
18. Slovakia	Yes				
19. Slovenia	Yes				
20. Sweden	Yes	Yes	Yes		Yes
21. United Kingdom	Yes	Yes		Yes	
22. Cyprus*					
23. Estonia*					
24. Greece	Yes			Yes	Yes
25. Hungary	Yes	Yes	Yes		
26. Italy	Yes		Yes		
27. Romania	Yes		Yes		
28. Spain	Yes	Yes		Yes	

* No surveillance system in place; ARNA countries: numbers 22-28.



3.4.6. Discussion

The Member States survey collected responses from all 28 Member States. The survey showed that they all have a legal framework that prohibits the sale of antibiotics OTC, although a number of Member States (six) report that there are exceptions for topical antibiotics such as creams and eye drops.

Despite the legal framework, a number of Member States reported that patients can obtain antibiotics OTC from pharmacies in their country. When asked about the levels of OTC sales, most Member States indicated it was 0 % or 1 %, with the exception of Belgium (0-10 %), Malta (1-5 %), Poland (3 %), Spain (4 %), Croatia (5 %), the Czech Republic (5 %), Lithuania (5 %), Portugal (5 %) and Bulgaria (8 %). Interestingly, the level of OTC sales may not be as bad as believed by the country experts, as the Eurobarometer findings for 2016 tended to show lower percentages (e.g. the Eurobarometer estimate for Belgium was 3 %, 1 % for Malta, 2 % for the Czech Republic and 3 % for Portugal).

The survey indicated that antibiotics are frequently available over the internet without a prescription, but the ARNA surveys have shown that this is not an important source in the seven Member States that were surveyed (see 4.3.2). Leftover antibiotics and antibiotics obtained from family or friends play a much more important role.

The survey showed that actions are being taken by all Member States to reduce the non-prudent use of antibiotics; but the type and intensity of actions differs by country. Only Slovenia indicated that there were no national measures. The most common measures were 'surveillance of resistance and antibiotic use', 'educational interventions' and 'media campaigns'. Antibiotic stewardship programmes were only reported by eight Member States.

The only clear differences between the ARNA countries and the other EU Member States were: (1) the existence of national antibiotic plans, of which there were fewer among the ARNA countries; and (2) national surveillance systems in outpatient care, of which again there were fewer among the ARNA countries.

Our survey had a number of limitations. First, we were dependent upon the knowledge of the national contact persons. We selected the contact persons carefully, but our survey covered some areas, such as the legal context and regulations, that may not have been fully covered by the respondent's expertise. A second limitation was that a couple of the questionnaires were not fully completed, so we are missing information for some Member States, for example Ireland. These factors may explain why we found fewer Member States had a national antibiotic plan compared to a survey carried out by the European Commission, which found that 21 Member States had a national plan (in addition, two reported that a plan was under preparation and another two indicated they were carrying out these activities although they have no formal action plans) ^(mm).

^(mm) http://ec.europa.eu/dgs/health_food-safety/amr/docs/amr_projects_3rd-report-councilrecprudent.pdf

4. The use of antibiotics without a prescription in seven EU Member States

Main findings

The results are based upon telephone interviews in seven Member States (Cyprus, Estonia, Greece, Hungary, Italy, Romania and Spain) with: 2 601 patients who had used an antibiotic without a prescription over the last 18 months; 712 GPs; and 702 pharmacists.

Patients

- The use of antibiotics without a prescription is still common in Cyprus, Greece, Hungary, Italy, Romania and Spain, but less common in Estonia.
- OTC buying is the most common source for obtaining antibiotics in Romania, Greece and Hungary. In the four other Member States (Cyprus, Estonia, Italy and Spain) most patients make use of antibiotics left over from previous courses. The internet is not an important source for obtaining antibiotics.
- Respondents from Greece and Cyprus are the most convinced that antibiotics can easily be obtained from GPs, pharmacists and members of their social network. Respondents from Estonia, Hungary and Italy are the least convinced.
- Knowledge about antibiotics among patients who use antibiotics without a prescription is lower than among the general population. As such, it is important to educate patients further on antibiotics.

HCPs

- A majority of GPs and pharmacists receive requests from patients to prescribe or dispense an antibiotic even though there is no medical indication. Most GPs and pharmacists do not always fulfil the requests from these patients. Yet some of them sometimes do prescribe or dispense an antibiotic in such cases, mainly because of patient pressure or as a result of shared decision-making with the patient. Pharmacists also fear that customers will go to another pharmacy.
- GPs and pharmacists are aware that the use of antibiotics is a problem in their respective Member States. A majority of the GPs and pharmacists interviewed believe that it is a greater problem in their own Member State than in others.
- Cooperation between pharmacists and GPs on the issue of antibiotic use is limited and could be strengthened.

4.1. Introduction

This chapter provides greater insight into the nature of non-prudent antibiotic use in seven EU Member States. We focus, especially, on the use of antibiotics without a prescription. The Member States we investigated are Cyprus, Estonia, Greece, Hungary, Italy, Romania and Spain. They were selected because they had a relatively high level of antibiotics that are used without a prescription (see also Section 2.4). Three surveys were carried out: one among patients who used an antibiotic without a prescription over the last 18 months, one with community pharmacists and one with GPs. A wide array of topics, all related to the use of antibiotics, were addressed in these surveys (see Section 4.2 and Annex A). The results were used as input for the country-dialogue meetings that were held in the ARNA countries. During these meetings stakeholders in each Member State discussed solutions to address the problem of the non-prudent use of antibiotics (see Chapter 6).



4.2. Methods

Three surveys were carried out between 1 December 2014 and 26 February 2015 by a research organisation in each individual Member State affiliated to the TNS NIPO. TNS NIPO coordinated the surveys. The following surveys were carried out.

- A patient survey in each Member State among a net sample of 400 patients who used an antibiotic without a prescription over the last 18 months (In Estonia 200 citizens were interviewed) (Section 4.2.1).
- A GP survey among a net sample of 100 GPs in each Member State (Section 4.2.2).
- A pharmacist survey among a net sample of 100 community pharmacists in each Member State (Section 4.2.2).

4.2.1. Patient survey

Data collection

Patients were approached for a telephone interview. Those respondents who wanted to participate were asked whether they had used antibiotics over the last 18 months and, if so, whether this was with or without a prescription. Respondents who answered that they either bought the antibiotic without a prescription (antibiotics bought OTC or via the internet) or used antibiotics left over from previous courses were included for further questions. All interviews were held in the national language of the respective Member State. Table 4.1 shows how the respondents were sampled for each Member State and when the fieldwork took place.

The data collection was concluded once 400 respondents had been interviewed who used antibiotics without a prescription. Between 4 000 and 20 000 people were called in each Member State in order to reach this number of patients. Of the 165 694 people who were approached, 65 103 agreed to participate in the survey and 29 647 of them had used an antibiotic over the last 18 months. A total of 2 601 respondents had used antibiotics without a prescription and were therefore involved in the interview. The other 62 502 had not used an antibiotic without a prescription. They were only asked for their age and gender. Appendix X includes a flow chart with more details about the response.

**Table 4.1.** Data collection among citizens in seven EU Member States (telephone interviews).

Member State	Sample selection	Number of interviews	Fieldwork dates		Number of citizens called
Cyprus	Random through telephone numbers	400	3.12.2014	16.1.2015	23 410
Estonia	Random through telephone numbers	200	21.1.2015	26.2.2015	26 780
Greece	Random through telephone numbers	400	15.12.2014	20.1.2015	28 358
Hungary	Random through telephone numbers	400	16.12.2014	23.2.2015	26 688
Italy	Random through telephone numbers	400	3.12.2014	9.2.2015	31 312
Romania	Random through telephone numbers	401	7.1.2015	20.2.2015	11 964
Spain	Random through national telephone number directories	400	9.12.2014	19.2.2015	17 182
<i>Total</i>		2 601			165 694

NB: The coverage for all Member States is national. For Cyprus and Estonia, the sample covers the areas under the control of the Republic of Cyprus and the Republic of Estonia.

Questionnaire

The questionnaire included 34 topics. Firstly, respondents were asked about the last course of antibiotics they had taken without a prescription during the previous 18 months. They were then questioned about where the antibiotic was obtained, the reasons for taking it and the length of the course. The second part of the questionnaire contained questions about potential side effects and information received on how to use the antibiotics in a prudent manner. Thirdly, questions were asked about knowledge and attitudes towards antibiotics. Finally, there were questions about the sociodemographic status of the respondents. This included: gender, age, urbanisation, employment status, educational level, health insurance, the patient's GP, smoking behaviour, perceived health and chronic conditions. The complete questionnaire can be found in Appendix B.

Statistical analyses

Descriptive analyses were performed (frequencies, means).

4.2.2. GPs and pharmacists survey

Data collection

In each Member State, except Cyprus, data from pharmacists and GPs were collected in telephone interviews in the national language. In Cyprus data were collected through face-to-face interviews in Greek. In all Member States, we aimed to achieve a net sample of about 100 pharmacists and 100 GPs interviewed. Tables 4.2 and 4.3 include more information about the data sample selection, the number of professionals approached for an interview and the dates of the fieldwork. It shows that the response rates vary widely between Member States. In Italy and Spain especially the response was low. Response among GPs was lower than among pharmacists.

**Table 4.2.** Data collection from GPs in seven EU Member States.

Member State	Method	Sample selection	Number of interviews	Fieldwork dates		Population
Cyprus	Face-to-face	Randomly selected from Cyprus GP list	100	5.12.2014	13.1.2015	123
Estonia	Telephone interviews	Randomly from full list of Estonian GPs	100	16.1.2015	19.1.2015	214
Greece	Telephone interviews	Own list of the NIPO team	100	16.12.2014	9.1.2015	1 903
Hungary	Telephone interviews	TNS Hoffmann database	111	1.12.2014	15.1.2015	1 560
Italy	Telephone interviews	Sample was selected from the database of the provider	100	15.12.2014	4.2.2015	8 773
Romania	Telephone interviews	Sample was based on the incidence reported by the National Medical College	101	7.1.2015	13.2.2015	147
Spain	Telephone interviews	Random through a list of 11 000 contacts	100	5.12.2014	22.12.2014	4 230
<i>Total</i>			712			16 950

NB: The coverage for all countries is national. For Cyprus and Estonia, the sample covers the areas under the control of the Republic of Cyprus and the Republic of Estonia.

Table 4.3. Data collection from pharmacists in seven EU Member States.

Member State	Method	Sample selection	Number of interviews	Fieldwork dates		Population
Cyprus	Face-to-face	Randomly from the list of registered pharmacies in Cyprus	100	3.12.2014	10.1.2015	120
Estonia	Telephone interviews	Randomly through full list of Estonian pharmacies	100	16.1.2015	19.1.2015	196
Greece	Telephone interviews	Out of the own list of the TNS NIPO team	100	16.12.2014	9.1.2015	487
Hungary	Telephone interviews	TNS Hoffmann database	102	1.12.2014	15.1.2015	363
Italy	Telephone interviews	Sample was selected from the database of the provider	100	15.12.2014	15.1.2015	662
Romania	Telephone interviews	Sample was based on the incidence reported by the National Medical College	100	7.1.2015	13.2.2015	172
Spain	Telephone interviews	Random through a list of 5 000 contacts	100	5.12.2014	22.12.2014	4 837
<i>Total</i>			702			6 837

NB: The coverage for all countries is national. For Cyprus and Estonia, the sample covers the areas under the control of the Republic of Cyprus and the Republic of Estonia.

Questionnaire

The questionnaires for GPs and pharmacists each contained 32 questions. The large majority of the questions were the same but some were different because of the different roles of GPs and pharmacists. Questions included seeking information on: patients who request antibiotics without a prescription; the response to these requests; the reasons patients buy antibiotics without a prescription; the information professionals provide to patients; misconceptions among patients; opinions on the use of antibiotics without a prescription; and possible solutions to diminish this use. Lastly, background information was gathered about age, gender, the year the HCP became qualified and the type of organisation they work in. The complete questionnaires for the GPs and pharmacists can be found in Appendix B.

Statistical analyses

Descriptive analyses were performed to identify frequencies and means. It is important to note that many pharmacists answered 'no' to the question: 'Can patients buy certain oral antibiotics at your pharmacy without a prescription?'. The response rates to some of the subsequent questions are low as the questions were not applicable if the pharmacist did not dispense antibiotics without a prescription.

4.3. The use of antibiotics without a prescription: patients

4.3.1. The frequency of non-prescription use

Respondents who had used antibiotics

Of all the citizens in the seven EU Member States who were interviewed (n = 65 103), almost half (45.5 %) had used oral antibiotics in the last 18 months. Among those who had used antibiotics (n = 29 647), 8.7 % had used them without a prescription. The highest percentages of patients who had used antibiotics without a prescription were found in Greece, Cyprus and Romania. The lowest percentages were found in Hungary and Estonia (Table 4.4). Three quarters of the respondents (75 %) used their last course of non-prescribed antibiotics for themselves, the other quarter for their child (25 %). The number of persons who had used antibiotics without a prescription for their children is highest in Italy (35 %), Spain (29 %) and Hungary (25 %) ⁽ⁿⁿ⁾.

Table 4.4. The number of people approached for an interview and the number of people who used antibiotics without a prescription in the last 18 months (percentage; calculated on the basis of the total number of respondents who used an antibiotic).

Country	Percentage of persons who used an antibiotics without a prescription of all interviewed respondents (n = 65 103)		Percentage of persons who used an antibiotics without a prescription of users of antibiotics (n = 29 647)	
	%	N*	%	N*
Cyprus	11.7 %	3 423	21.3 %	1 882
Estonia	1.2 %	16 779	3.0 %	6 312
Greece	12.0 %	3 330	26.9 %	1 487
Hungary	2.3 %	17 205	5.9 %	6 676
Italy	4.3 %	9 313	8.5 %	4 687
Romania	10.2 %	3 936	26.9 %	2 300
Spain	3.4 %	11 795	6.3 %	6 303

* N for which percentage is calculated.

NB: From now on, all results refer to the respondents who used antibiotics without a prescription as they are the respondents who completed the full interview (n = 2 601).

⁽ⁿⁿ⁾ The figures differ from those in the Eurobarometer data, as the Eurobarometer data ask for the last 12 months, whereas in this survey we asked for the last 18 months.



Among patients who took antibiotics without a prescription themselves, more than two thirds were aware of other antibiotic users in their social environment, such as their partner or family. Around one third of patients in Greece (34 %), Hungary (37 %) and Romania (32 %) were aware of others who use antibiotics without a prescription. Among patients who were aware of antibiotic users in their environment, over half of the respondents mentioned their extended family (56 %) and almost half mentioned their partner (46 %). The partner was most frequently mentioned in Hungary (49 %) and Italy (65 %); in other Member States, this was the extended family (Cyprus (57 %), Estonia (47 %), Greece (71 %), Spain (65 %) and Romania (53 %)).

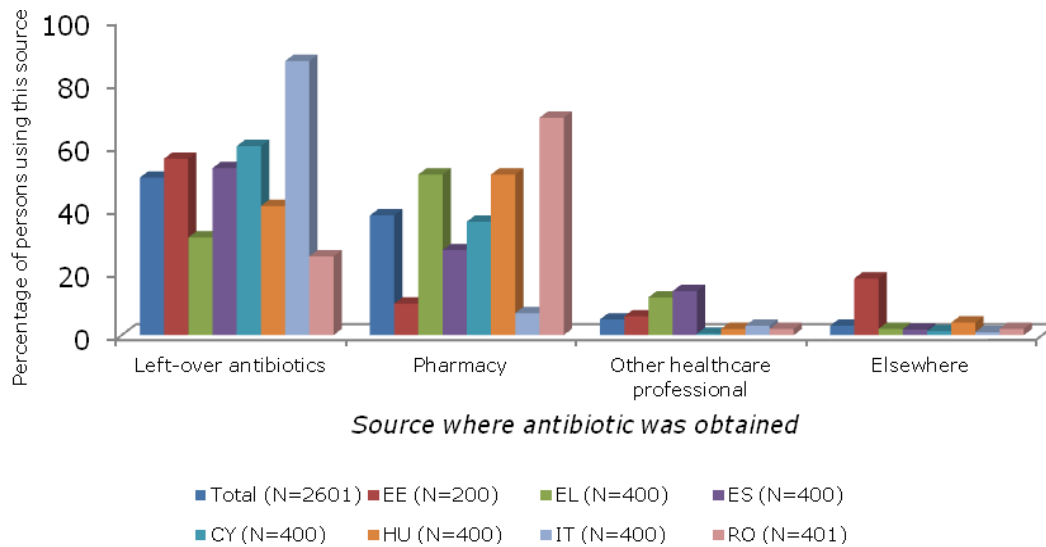
4.3.2. Where do patients get antibiotics without a prescription?

The source of the last course of antibiotics in the previous 18 months

Respondents who used antibiotics without a prescription were asked how they obtained their last course (Figure 4.1). The pharmacy was the most frequently mentioned source in Romania (69 %), Greece (51 %), and Hungary (51 %). In the other Member States most people reported using antibiotics left over from previous courses (Italy (87 %), Cyprus (60 %), Estonia (56 %), Spain (53 %)). Internet sources such as e-pharmacies were hardly ever mentioned (not shown in Figure 4.1). The other sources are: without a prescription from a pharmacy during my holiday in my own country (1.5 %); without a prescription from a pharmacy during my holiday in another country (1.2 %); and without a prescription from a dentist, nurse or other HCP (5 %).

When patients use leftover antibiotics they most frequently use those antibiotics remaining from a previous course (71 %), followed by those remaining from their children's treatment (14 %). Other ways of obtaining such leftover antibiotics are through their partner (4 %), friends (0.5 %) or family (6 %). This trend is the same for all countries.

Figure 4.1. Source from which patients obtained the last course of antibiotics without a prescription in the previous 18 months ^(oo) (as a percentage of all persons who used an antibiotic without a prescription). (Source: ARNA patient survey among users of antibiotics without a prescription.)

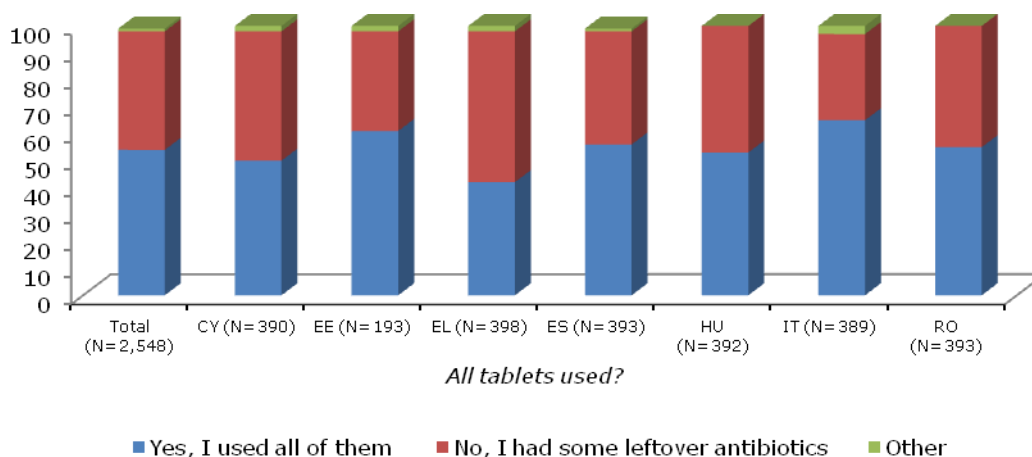


Respondents who store leftover antibiotics

More than half of the respondents from Greece (56 %) reported that they had leftover antibiotics from a previous course (Figure 4.2). In the six other Member States, the percentage of respondents who reported having leftover antibiotics is below 50 %, but is still one third in Italy (32 %) and more than one third in the other Member States.

^(oo) The figure only presents the categories which included more than three per cent of the respondents.

Figure 4.2. Did the patient use all antibiotics dispensed for the last treatment or not? (As a percentage of all persons who used an antibiotic without a prescription.) (Source: ARNA patient survey among users of antibiotics without a prescription.)



4.3.3. Reasons for use and side effects

Patients use antibiotics without a prescription for various reasons. Influenza, the common cold, sore throat, cough, fever and headache are all common reasons to use antibiotics without a prescription (45 % of users). Furthermore, patients use antibiotics on their own initiative for bronchitis (11 %) or urinary tract infections (6 %). Antibiotics are less often used for diseases such as pneumonia (3 %) or skin infections (4 %). There are no major differences between the Member States with regard to the reasons why patients use antibiotics without a prescription.

Side effects of non-prescription antibiotics are experienced by 7 % of all interviewed patients. The highest percentage of patients reporting side effects was found in Italy (8 %), the lowest in Romania (5 %). Because a small proportion mentioned side effects the absolute number of patients per Member State reporting a side effect was low (ranging from 14 in Estonia to 31 in Italy). Therefore, we only provide figures for the total group of patients ($n = 169$). The most frequently mentioned side effect was an upset stomach (33 % of all patients who reported a side effect), followed by diarrhoea (30 %) and allergic reactions (12 %). Rash was mentioned by 5 % of the patients and two patients mentioned having experienced renal failure. It should be noted that 38 % reported 'other side effects' ^(pp). Six patients (4 %) refused to answer the question or did not know.

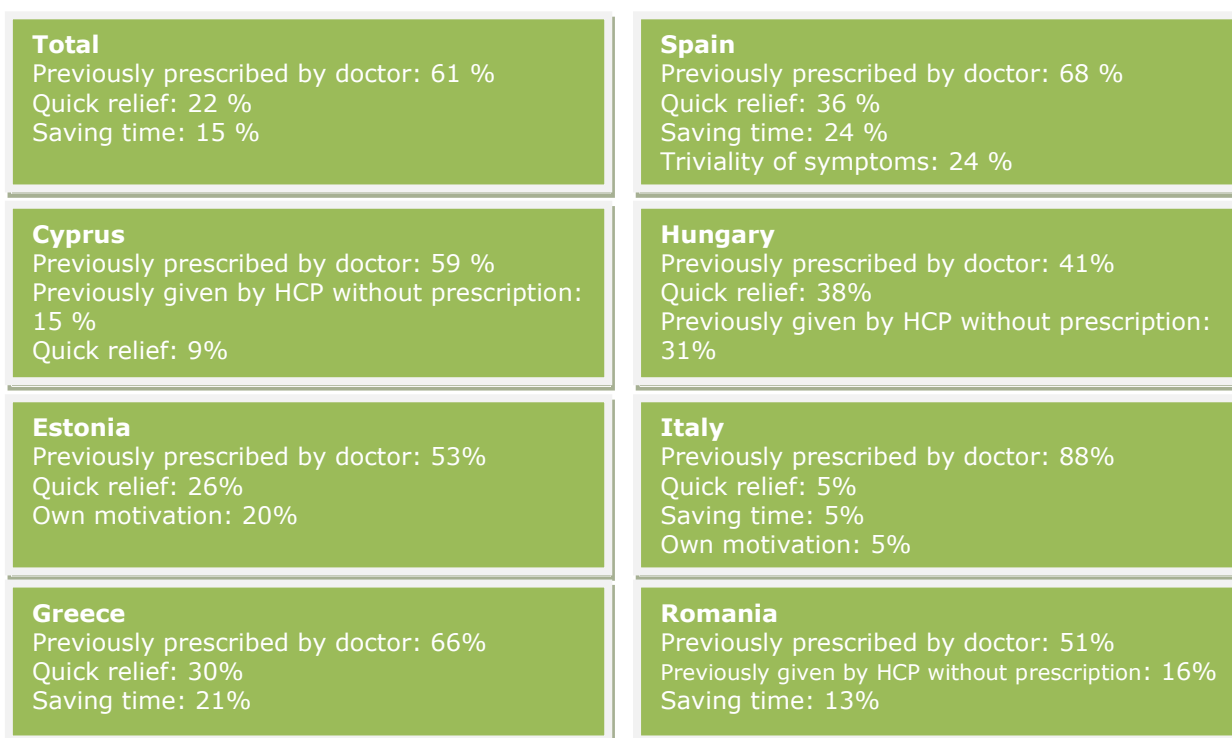
4.3.4. Why do patients self-medicate?

Patients have different motivations for using antibiotics without a prescription (Figure 4.3). The most frequently mentioned is that the same antibiotics were previously prescribed by a qualified doctor (61 % overall). In Italy, the percentage of patients who mentioned this as a reason was 88 %, which is the highest of all Member States. Other important reasons mentioned included an expectation of quick relief (22 %) and saving time instead of first going to the doctor (15 %). In Cyprus and Hungary, respectively 15 % and 31 % of patients indicated that they used leftover antibiotics without a prescription because they were previously provided by a pharmacist or chemist personnel without prescription. In Hungary, almost one quarter

^(pp) These side effects were not further specified.

of patients (24 %) also mentioned that the triviality of their symptoms was a motivation.

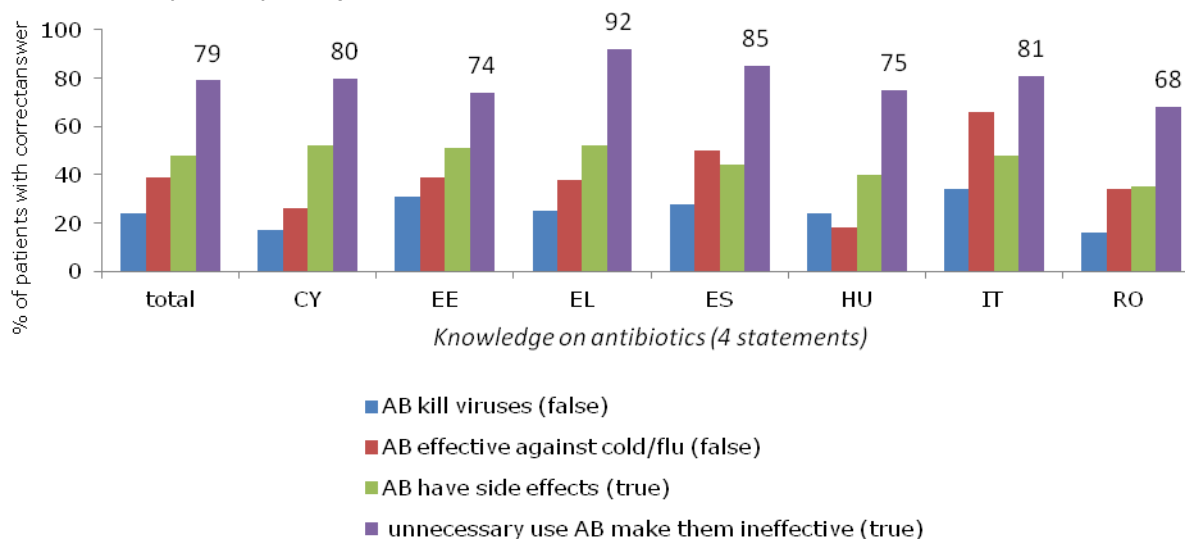
Figure 4.3. Most commonly mentioned motivations for using antibiotics without a prescription by users of non-prescription antibiotics (as a percentage of all persons who used an antibiotic without a prescription). (Source: ARNA patient survey among users of antibiotics without a prescription.)



Does knowledge about antibiotics influence their effectiveness and appropriate use?

The respondents, who had all used an antibiotic without a prescription over the last 18 months, were asked about their knowledge of antibiotics. A minority of the respondents (24 %) knew that antibiotics are not effective against viruses. This is clearly lower than the percentage that was found among the general population in the 2016 Eurobarometer survey. Here 43 % provided the correct answer.⁸ Respondents from Estonia (31 %) and Italy (34 %) most often provided the correct answer. Four out of ten respondents (39 %) correctly knew that antibiotics are ineffective against the flu and colds. Again, this percentage is lower than in the general population as measured in the Eurobarometer (56 %).⁸ A large variation exists between the seven Member States in our survey. In Italy, two thirds of the users of antibiotics without a prescription provided the correct answer, while in Hungary this was only 18 %. There is less variation between Member States concerning the knowledge of side effects such as diarrhoea. Overall, 48 % of the respondents provided the correct answer. This figure was 66 % in the general population in the 2016 Eurobarometer data. In the ARNA survey, Romania stands out. There only 35 % of the users of antibiotics without a prescription correctly knew about side effects. A majority of users of antibiotics without a prescription knew that antibiotics become ineffective when used inappropriately (79 %). This is only slightly lower than in the general population in 2016 (84 %).⁸ In Greece, 92 % of the users of antibiotics without a prescription knew antibiotics can become ineffective if used inappropriately. In Romania this is only 68 %.

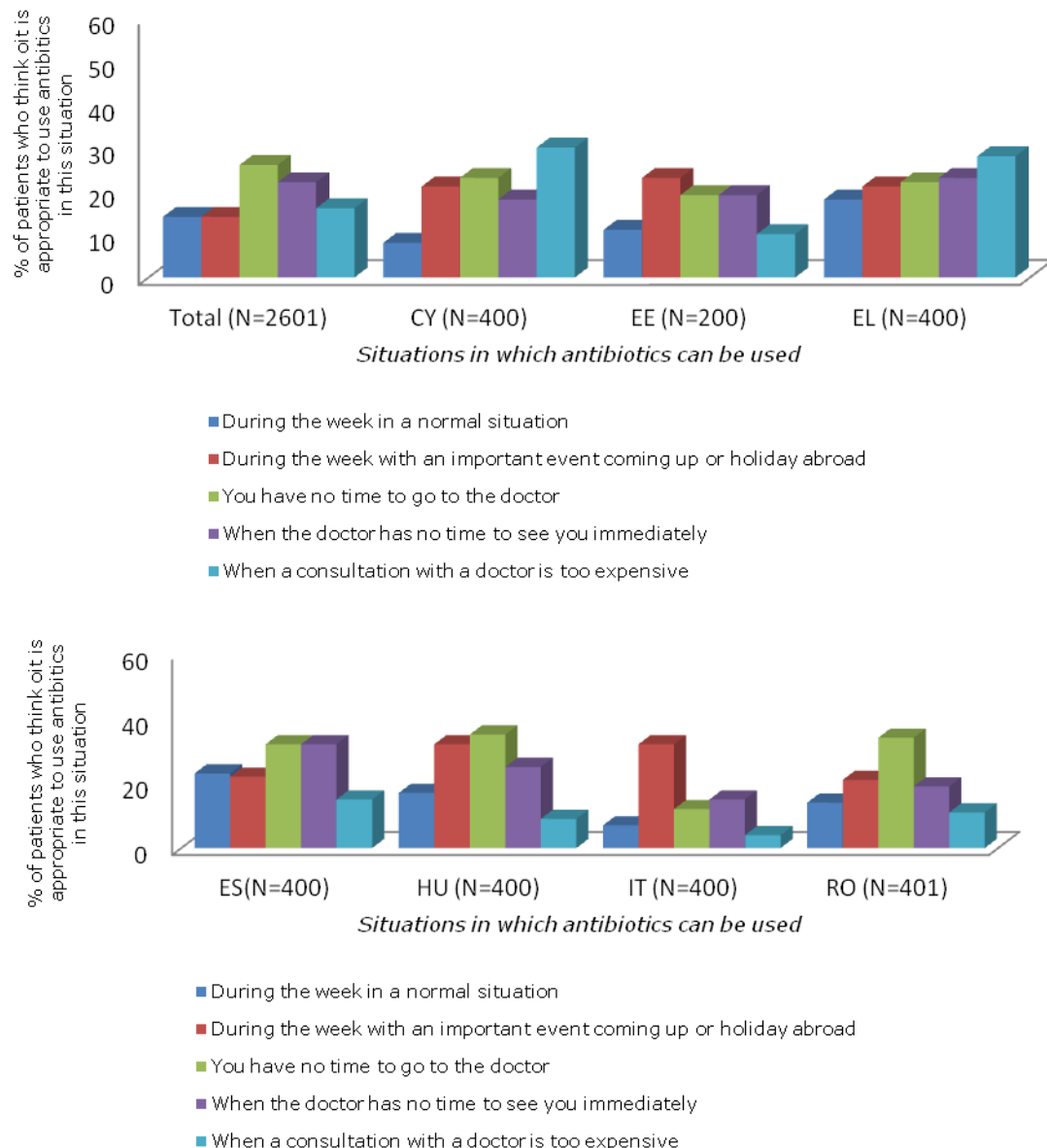
Figure 4.4. Knowledge about antibiotics among users of antibiotics without a prescription: percentage of respondents with correct answer (as a percentage of all persons who used an antibiotic without a prescription). (Source: ARNA patient survey among users of antibiotics without a prescription.)



Can antibiotics treat bronchitis?

Respondents were asked whether, in a variety of situations, they believed it to be appropriate to get antibiotics without a prescription to treat bronchitis. (Figure 4.5). More than a quarter of the respondents thought it is appropriate to get antibiotics for bronchitis in cases where they have no time to go to the doctor (26 %). This percentage was highest in Hungary (35 %), Romania (34 %) and Spain (32 %). For other situations, the opinions of respondents from the different Member States were more specific. In Spain, almost a quarter of the respondents believed it to be appropriate to get antibiotics without a prescription in a normal situation during the week (23 %) and one third believed it to be appropriate in cases where the doctor has no time to see the patient immediately (32 %). One third of respondents from Hungary (32 %) and Italy (32 %) believed it to be appropriate to obtain antibiotics during the week without a prescription when there was an important event coming up or a holiday abroad. Respondents from Cyprus (30 %) and Greece (28 %) think non-prescription use is appropriate when a consultation with a doctor is too expensive. Again, it should be stressed that these figures apply to patients who had used an antibiotic without a prescription over the last 18 months.

Figure 4.5. The use of antibiotics without a prescription for bronchitis in different situations: percentage of patients who think it is appropriate to use an antibiotic in this situation (as a percentage of all persons who had used an antibiotic without a prescription.) (Source: ARNA patient survey among users of antibiotics without a prescription.)

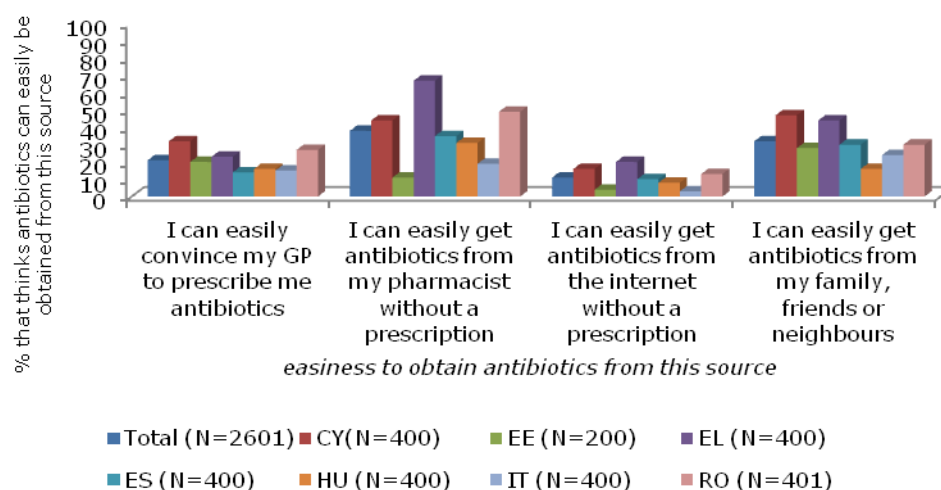


The perceived availability of antibiotics among non-prescription users

Respondents were asked about the availability of antibiotics (Figure 4.6). One in five respondents (21 %) stated that they can easily convince their GP to prescribe an antibiotic. The highest percentage of respondents who stated they can convince their GP is found in Cyprus (32 %). The lowest is found in Spain (14 %), Italy (15 %) and Hungary (16 %). More than one third of all respondents (38 %) agreed that they can easily obtain antibiotics from their pharmacist without having a prescription. This opinion was most strongly held in Greece (67 %), Romania (49 %) and Cyprus (44 %), and least strongly held in Estonia (11 %). The internet is not considered a source from which antibiotics can easily be obtained according to the respondents.

Only one out of ten respondents (11 %) agreed with the statement that antibiotics are easily obtained via the internet. In Greece and Cyprus this percentage was higher than the average: 20 % and 16 % respectively. Family, friends and neighbours are a source where antibiotics without a prescription can easily be obtained according to one third (32 %) of all respondents. Again, in Greece (44 %) and Cyprus (47 %), more respondents than in the other countries state that they can easily obtain antibiotics without a prescription from family, friends and neighbours. In Hungary, for example, this percentage is only 16 %. Overall, respondents in Greece and Cyprus were most convinced that antibiotics can easily be obtained from the different sources, while respondents in Estonia, Hungary and Italy were least convinced. This pattern is in line with the level of antibiotic use without a prescription.

Figure 4.6. Percentage of persons who agree that antibiotics can easily be obtained from different sources* (as a percentage of all persons who used an antibiotic without a prescription). (Source: ARNA patient survey among users of antibiotics without a prescription.)



* Figures include respondents who agreed or strongly agreed with the statement.

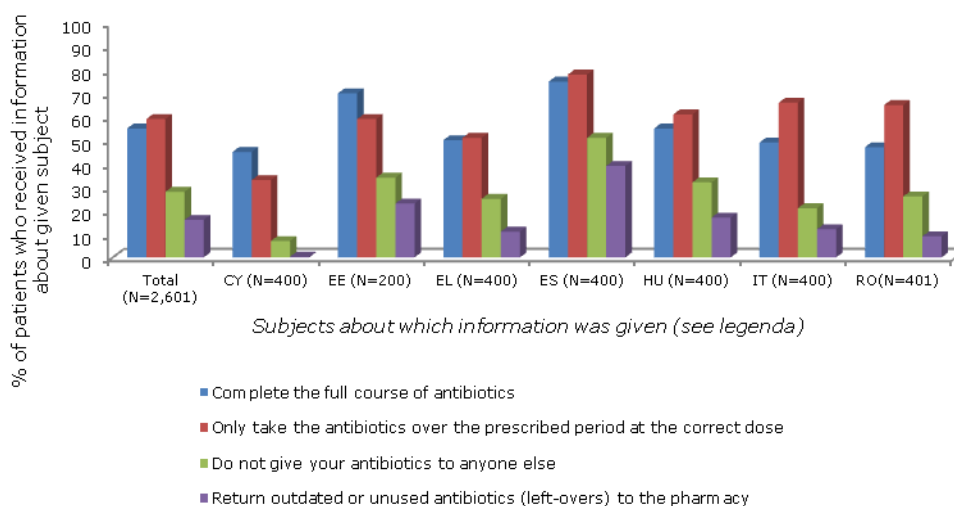
4.3.5. Information provision

The provision of information on how to use antibiotics

Among the respondents who obtained an antibiotic without a prescription, three quarters (74 %) received information about how to use them (Figure 4.7). The number of people who received information was highest in Hungary and Estonia (respectively 83 % and 81 %) and lowest in Greece and Italy (respectively 64 % and 67 %). In Romania this percentage was 79 %, in Spain 76 % and in Cyprus 69 %.

The highest proportion of respondents were instructed about the importance of completing the full course of antibiotics (55 % of all respondents) and the requirement to only take the antibiotics for the prescribed period and at the correct dosage (59 %) (Figure 4.6). About a quarter (28 %) of all respondents were told not to give the antibiotics to others such as family and friends. Only 16 % of all respondents were asked to return unused antibiotics to the pharmacy. For all items, the lowest proportion of respondents who reported being informed about these issues was found in Cyprus and the highest proportion in Spain.

Figure 4.7. Percentage of patients who received information on antibiotics (as a percentage of all persons who used an antibiotic without a prescription) (multiple answer question). (Source: ARNA patient survey among users of antibiotics without a prescription.)



* Figures include respondents who said 'yes' to the statement.

Who provides information?

Half of respondents who obtained antibiotics without a prescription received information about their proper use from a GP. For those receiving them from pharmacy staff, the figure was 43 %. The reason that the GP is the most mentioned source of information may be that respondents have previously obtained an antibiotic from their doctor for the same or another health symptom and as such received information about its use. Sources including other HCPs (9 %), the internet (3 %) or other media (1 %) seem to be less relevant. There were differences between the seven Member States in what the main source of information was. The GP was the most frequently mentioned source of information in Cyprus (57 %), Estonia (53 %), Greece (58 %), Spain (50 %) and Italy (87 %). In Hungary (57 %) and Romania (74 %), pharmacy staff members were the most frequently mentioned source for information.

4.4. Views from GPs and pharmacists

In total, 712 general practitioners and 702 pharmacists were interviewed about the use of antibiotics without a prescription.

4.4.1. The use of antibiotics without a prescription

Over the last 12 months, the majority of GPs (73 %) and of pharmacists (87 %) were confronted with patients who requested oral antibiotics even though these were not indicated for use with their diagnosis (Table 4.5a). The proportion of HCPs with this experience is highest in Cyprus (pharmacists: 98 %; GPs: 89 %) and lowest in Estonia (pharmacists: 53 %, GPs: 39 %).

Table 4.5a. The percentage of GPs who stated they have been asked by patients to prescribe an oral antibiotic for reasons that are not indicated by their diagnosis total and by Member State (as a percentage of all GPs interviewed). (Source: ARNA GP survey.)

	Total	Cyprus	Estonia	Greece	Hungary	Italy	Romania	Spain
Percentage of GPs	73	89	39	97	58	75	86	74
Number of respondents*	711	100	100	99	111	100	101	100

* Total number that answered the question.

Table 4.5b. The percentage of pharmacists who stated they have been asked by patients to deliver an oral antibiotic without a prescription, total and by Member State (as a percentage of all pharmacists interviewed). (Source: ARNA pharmacist survey.)

	Total	Cyprus	Estonia	Greece	Hungary	Italy	Romania	Spain
Percentage of pharmacists	87	98	53	96	82	90	97	98
Number of respondents*	702	100	100	100	102	100	100	100

* Total number that answered the question.

There are also differences between Member States and between HCPs in the average number of patients who had requested oral antibiotics in the last month as estimated by GPs and pharmacists (Tables 4.6a and 4.6b). Pharmacists who reported the highest numbers of patients during the last month are located in Greece (21 patients on average) and Italy (18). GPs in Romania (43) and Spain (34) reported the most requests for an antibiotic when their patient's diagnosis does not indicate prescribing one.

Table 4.6a. The average number of patients per month who, according to GPs, ask their GP for an oral antibiotic for reasons that are not indicated by their diagnosis, total and by Member State (n = 497 GPs). (Source: ARNA GP survey.)

	Total	Cyprus	Estonia	Greece	Hungary	Italy	Romania	Spain
Mean	12.9	10.6	4.3	21.2	6.0	17.6	12.1	10.7
Number of respondents	497	81	36	92	55	74	86	73

Table 4.6b. The average number of patients per month who, according to pharmacists, ask the pharmacist for oral antibiotics without having a prescription, total and by Member State (n = 594 pharmacists). (Source: ARNA pharmacist survey.)

	Total	Cyprus	Estonia	Greece	Hungary	Italy	Romania	Spain
Mean	21.2	14.3	4.0	14.9	3.7	23.8	43.4	34.3
Number of respondents	594	92	50	96	82	88	97	89

Pharmacists who sell OTC were asked which types of antibiotics they sell without a prescription. Table 4.7 shows that amoxicillin is clearly the most dispensed oral antibiotic without a prescription in all Member States. It is dispensed as monotherapy and as combination therapy. Other antibiotics that were frequently mentioned are clarithromycin, ciprofloxacin and azithromycin.

Table 4.7. Top five most-sold antibiotics without a prescription, percentage of by pharmacists who state that they sell over the counter, total and per Member State. (Source: ARNA pharmacist survey.)*

Total (n = 136)	Amoxicillin	89 %
	Amoxicillin and enzyme inhibitor	29 %
	Clarithromycin	22 %
	Ciprofloxacin	17 %
	Azithromycin	15 %
Cyprus (n = 27)	Amoxicillin	93 %
	Amoxicillin and enzyme inhibitor	37 %
	Clarithromycin	22 %
	Ciprofloxacin	26 %
	Azithromycin	22 %
Greece (n = 62)	Amoxicillin	90 %
	Clarithromycin	32 %
	Cefaclor	19 %
	Amoxicillin and enzyme inhibitor	16 %
	Azithromycin	15 %
Italy (n = 13)	Amoxicillin	69 %
	Amoxicillin and enzyme inhibitor	46 %
	Cefixime	8 %
	Ciprofloxacin	15 %
	Clarithromycin	8 %
Romania (n = 26)	Amoxicillin	96 %
	Amoxicillin and enzyme inhibitor	50 %
	Ciprofloxacin	42 %
	Clarithromycin	31 %
	Cefalexin	27 %
	Cefuroxime	27 %
	Sulfamethoxazole-trimethoprim	27 %
	Clarithromycin	27 %

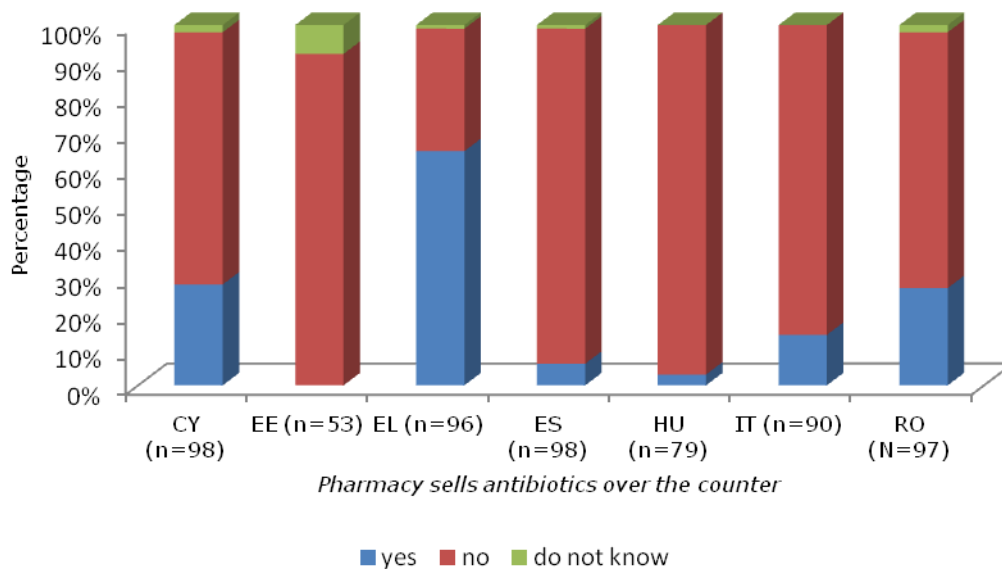
* The number of pharmacists in Estonia, Hungary and Spain was too low to include them in this table but their answers are included in the total group.

4.4.2. Where do patients get antibiotics without a prescription?

Buying antibiotics without a prescription at the pharmacy

Greece is the only Member State where a majority of pharmacists (65 %) indicated that patients can buy antibiotics without a prescription in their pharmacy. In Estonia, all the pharmacists we interviewed indicated that patients cannot buy antibiotics without a prescription. The same was true for a large majority of the pharmacists in the other five ARNA countries (Figure 4.8).

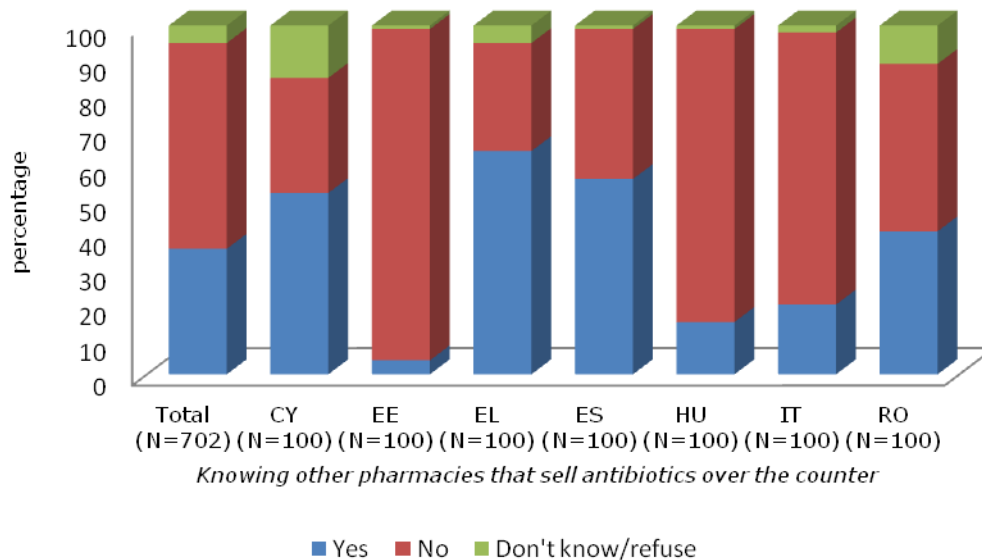
Figure 4.8. The proportion of pharmacists who indicated that customers can buy certain oral antibiotics at their pharmacy without a prescription (as a percentage of all pharmacists; n = 611 pharmacists). (Source: ARNA pharmacist survey.)



The number of other pharmacists who sell antibiotics OTC

Almost half of the GPs interviewed (46 %) stated that they know pharmacists who sell antibiotics without a prescription (Figure 4.9). This percentage is highest in Greece (97 %) and lowest in Estonia (3 %). These percentages are higher than those that pharmacists report about themselves. However, when asking pharmacists about OTC dispensing of antibiotics by other pharmacists, a similar pattern can be seen. They estimate that colleague pharmacists are more often inclined to sell antibiotics OTC (Figure 4.8). More than one third of the pharmacists stated that they know other pharmacists who sell antibiotics OTC (36 %). Again, this percentage is highest in Greece (64 %) and lowest in Estonia (4 %).

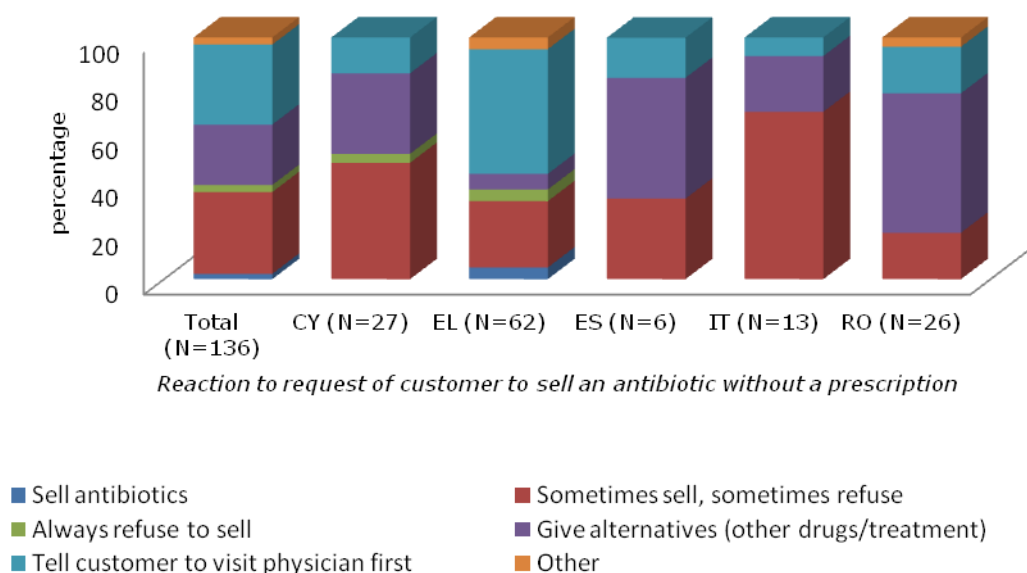
Figure 4.9. The number of pharmacists, total and by Member State, who personally know colleagues in their Member State who sell antibiotics OTC (as a percentage of all pharmacists; n = 702 pharmacists). (Source: ARNA pharmacist survey.)



How do pharmacists react to patients' requests for antibiotics without a prescription?

Pharmacists who indicated that they sometimes sell antibiotics were asked what their principal reaction is to requests from patients who want antibiotics without a prescription (Figure 4.10). One-third (34 %) said that they sometimes do sell them and sometimes do not. One-third (33 %) advise customers to first visit a GP. A quarter (25 %) advise using alternatives. In Cyprus and Italy the most frequently mentioned reaction is to sometimes sell and sometimes not. In Greece, the most frequently mentioned reaction is to advise the customer to go to the GP first, whereas in Spain and Romania it is to provide alternatives for antibiotics. These results should be interpreted with caution, however, given the small number of respondents.

Figure 4.10. The reaction of pharmacists, total and by Member State, to requests from patients for an antibiotic without a prescription^(qq) as reported by pharmacists (as a percentage of pharmacists who sell antibiotics OTC; n = 136 pharmacists). (Source: ARNA pharmacist survey; Estonia and Hungary are excluded from the figure as the number of respondents was fewer than five.)

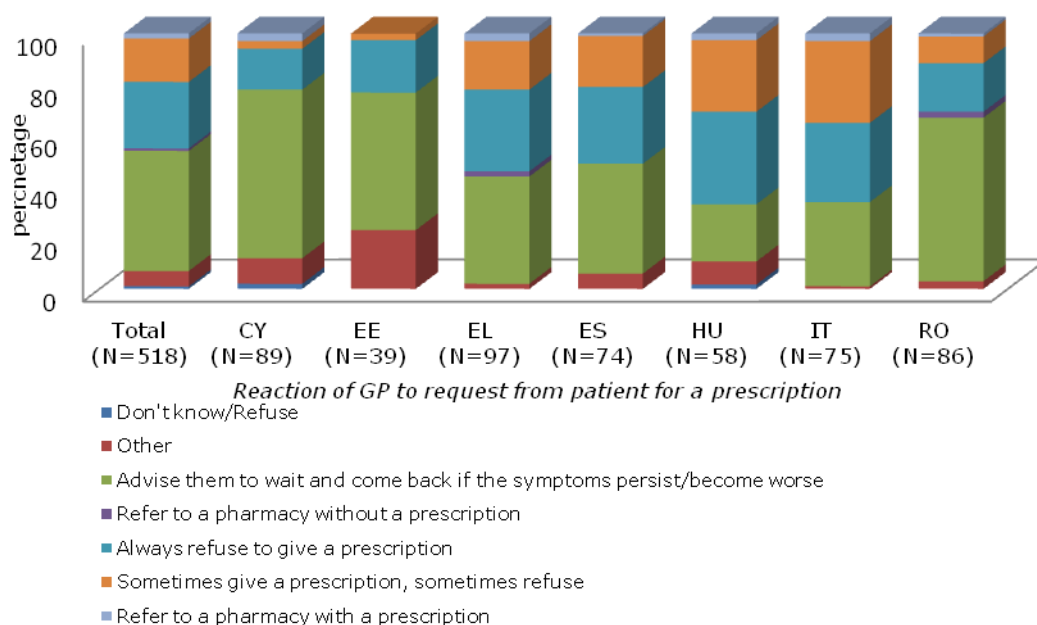


How do GPs react to patients' requests for antibiotics?

GPs were asked what their principal reaction is when a patient asks for a prescription for antibiotics when there is no indication to use an antibiotic (Figure 4.11). The principal reaction of almost half of the GPs (47 %) is to advise the patient to wait and come back if the symptoms persist or become worse. A quarter (26 %) always refuse to prescribe an antibiotic, while 17 % sometimes prescribe an antibiotic and sometimes refuse. In Estonia (54 %), Cyprus (66 %), Romania (64 %), Spain (43 %) and Greece (42 %), the most frequently mentioned principal reaction is to advise the patient to wait and come back if the symptoms continue or become worse. In Hungary and Italy three reactions are equally common. These are: sometimes to give a prescription and sometimes not; always to refuse; and to advise to wait and come back if the symptoms persist or get worse (Figure 4.10).

^(qq) There were no responses from Estonia to this question.

Figure 4.11. The reaction of GPs, total and by Member State, to requests from patients for an antibiotic when an antibiotic is not indicated as reported by GPs themselves (as a percentage of all GPs; n = 518 GPs). (Source: ARNA GP survey.)



Reasons for prescribing or dispensing antibiotics even though there was no medical indication

GPs and pharmacists who prescribed or delivered antibiotics when they were not indicated were asked why they did so. Not all GPs and pharmacists answered this question as not all of them reported prescribing or dispensing antibiotics when not indicated. The results are only presented for Member States where more than 10 GPs or pharmacists responded. For GPs these were: Greece (12); Estonia (16); Hungary (18); and Italy (26). For pharmacists these were: Cyprus (13); Greece (20); and Italy (13). The main reasons given by both GPs and pharmacists for prescribing or dispensing antibiotics while not indicated are pressure from the customer (GPs: 45 %, pharmacists: 39 %) and as a result of shared decision-making with the customer (GPs: 41 %, pharmacists: 45 %). The fear that customers will go to another pharmacy where they would probably get the antibiotics anyway is a reason for 29 % of the pharmacists to sell antibiotics in cases where these are not indicated.

Guidelines

GPs were asked if their colleagues generally adhere to antibiotic prescribing guidelines. Overall, more than two thirds of GPs (68 %) have the impression that their colleagues always, or mostly, adhere to national guidelines. GPs are most confident in Estonia, with 93 % believing that their colleagues always or mostly follow the guidelines. Other Member States where two thirds or more of the GPs think that their colleagues always or mostly follow the guidelines include: Spain (90 %); Hungary (71 %); Romania (70 %); and Italy (67 %). In Greece (45 %) and Cyprus (37 %), fewer than half of the GPs interviewed believe that their colleagues always or mostly follow the guidelines. In Cyprus, 23 % of the GPs interviewed believe that their colleagues do not follow the guidelines at all. In Greece this percentage is 7 %.

4.4.3. Opinions on the use of antibiotics

Pharmacists and GPs were asked about their opinion on five statements regarding antibiotic use. The statement most widely supported is that the use of antibiotics without a prescription increases the risk of antibiotic resistance (Figures 4.12 and 4.13). In almost all Member States over 90 % of pharmacists and GPs agreed with this statement. A majority of pharmacists in all Member States (from 52 % in Estonia to 95 % in Italy) and GPs (from 60 % in Estonia to 98 % in Cyprus) agreed that the use of antibiotics without a prescription is a problem in the treatment of respiratory infections.

Pharmacists and GPs were more divided over whether the use of antibiotics without a prescription is not an issue among the population visiting their respective pharmacies or practices. A majority of pharmacists and GPs in Estonia (80 %/81 %), Hungary (55 %/53 %) and Italy (55 %/64 %) agreed with this statement, whereas a majority of pharmacists and GPs in Greece disagreed (61 %/73 %).

In all Member States except for Estonia and Hungary, the majority of pharmacists and GPs agreed that the use of antibiotics without a prescription is a significant problem in their own Member State. In Hungary, almost half of the GPs and pharmacists thought that the use of antibiotics without a prescription is a problem, whereas in Estonia only a small minority believe there is a problem. GPs and pharmacists were also asked whether the use of antibiotics without a prescription is a significant problem in Member States other than their own. Except for Estonia, GPs and pharmacists in all Member States believe that other Member States have fewer problems than their own when it comes to the use of antibiotics.

Figure 4.12. The percentage of pharmacists (strongly) agreeing with five statements on antibiotic use, total and by Member State (as a percentage of all pharmacists; n = 702 pharmacists). (Source: ARNA pharmacist survey.)

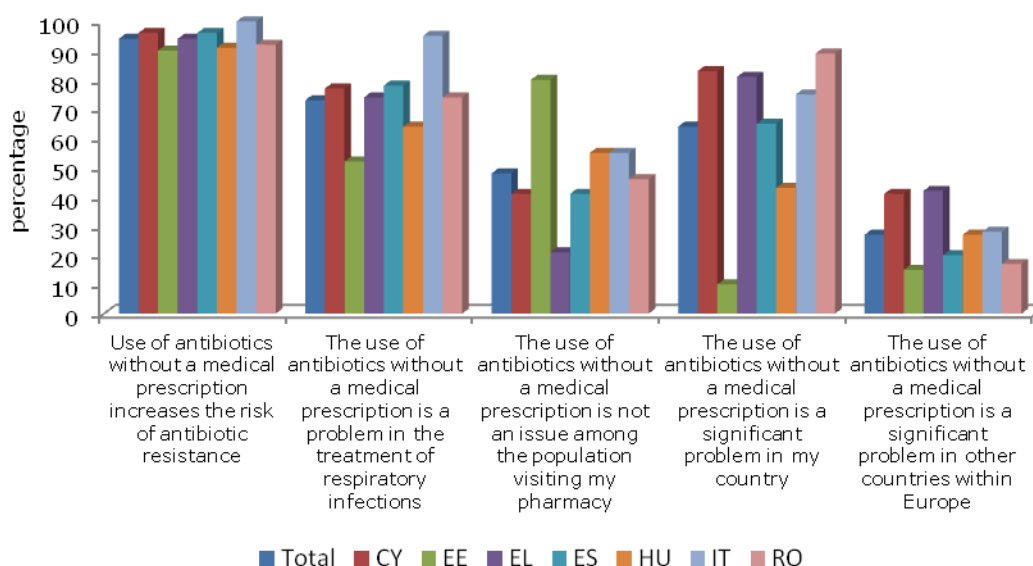
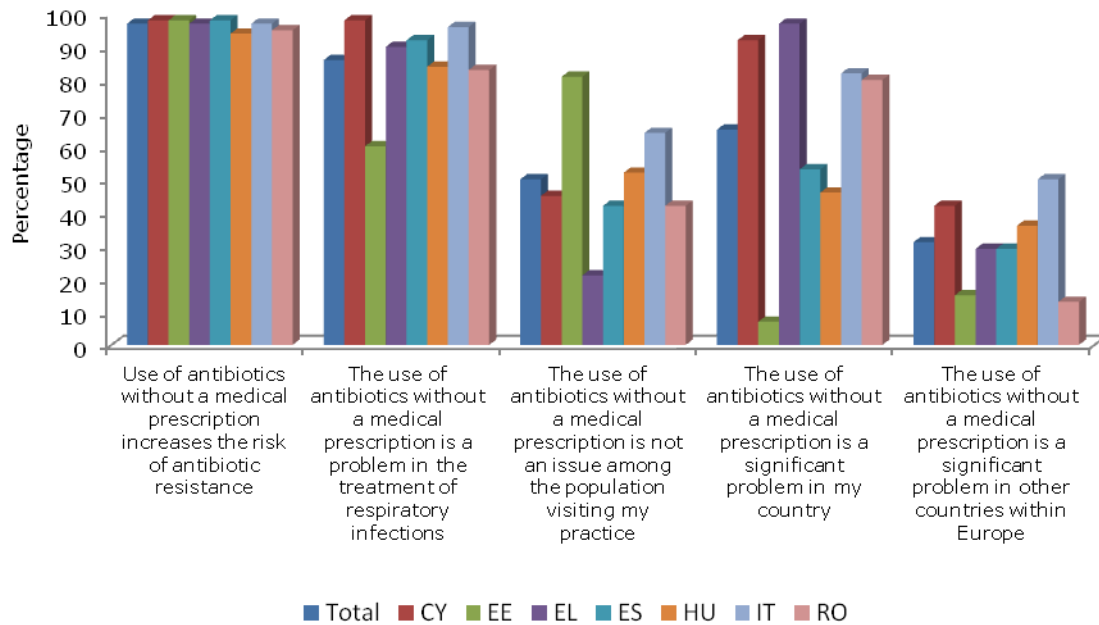


Figure 4.13. Number of GPs (strongly) agreeing with five statements on antibiotic use, total and by Member State (as a percentage of all GPs; n = 712 GPs). (Source: ARNA GP survey.)

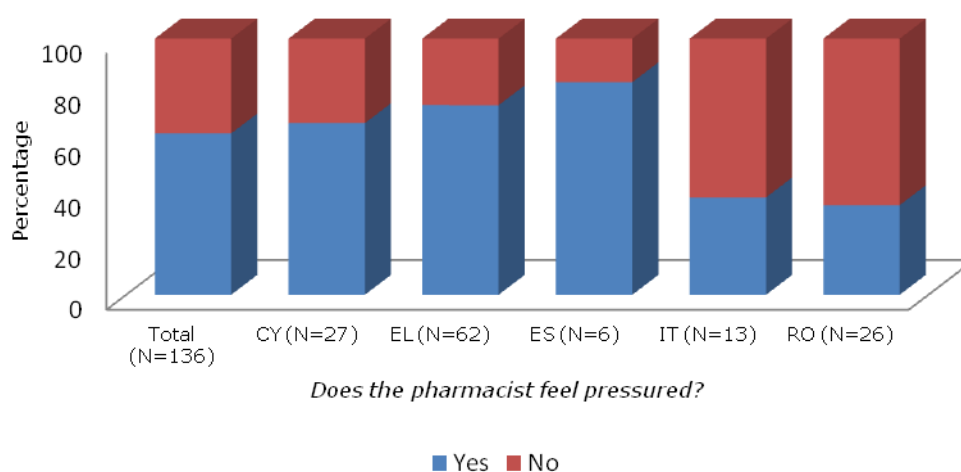


Pressure to prescribe or dispense antibiotics

Pharmacists

In Greece, Spain and Cyprus, a majority of pharmacists who sell antibiotics OTC reported feeling under pressure to do so. In Italy and Romania, a majority of pharmacists who sell antibiotics OTC indicated that they did not feel this pressure (Figure 4.14). Overall, empowered customers (80 %) and the fear that customers will go to another pharmacy (36 %) are the most important reasons for feeling this pressure. This was the case in all Member States.

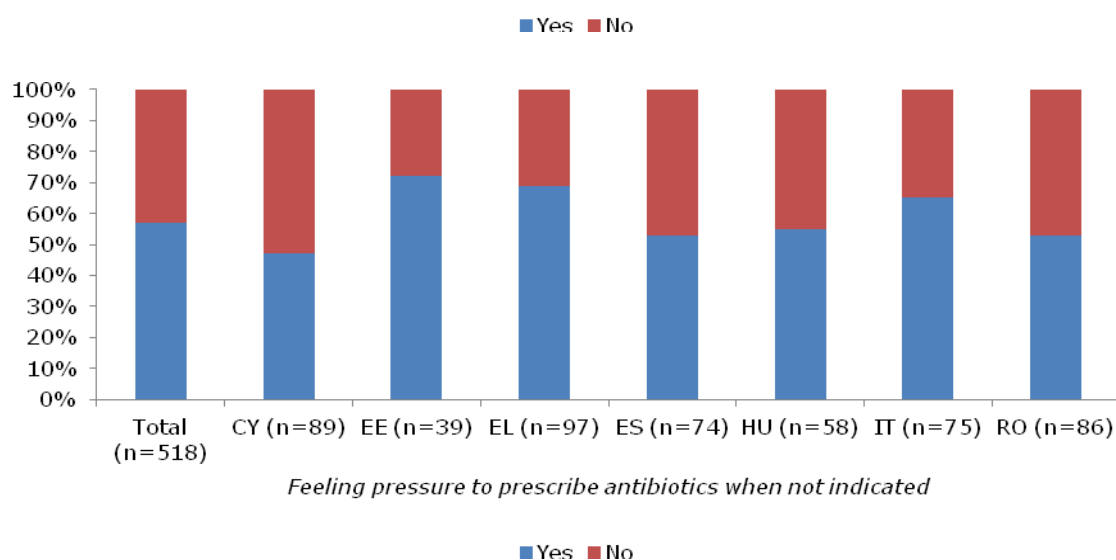
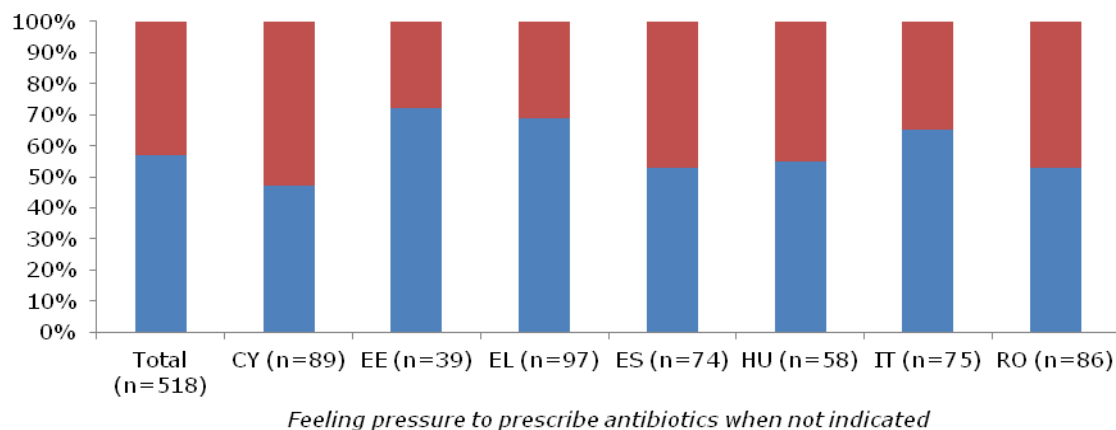
Figure 4.14. The percentage of pharmacists who feel pressured by patients to sell antibiotics without a prescription, total and by Member State (as a percentage of all pharmacist who sell antibiotics over the counter; n = 136 pharmacists). (Source: ARNA pharmacist survey; Estonia and Hungary were excluded because there were fewer than five respondents.)



GPs

A clear majority of GPs in Estonia (72 %), Greece (69 %) and Italy (65 %) reported that they sometimes felt under pressure to prescribe antibiotics when they are not indicated. In Spain (53 %) and Hungary (55 %) just over half of the GPs indicated that they felt the same, while in Cyprus (47 %) and Romania (41 %) slightly fewer than half of the GPs feel this pressure (Figure 4.15). The main reasons for feeling pressured are comparable to those that were mentioned by the pharmacists: empowered patients (63 %) and the fear that patients will go to another GP (18 %).

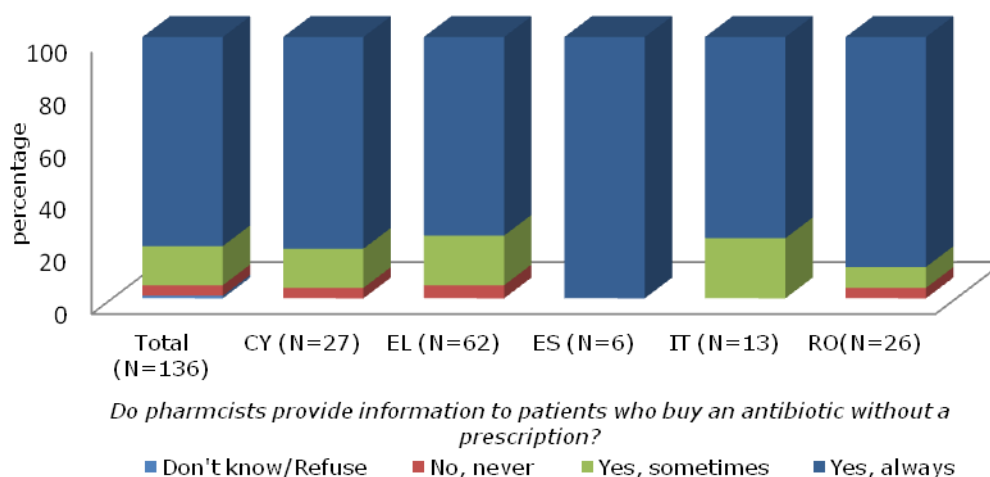
Figure 4.15. The percentage of GPs who feel under pressure to prescribe antibiotics when not indicated, total and by Member State (as a percentage of all GPs; n = 518 GPs). (Source: ARNA GP survey.)



Pharmacists who reported selling antibiotics OTC and all GPs were asked whether or not they feel constraints put upon them in what they can do as an HCP to prevent the use of antibiotics without a prescription. More than half of the GPs (59 %) and pharmacists (52 %; n = 49) stated that they do not feel constrained in what they can do. Among those who feel constrained, the most frequently mentioned reasons were patient pressure (GPs: 50 %; pharmacists: 52 %) and, for pharmacists, the feeling they have to do everything possible to cure the patient (50 %). GPs from Cyprus, Greece and Spain appear to believe that there need to be changes in the behaviour of pharmacists as almost half of these GPs (49 %) feel constrained because of OTC selling of antibiotics by pharmacists.

A majority, 80 % on average, of pharmacists who dispense antibiotics OTC reported that they always provide information about the use and side effects of antibiotics to patients who buy them without a prescription. Only 4 %, on average, say they never provide information (Figure 4.16).

Figure 4.16. Pharmacists providing information to patients who receive an antibiotic without a prescription as reported by pharmacists, total and by Member State (percentage of all pharmacists who sell over the counter; n = 136 pharmacists). (*Source:* ARNA pharmacist survey; Estonia and Hungary excluded because there were fewer than five respondents.)

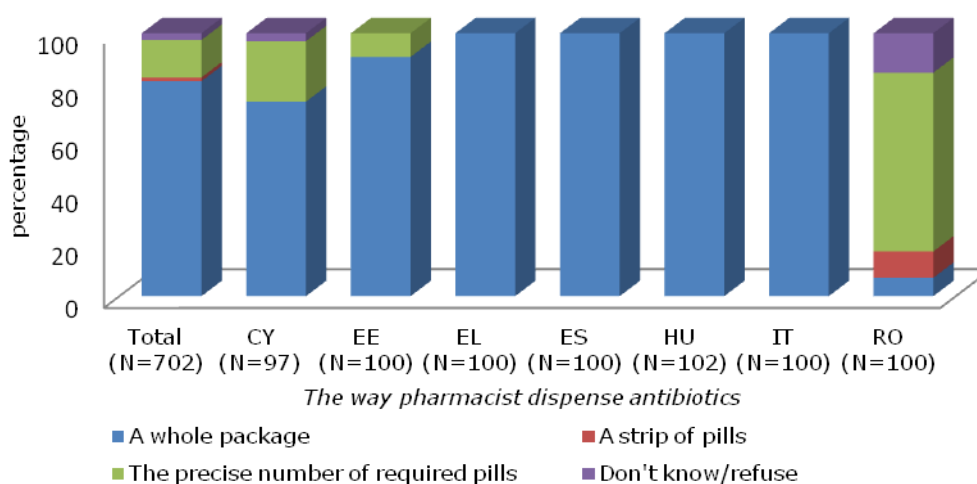


4.4.4. Interventions by GPs and pharmacists

The system of dispensing antibiotics

It was shown in Chapter 3 that in some Member States whole packages of antibiotics are dispensed even when they contain more antibiotics than needed. This is reflected in the answers given by the pharmacists in the surveys. In all Member States, a large majority of pharmacists dispense antibiotics in whole packages. The exception was Romania, where more than two thirds of the pharmacists said they dispense the precise number of prescribed units (tablets, capsules). In Greece, Spain, Hungary and Italy all pharmacists said they dispensed a whole package. In Estonia this was 91 % and in Cyprus 74 % (Figure 4.17).

Figure 4.17. The way pharmacists dispense antibiotics (precise number of pills, strip of pills, whole package), total and by Member State (as a percentage of all pharmacists; n = 702 pharmacists). (Source: ARNA pharmacist survey.)



Professional meetings between HCPs

In all seven Member States where the survey was held a minority of the GPs and pharmacists stated that they collaborate with the other profession. Overall, 3 % of GPs (range 1 %-9 %) and 7 % of pharmacists (range 1 %-18 %) reported participating in a meeting together with the other profession. Having meetings with colleagues from the same profession (only pharmacists or only GPs) is more common. The figure was 20 % among GPs and 17 % among pharmacists.

National campaigns to reduce the use of OTC antibiotics

Four out of ten pharmacists are aware of national campaigns in their Member State to reduce the use of OTC antibiotics. More than half of the pharmacists are aware of such campaigns in Cyprus (56 %), Greece (55 %), Italy (59 %) and Spain (58 %). In the other Member States this percentage is lower: Romania (29 %), Hungary (14 %), Estonia (8 %). For GPs the pattern is the same.

The need to reduce non-prescription antibiotics

The majority of GPs (89 %) and pharmacists (81 %) interviewed believe that patients should use fewer non-prescription antibiotics. Both professions agree that public education is an absolute necessity if this goal is to be attained (GPs: 83 %; pharmacists: 88 %). However, GPs and pharmacists do not agree on other ways to achieve a reduction in non-prescription antibiotics. While GPs consider it necessary to enforce the law by regulating the sale of antibiotics (56 %) and strengthening pharmacy regulations (49 %), pharmacists believe it is more important to prevent self-medication from other sources (54 %) and to provide information on local patterns of antibiotic resistance (54 %).

4.5. Summary and discussion

Chapter 2 showed that, in 2016, between 2 % (Sweden) and 20 % (Greece) of all antibiotics that were used in EU Member States were used without a prescription. The ARNA survey was performed in seven Member States with a relatively high level of non-prescription use of antibiotics. It specifically focused on use without a prescription during the last 18 months. The results showed that in the seven Member States selected, the use of antibiotics without a prescription is still common in all except



Estonia. Purchasing antibiotics OTC is the most common source in Romania, Greece, and Hungary. In the four other Member States (Cyprus, Estonia, Italy, Spain), most people make use of leftover antibiotics from previous courses. The internet is not an important source for obtaining antibiotics.

Respondents from Greece and Cyprus were most convinced that antibiotics can easily be obtained from GPs, pharmacists and members of their social network, while respondents from Estonia, Hungary and Italy were least convinced about this. Influenza, the common cold, sore throat, cough, fever and headache were all common reasons to use antibiotics without a prescription. A previously prescribed antibiotic treatment is the main motivation for patients in all seven Member States to use antibiotics without a prescription.

Knowledge about antibiotics among patients who use antibiotics without a prescription is lower than among the general population (Eurobarometer 2016). In Chapter 3 it is shown that knowledge is an important determinant of antibiotic use without a prescription. As such, it is important to educate patients further about antibiotic use. Pharmacists and GPs can play an important role in this process.

Pharmacists and GPs were also interviewed within the context of the ARNA project, and an important finding was that a large majority are asked by their patients to prescribe or dispense an antibiotic even though there is no medical indication. Most GPs and pharmacists do not always fulfil these requests. As such, they try to avoid irrational use of antibiotics. However, some agree that they sometimes prescribe or deliver an antibiotic in such a situation, mainly because of patient pressure or as a result of shared decision-making with the patient. Moreover, in some Member States pharmacists fear that patients will otherwise simply go to another pharmacy. The surveys also found that GPs and pharmacists are aware that the use of antibiotics is a problem in their respective Member States. Interestingly, a majority of the GPs and pharmacists interviewed believe that it is a bigger problem in their own Member State than in other countries in Europe.

There are some limitations to the surveys, such as the low response rates, especially in the GP and pharmacist surveys (e.g. Estonia). As a non-response analysis was not possible, it is not clear whether the GPs and pharmacists who participated in the surveys are representative of their overall group. Moreover, self-reports are known to sometimes lead to outcomes that are too positive, for example because of a tendency towards providing socially desirable answers. In addition, despite the explanation about what an antibiotic is, we are not sure that every respondent has understood this well, and that they may have confused antibiotics with other medicines. Nevertheless, the findings provide insights into the views of patients, GPs and pharmacists on antibiotics. It also showed that they find antibiotic use without a prescription a problem in their respective Member States. As such, the findings were valuable for the rest of the ARNA project where solutions and interventions were discussed with stakeholders in the country-dialogue meetings (see Chapter 6). For each Member State, factsheets were made with the results from the surveys comparing the results for the country to the overall results for all Member States. It should be noted that Estonia stood out in all three surveys, indicating that the problem of antibiotic use without a prescription was less important than anticipated. On the basis of these results, it was decided that no country-dialogue meeting was necessary in Estonia.

5. Good practices in the EU

Main findings

- Our literature review and EU Member State survey showed a wide variety of interventions that have been implemented across the EU to promote more prudent use of antibiotics.
- Most of the interventions, which have been evaluated and shown to be effective, focus on education and information provision for the general public and HCPs (GPs and pharmacists).
- For HCPs there are other effective interventions, such as providing assistance through technological support tools or guidelines.
- On a policy level, cooperation is important, alongside the creation of local and national committees, stimulating research and monitoring AMR.
- Multifaceted campaigns, comprising a combination of interventions on different levels, implemented simultaneously and repeated over time, have proven to be most effective.
- Despite these findings, effectiveness studies that could provide evidence are lacking for some interventions. There is a need for better-quality evaluation studies.

5.1. Introduction

Member States across the EU are implementing a diverse range of interventions in response to the threat of rising AMR rates. These aim to promote more prudent use of antimicrobial agents. They range from broad multisectoral and multifaceted national programmes to combat AMR to, at the other end of the scale, educational interventions aimed at specific target populations or HCPs.

In this chapter we will provide an overview of the different interventions based on two sources of information: a comprehensive literature review (2000-2015); and a survey of experts in all 28 EU Member States (see 'Methods' below). The interventions will be presented on three levels: (1) patients and the general public; (2) HCPs; and (3) general policy options.

The overall aim of this chapter is to provide an overview of good practices in the EU and to identify what actions Member States can take to reduce the non-prudent use of antimicrobial agents in the EU.

5.2. Methods

5.2.1. Review of reviews

We performed a comprehensive search in Pubmed for systematic literature reviews published between January 2000 and December 2015, with no limit on the language. The search string included the following search terms and their equivalents: (antibacterial agents OR drug resistance OR antibiotic) AND (outcome assessment OR health promotion OR intervention studies) AND (review literature as topic OR meta-analysis as topic) AND (Europe OR Anglo-Saxon countries OR America).

We chose a review of reviews as we wanted to obtain a comprehensive overview of interventions and to avoid unnecessary duplication of effort. The search was restricted to the outpatient setting as the vast majority of antibiotics are prescribed in this setting and the ARNA project had an outpatient focus.



Titles and abstracts were screened by two readers. The first reader extracted data from the publications and these were checked by the other reader. Disagreements were resolved by discussion between the two review authors.

The following information was extracted for each review: first author; year of publication; type of interventions; number of studies included; time period; patient group and main conclusions; level of intervention, such as patient, HCP, healthcare system or EU-wide; specific area; content of intervention; and, if possible, whether the intervention was effective. An intervention was defined as effective if the evaluation showed any influence on the consumption, prescription or dispensing of antibiotics. This could either be a general effect, such as a decrease in the prescribing of antibiotics, or a specific effect, such as a reduction in the mean number of units of a specific antibiotic prescribed.

The PubMed search, carried out from August to December 2015, resulted in a total of 206 hits. Screening of titles and abstracts resulted in a total of eight potentially relevant abstracts. After reading the full texts, one article (Kaki, 2011) was excluded as it only focused on studies within an intensive-care setting. This resulted in a total of **seven relevant reviews** (see Table 5.1).

5.2.2. Member State survey

National contact persons were identified by the ARNA team in all 28 EU Member States. These were mostly people working at ministries of health, national health insurance boards, national institutes of public health and, where applicable, institutes for the rational use of medicines. The people were contacted by email. At a later stage they were also contacted directly by phone.

An online questionnaire included 32 questions covering the following topics.

1. National antibiotic plans.
2. National measures to enhance the prudent use of antibiotics, including laws and legal regulations, national policy measures, surveillance and auditing.
3. Legal provisions for the prescription of antibiotics in each Member State, including laws and regulations regarding outpatient care and the sale of OTC antibiotics.

The Member State survey collected a total of 70 documents and websites related to national policy measures obtained from 15 Member States: Austria, Croatia, Cyprus, Denmark, French, Hungary, Germany, Ireland, Italy, Lithuania, Malta, the Netherlands, Slovenia, Sweden and Spain.

After reviewing the full texts of the documents and websites, 56 documents/websites were considered relevant and provided additional information to the review of reviews.

**Table 5.1.** Characteristics of the seven articles included in the review of reviews on good practices.

Author	Type of interventions	Number of studies	Period	Patient group	Conclusions
Arnold (2005) ⁸²	Interventions to improve antibiotic prescribing practices in outpatient care	79	1966-2000	General population	<ul style="list-style-type: none"> — Simple, single intervention studies (printed educational materials) generally resulted in small, sometimes statistically significant, changes in prescribing behaviour — All studies examining the effect of educational meetings utilising interactive workshops had statistically significant results — The effects of doctors' reminders were mixed and the number of studies too small to draw any clear conclusions — Patient educational materials, along with limited physician education, produced small changes in the prescribing rate of antibiotics for viral respiratory tract infections — Multifaceted interventions involving doctors, patient and community education consistently produced moderate changes in prescribing behaviours — All studies demonstrated that when patients were asked to delay obtaining or collecting an antibiotic prescription, they were much less likely to collect it than those offered an immediate prescription — It appears that interventions aimed at increasing the prescribing of certain recommended first-line antibiotics for specific infections are more likely to produce substantial changes in prescribing than those interventions targeting overall inappropriate antibiotic use
Arroll (2003) ⁸³	Delayed prescriptions	5	1966-2003	Patients with upper respiratory tract infections	<ul style="list-style-type: none"> — There is a consistent reduction in the use of antibiotics in all five controlled trials
Drekonja (2015) ⁸⁴	Effect of outpatient antimicrobial stewardship programmes on prescribing, microbial outcomes and costs	50	2000-2013	General population	<ul style="list-style-type: none"> — Outpatient antimicrobial stewardship interventions of all types were associated with favourable changes in antimicrobial prescribing — Changes in prescribing did not adversely affect patient outcomes or drug costs, although these outcomes were not universally reported — Laboratory testing to aid antimicrobial stewardship, especially procalcitonin and CRP assays, appears to be a promising tool that can be used to decrease antimicrobial prescribing — Efforts to improve provider communication with patients also showed promising results
Holstiege (2014) ⁸⁵	Computer-aided clinical decision support systems (CDSS) for improving antibiotic prescribing in primary care	7	From inception to 2013	General population	<ul style="list-style-type: none"> — Five out of seven trials showed significant effects in improving antibiotic-prescribing behaviour — CDSS show a promising effectiveness in improving antibiotic-prescribing behaviour in primary care



Huttner ⁸⁶ (2010)	Large-scale public campaigns in high-income countries	22	2007-2008	All campaigns focused on respiratory tract infections	—The evaluation of effectiveness is a weak point of numerous campaigns. Several campaigns have not been evaluated and the scope and quality of evaluation of the remaining ones varied greatly
Wang (2015) ⁸⁷	Antibiotic stewardship programmes with a specific focus on France	61	2000-2014 + letters to relevant organisations	General population	—The measures implemented in France and abroad were usually more persuasive than restrictive —The positive impact of the campaigns on antibiotic use was demonstrated. But it is not clear if it was positive in all countries
Wirtz (2013) ⁸⁸	Policy interventions to prohibit OTC antibiotic sales in four Latin American countries	Documents and legislation from the four countries	1995-2009 + review of legislation	General population	—It seems that a more comprehensive set of interventions including the involvement of stakeholders, promoting changes in prescribing behaviour and a public education campaign, can enhance the uptake of the policies. However, the interventions have to be sustained over time

5.3. Good practices on the patient and public health levels

The review of reviews and Member State survey showed that interventions on the patient and public health levels have predominantly focused on providing patients with information and education to increase their knowledge about antibiotics and AMR (see Table 5.2).

Table 5.2. Overview of interventions on the patient and public health levels and source.

		Source
Patient information and education	Patient educational materials ⁸² (information documents, flyers)	Literature
	Combination of pamphlets, posters, website, letters, guidelines, seminars, distribution of cold care kits to administer the correct medication at home (no use of mass media) ⁸⁶	Literature
	Facebook page with information about antibiotics and how to use them properly (see example)	Survey: HR
	School materials for children (see example)	Survey: SE
	Online campaign about antibiotics (see example)	Survey: IT
	Posters for waiting rooms, brochures and handouts focusing on the appropriate use of antibiotics	Survey: DK
	Television spots ⁸⁶	Literature

Example: public health campaign in Croatia – Facebook

Croatia created a Facebook page with information about antibiotics and how they should be used properly.



Source (Croatia): <https://www.facebook.com/reciNEantibioticima?fref=ts>

Example: online public health campaign in Italy

A website was created for an online campaign in the Italian Region of Emilia-Romagna (in the north of Italy) about: 'Antibiotics. It's a shame to use them badly. Effective if necessary, harmful if abused', which consists of posters, brochures and YouTube videos.



Source (Italy): <http://salute.regione.emilia-romagna.it/antibiotici>

Example: EU project – public health campaign for children

The 'e-Bug' project is led by Public Health England's Primary Care Unit and involves a consortium of 28 international partner countries (mostly EU Member States).



Source (United Kingdom): <http://www.e-bug.eu>

5.4. Good practices on the HCP level

The review of reviews and Member State survey showed that various interventions are being implemented on the HCP level to promote more prudent use of antibiotics (Table 5.3).

Table 5.3. Overview of interventions on the HCP level and source.

		Source
Education	Campaigns ⁸⁶	Literature
	Printed educational materials ⁸²	Literature
	Academic detailing ⁸²	Literature
	Educational meetings ⁸⁹	Literature
	Audit and individualised feedback ^{82 84}	Literature
	Communication skill training for providers ⁸²	Literature
	Practical training in the field of antimicrobial stewardship	Survey: AT
Techno-logical support tools	Computer-aided clinical decision support systems ^{84 85}	Literature
	Online resources for information (material available to GP for patient education) ⁸⁷	Literature
	E-learning course about AMR or antibiotic prescribing	Survey: NL, DE
	Online toolkit for responsible use of antibiotics	Survey: NL
	Anti-infection tool IT system: registering antibiotic prescriptions, healthcare associated infections	Survey: SE
Prescribing antibiotics and diagnostics	Delayed prescribing ^{82 84 90}	Literature
	GP charter sign confirming compliance with official recommendations for prescribing antibiotics ⁸⁷	Literature
	Doctor's reminder (offering summary of evidence for prescribing for acute otitis media) ⁸²	Literature
	Documents allowing doctors to help patients who do not speak English (guidance, education, tools) ⁸⁷	Literature
	Rapid antigen testing/C-reactive protein testing/point-of-care tests ⁸²	Literature
Guidelines	Development and implementation of antimicrobial prescribing guidelines with evidence-based recommendations for diagnosis and treatment ⁸²	Literature
	Online guidelines for the treatment of different kinds of diseases	Survey: AT, HR, MT, NL, SE, DK, FR, IE
	Local guidelines and memoranda, adapted to local needs, are produced based on national recommendations	Survey: SE
Professional meetings	Organisation of conferences and meetings with GPs to raise awareness for the need to reduce antibiotic use ⁸²	Literature
Financial incentive	One-off payment (independent of practice performance) ⁸²	Literature
Surveillance	Strengthening control measures and prevention of infections by intensifying surveillance of the implementation of measures by health professionals	Survey: CY
	Strengthen the surveillance of antibiotic consumption	Survey: CY
Financial constraints	A policy of not reimbursing some agents, such as cefuroxime, was implemented to discourage its prescription ⁸⁷	Literature

Educational interventions

We found that EU Member States often target HCPs with a wide range of interventions to stimulate the prudent use of antibiotics (see Table 5.3). Many of the interventions focus on the continuous education of HCPs through, for example, the use of campaigns. This has been proved to have a positive effect.⁸²

Material available to GPs for patient education by country (Wang et al. 2015)

Material available to GP for patient education		
Country	Region, year	Available material
Canada	National, 2010 Regional, 2010	Recommendations, models of delayed prescriptions Recommendations, mobile applications, information for patients in case of otitis and other health symptoms
Ireland	National, 1999 National, 2013	Online recommendations Posters, advice for patients when antibiotics are not prescribed, in case of delayed prescription
Luxembourg	National, 2012	Advice for patients given by the doctor when antibiotics are not prescribed, and in case of viral infection
Norway	Regional, 2006	Articles, recommendations
Sweden	National, 1995	Advice for patients concerning common infections in primary care settings, available in several languages
United Kingdom	National, 2012	Recommendations, training for doctors, advice for patients in several languages
United States	Regional, 1997 Regional, 1995	Training for HCPs, online resources for patients Advice for patients given by the doctor when antibiotics are not prescribed, and in case of viral infection, posters

Feedback on antibiotic prescribing and dispensing is another common intervention. The feedback is provided to give HCPs insight into their own behaviour. Part of the Swedish strategic programme against antibiotic resistance is to give feedback on the personal prescribing patterns of GPs, allowing them to compare their prescribing pattern with their closest colleagues^(rr). The same happens in peer review groups in the Netherlands^(ss).

Technological interventions

Evidence demonstrates the importance of technological support tools for improving antibiotic prescribing and dispensing. Computer-aided clinical decision support systems are popular and effective.^{84 85} Another example is that HCPs can find online support on how to communicate with targeted patient groups.⁸⁷

^(rr) Source: Member State survey, see: <http://strama.se/?lang=en>

^(ss) Source: Member State survey, see: <http://www.medicijngebruik.nl/fto> (in Dutch).

Prescribing and diagnostics

A number of interventions give guidance on antibiotic prescribing. Rapid antigen testing⁸² and delayed prescribing^{82 84 90} especially are seen as effective measures to stimulate more prudent use of antibiotics. The latter is a strategy in which the patient is asked to wait, usually 24 to 48 hours after a visit to a clinic, in order to determine if an antibiotic is needed for an illness. Another example is the signature of a charter by the GP in which he or she pledges to comply with official recommendations for prescribing antibiotics.⁸⁷

Training of GPs/guidelines for good practices by country (Wang et al. 2015)

Training of GPs/guidelines for good practice	
Country	Intervention
United States	Computerised decision aids: these tools help to choose an agent better, rather than decrease the amount of prescribed antibiotics
Denmark, some Canadian provinces (Alberta), United States, Finland, Norway, Sweden	Mobile applications to assist doctors in their practice
Scotland	Courses for HCPs are available on the internet to teach them about antibiotic use and bacterial resistance
The Netherlands	GPs regularly organise peer groups to discuss their prescription profiles with pharmacists
North Carolina (United States), United Kingdom, the Netherlands	Raising awareness among GPs and training them in antibiotic stewardship begins in the course of their studies. Courses on this issue and a final examination have already been implemented

Diagnostic tests by country (Wang et al. 2015)

Diagnostic tests	
Country	Intervention
France, United States, Italy, Luxembourg, Germany, Finland, Norway, Sweden	Recommend use of diagnostic tests to determine whether or not antibiotic therapy is required
Belgium, the Netherlands	Do not recommend any diagnostic tests and antibiotics, except in very specific cases
Ireland	Delayed prescription

Guidelines

Making clear and easily available treatment guidelines available for all HCPs is another intervention that has been identified to promote the prudent prescribing and dispensing of antibiotics.⁸² The guidelines should be kept up to date by using new scientific evidence. They should also be adapted to local needs. Some countries have already integrated this into their national antibiotic plans. For example, the national programme for control of antibiotic resistance in Croatia states that good clinical practice in the use of antibiotics should be promoted. This is to be achieved by developing guidelines based on evidence related to the rational use of antibiotics and through encouraging the adoption of these evidence-based guidelines^(tt).

Guidelines For Antimicrobial Prescribing
In Primary Care In Ireland

Useful Links Background Principles

Home Upper Resp. Lower Resp. Flu Meningitis Urinary Gastro Genital Skin/Soft Tissue Useful Info

In Primary Care In Ireland 2014/2015

Choose a condition above, or press the menu icon on the top right of your screen to start

[Principles for Antimicrobial Prescribing](#)

[About these Guidelines](#)

Aims

- 1 To provide a simple, best guess approach to the treatment of common infections
- 2 To promote the safe and effective use of antibiotics
- 3 To minimise the emergence of bacterial resistance in the community

This site is provided by the HSE and RCPI Clinical Programme on HCAI and AMR Prevention, working with the ICGP. It aims to provide GPs with a quick reference guide to antibiotic prescribing.

Useful Links

Visit the HSE's [Antibiotics Home Page](#).

Visit the [Health Protection Surveillance Centre](#).

Visit the [ICGP website](#).

Visit the [Health Products Regulatory Authority](#) for SPCs for products licensed in Ireland.

Send feedback on these guidelines to antibiotics@hpsc.ie.

Source (Ireland): <http://www.antibioticprescribing.ie>

Other

Further interventions include surveillance and those involving financial incentives to promote evidence-based prescribing. This is the case with Sweden's Strama programme^(uu). Other finance-related interventions involve simply not reimbursing certain antibiotics.⁸⁷

^(tt) Source: Member State survey.

^(uu) <http://strama.se/?lang=en>

5.5. Policy options

The review of reviews and Member State survey showed that a range of interventions are being used on a policy level to promote more prudent use of antibiotics (Table 5.4).

Table 5.4. Overview of interventions on the policy level and their source.

		Source
Regulatory measures	Prohibition of OTC antibiotic sale	Literature
	Enforce nationwide and involve pharmacies in promoting this ⁸⁸	Literature
	Inspections of pharmacies	Literature
	Prohibit the splitting up of packages in order to sell antibiotic pills individually	
	Changes to the financial or healthcare system such as the reform of primary care ⁸²	Literature
Cooperation	Develop, strengthen and maintain intersectoral and international cooperation and commitments	Survey: HR, CY, SE
	Establishment of multidisciplinary networks dedicated to the correct use of antibiotics	Survey: FR, SE, ES
	Political support and involvement of stakeholders and politicians	Survey: SE
Local committees	Local committees to monitor antibiotic use	Survey: CY
	Establishment of local strategic programmes against AMR responsible for such things as the surveillance of antibiotic consumption	Survey: SE
	Development of platforms to exchange information between local and national levels	Survey: SE
	Reimbursement based on performance to encourage, strengthen and intensify the efforts towards promoting patient safety in the county councils	Survey: SE
Improve prudent use	Set national targets for the reduction of antibiotic prescriptions	Survey: FR
	e-Health Agency: pharmaceutical sales statistics, delivered by all registered pharmacies	Survey: SE
	Provide prescribers with an overview of their personal prescribing of antibiotics, conduct analysis of prescribing and draw conclusions on compliance with local treatment recommendations	Survey: SE
	Supervise and monitor the use of antibiotics in order to preserve their effectiveness	Survey: HR
	Collaboration between the public health agency and local laboratories, which enables national and local monitoring with good geographic coverage	Survey: SE
	Encourage professional associations to identify and monitor indicators of rational prescribing or control of sales of antibiotics	Survey: HR
Publicity	Annual report with, for example, data on human surveillance of antibiotic use and resistance	Survey: NL, SE
	The marketing and promotion of antibiotics should not work against the aims of the plan of action. Prescribers of antibiotics should have access to impartial information	Survey: SE
	Exploitation and dissemination of information and knowledge generated	Survey: ES
	Website support, for example with information about campaigns, symposiums, European Antibiotic Awareness Days (EAAD) and other EU initiatives such as e-Bug	Survey: HR, HU, ES

Regulatory measures

Regulatory measures can contribute to more prudent use of antibiotics. Examples include the prohibition of OTC antibiotic sales, together with the inspection of pharmacies and the nationwide enforcement of laws.⁸⁸ In the EU, OTC sales are illegal but the Member State survey showed that countries differ in the extent to which they enforce this law. Another regulatory measure is related to the delivery of the precise number of pills/items/flacons needed for a treatment course.¹⁶

The last point has been assessed in Spain by the national antibiotic plan and it was found to be a complicated issue as it involves a number of changes to the delivery chain (e.g. opening packages, repackaging and adding product instructions), some of which are regulatory (e.g. cutting the blister packages for distribution to patients). Spain has also looked at changing the way primary packages are produced (e.g. packages in different sizes or delivery of large batches plus product instructions), but this is also complicated and poses a number of challenges.

When this point was discussed by the ARNA Expert Group it was noted that there are concerns from pharmacists about opening packages, cutting the blisters and adding product instruction (e.g. it will slow down the dispensing process). Furthermore, pharmacies do not receive reimbursement to print the extra product leaflets and some Member States reported pharmacies do not have the technology to print the product leaflets.

Cooperation

In order to implement interventions, cooperation and collaboration are needed. For instance, international cooperation is needed for pan-European campaigns, while national plans to combat AMR require collaboration from various stakeholders in different sectors such as the healthcare, regulatory and agricultural ones. Additionally, support from relevant stakeholders is important. An important example is the EAAD, which is an annual European public health initiative that takes place on 18 November to raise awareness about the threat to public health of antibiotic resistance and the importance of prudent antibiotic use (see below). This initiative also supports national and local committees and encourages the exchange of information between the local and the national levels^(vv). Furthermore, the Swedish survey results indicated that cooperation between professional associations should be encouraged in order to identify and monitor the indicators of rational prescribing and to control sales of antibiotics^(ww).

^(vv) <http://ecdc.europa.eu/en/eaad/Pages/Home.aspx>

^(ww) Source: Member State survey.

This website is part of the ECDC (European Centre for Disease Prevention and Control) network. See entire ECDC network.

EUROPEAN ANTIBIOTIC AWARENESS DAY A EUROPEAN HEALTH INITIATIVE

English (en)

Plan a campaign | For prescribers | Get informed | Get involved | Campaigns in Europe | News | About

Do not self-medicate with antibiotics

New infographic

Patient stories

EAAD 2015

What is antibiotic resistance?

TWEET #EAAD

#EAAD Tweets

WHAT'S NEW

EU Health Award for NGOs fighting Antimicrobial Resistance launched! 31 May 2016

European Parliament approves plan to prevent unnecessary use of antibiotics in farm animals 16 Mar 2016

Supporting the countries in fighting antimicrobial resistance: WHO manual for national plans and library of best practices 03 Mar 2016

Dutch EU Presidency: Ministerial Conference on Antimicrobial Resistance (AMR) 10 Feb 2016

EAAD 2015
Combating resistance to last-line antibiotics in the EU still a priority

1/6 of Europeans are not aware that the misuse of antibiotics makes them less effective

00:32 HD

What is antibiotic resistance and prudent antibiotic use? How to use antibiotics responsibly?
See patient stories, infographics, videos

Planning a campaign to promote responsible use of antibiotics?
Toolkits with template communication materials aimed at the general public, prescribers in hospitals and primary care

Source (ECDC): <http://ecdc.europa.eu/en/eaad/Pages/Home.aspx>

Supporting prudent use by national stakeholders

The Member State survey showed that national stakeholders, such as professional organisations, the ministry of health or the medicines agency, can support HCPs and patients to enhance the prudent use of antibiotics. Examples include the setting of targets for a reduction in the number of antibiotic prescriptions and to measure adherence to treatment recommendations^(xx). Another example is to provide the infrastructure for monitoring the use of antibiotics both nationally and regionally^(yy). Moreover, policymakers can encourage professional associations to identify and monitor the indicators of rational prescribing and the control of antibiotic sales^(zz).

ANTIBIOCLIC Antibiothérapie rationnelle en soins primaires

Dernière Màj : 30/06/2016

NOUVELLE RECHERCHE | SOURCES | ACTUALITÉ | À PROPOS | CONTACT

* Les IST et les infections urinaires de la femme enceinte ont été mises à jour *

RECHERCHE ANTIBIOTIQUE

Domaine anatomique

Choisissez ...

Pathologie

Choisissez ...

CHERCHER

Modifications récentes

Oite moyenne aiguë - 30 juin 2016

Cystite - 14 avril 2016

Colonisation urinaire - 14 avril 2016

En préambule

ANTIBIOCLIC est un outil indépendant d'aide à la décision thérapeutique en antibiothérapie, pour un bon usage des antibiotiques.

Ce site est à usage des professionnels de santé.

Son contenu suit les dernières recommandations françaises en vigueur.

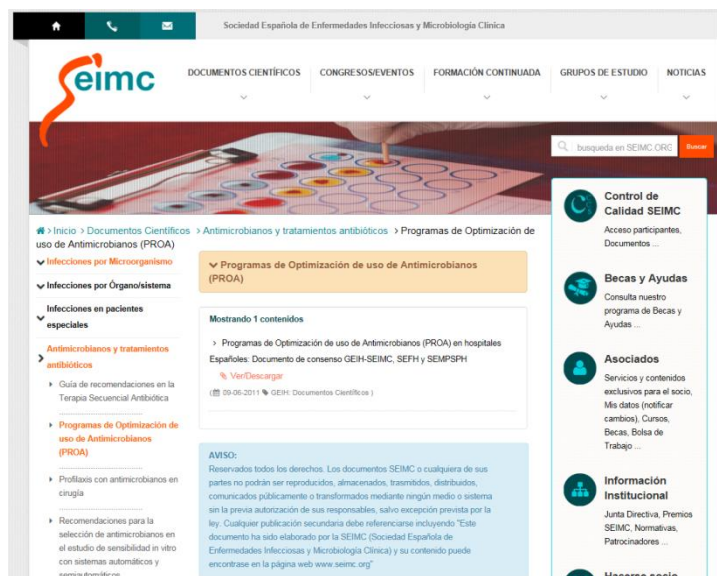
Le contenu du site ne se substitue pas à la responsabilité de prescription du médecin.

Source (France): <http://antibiocllic.com/>

^(xx) E.g. <http://strama.se/about-strama/?lang=en>; <https://guidelines.nhg.org/>

^(yy) E.g. <http://www.eurosurveillance.org/viewArticle.aspx?ArticleId=19036>

^(zz) E.g. <http://fingertips.phe.org.uk/profile/amr-local-indicators>



Source (Spanish Society of Medical Microbiology):
http://seimc.org/documentoscientificos.php?mn_MP=3&mn_MS=117

Public health campaigns

Public health campaigns can contribute to the raising of awareness of the problem of AMR (see example below).⁸⁶ Annual surveillance data can also be published in order to help raise awareness.⁹¹

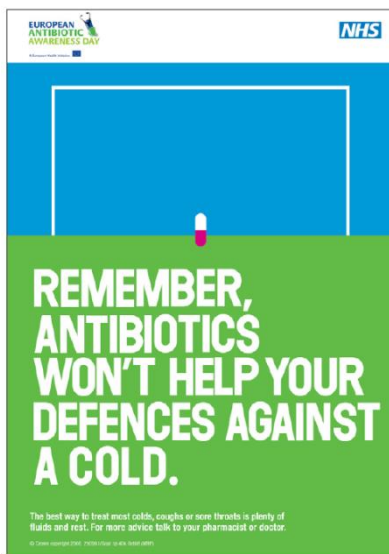


Figure 1: Poster of the English campaign
Source (United Kingdom): Huttner et al. 2012

5.6. Multifaceted interventions

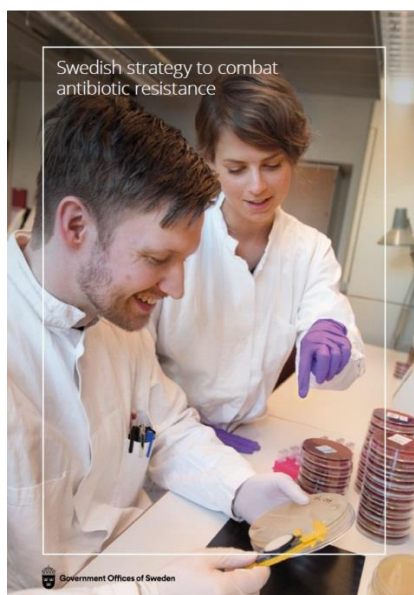
One important finding from the review of reviews is that multifaceted campaigns with their interventions on both the patient or public health level and the HCP level are more often effective. Examples include:

- the combination of printed educational materials for both doctors and their patients, together with educational meetings led by opinion leaders;
- the combination of group discussions on guidelines, training in communication skills and providing information regarding C-reactive protein (CRP) testing;⁸⁴
- the combination of at least four interventions in the areas of pamphlets and posters, print media, billboards, radio, television, websites, letters, guidelines, academic

detailing or educational outreach, seminars and individual feedback about prescribing behaviour.⁸²

An example of a Member State where multifaceted interventions are implemented is Slovenia, where there have been a number of activities in which the Ministry of Health, the National Committee for the Rational Use of Antimicrobials and academic units are involved. The focus is on four areas: education, engineering, economics and enforcement. They target patients and HCPs with interventions in each of these four areas (^{aaa}).

Having a national action plan can often clarify the roles of each organisation or individual, encourage work in an multifaceted manner and establish clear targets (see example below for Sweden).



Source (Sweden): <http://strama.se/wp-content/uploads/2016/06/swedish-strategy-to-combat-antibiotic-resistance-1.pdf>

5.7. The effectiveness of the interventions

Evidence regarding the effectiveness of the interventions was often weak because they were not, or were not properly, evaluated. Furthermore, the quality of the published studies varied greatly.⁸¹ In addition, studies provided limited information on the sustainability of interventions or whether they could increase in size to accommodate a growing amount of work.

There is a need to have better knowledge about the effectiveness of interventions.⁸¹ This will help decisions on whether an intervention should be implemented or continued. One area where there was an important lack of evidence of effectiveness was the healthcare-system level.

(^{aaa}) Source: Member State survey.

5.8. Summary and discussion

The review of reviews and the Member State survey showed that a large number and variety of interventions have been initiated across the EU to promote the prudent use of antibiotics, of which some examples are summarised in the box below. The interventions range from fully coordinated activities within a national antibiotic plan to combat AMR, to actions aimed at certain groups, such as healthcare workers, or even smaller interventions targeted at specific populations, such as children.

It is difficult, however, to be sure whether many of the interventions are effective. This is because many of the interventions have not been properly evaluated, especially those on a healthcare-system level. This, therefore, is an area that requires further attention. However, we found that many initiatives exist, and Member States across the EU can learn from each other in order to better develop activities that will promote the prudent use of antibiotics in each of them.

Box 5.1. Examples of good practice across the EU.

Patient level

- **Croatia** created a Facebook page with information about antibiotics and how they should be used properly.
- The **Italian** region of Emilia-Romagna (in the north of Italy) held an online campaign about: 'Antibiotics. It's a shame to use them badly: effective if necessary, harmful if abused', which consists of posters, brochures and YouTube videos: <http://www.salute.regione.emilia-romagna.it/antibiotici>
- The e-Bug project is led by Public Health England's Primary Care Unit and involves a consortium of 28 international partner countries (mostly **EU Member States**): <http://www.e-bug.eu/>

HCP level

- **The Netherlands** has a strong system of peer review groups where GPs and pharmacists meet to discuss pharmacotherapy. Those groups strengthen the cooperation between GPs and pharmacists: <https://www.medicijngebruik.nl/fto>
- The **Swedish** strategic programme against antibiotic resistance (Strama) includes feedback on the personal prescribing patterns of GPs, allowing them to compare their prescribing pattern with their closest colleagues, for example to avoid over-prescription: <http://strama.se/?lang=en>

Healthcare-system level

- The European Antibiotics Awareness Day is an annual **European** public health initiative that takes place on 18 November to raise awareness about the threat to public health of antibiotic resistance and the importance of prudent antibiotic use: <http://ecdc.europa.eu/en/eaad/Pages/Home.aspx>

Multifaceted

- In **Slovenia** there have been a number of activities in which the Ministry of Health, the National Committee for the Rational Use of Antimicrobials and academic units are involved. The focus is on four areas: education, engineering, economics and enforcement. They target patients and HCPs with interventions in each of these four areas.
- In **Spain** the national antibiotic plan was introduced in 2014, with its main aim being to enhance the prudent use of antibiotics using a One Health approach. As such, a lot of initiatives are already developed in Spain. The national antibiotic plan is coordinated by the Medicines Agency (AEMPS).

6. Expert opinions and consensus statement on policy options

The main findings of the expert meeting

Twenty experts discussed and agreed a set of interventions that could reduce the use of antibiotics without a prescription in EU Member States:

Public health campaigns

- There is a need to implement multifaceted interventions that are evaluated correctly.
- It is important to take into account people's health literacy.
- Messages in mass-media campaigns should be consistent with information from pharmacists and GPs.

HCPs

- Efforts should be made to strengthen collaboration between HCPs, and especially between GPs and pharmacists.
- Rapid diagnostic tests such as those performed at the patient's bedside, rather than in a laboratory, could help, but more research is needed to assess their integration into outpatient care.

Policy options

- National antibiotic plans or national plans to combat AMR help support activities in the field and the prudent use of antibiotics.
- Where OTC sales are occurring in EU Member States, enforcement practices need to be strengthened. The use of sanctions, positive or negative, needs to be considered, but positive incentives are preferable.
- It is advisable that antibiotic packages be tailored to the course of treatment. This, however, would be a complicated issue for countries to address and implement, as it will require a number of regulatory modifications because the legal framework would need to be adapted.
- The length of time that antibiotic prescriptions are valid should be shorter than is traditional, as this would help avoid the misuse of antibiotics.
- Appropriate use of delayed prescribing should be encouraged.

6.1. Introduction

We gathered 20 experts from nine EU Member States. One was representing a European organisation — the Pharmaceutical Group of the EU — and two were from countries outside of the EU — Norway and Switzerland. They discussed and agreed a set of interventions that could reduce the use of antibiotics without a prescription in EU Member States.

The experts reviewed four types of interventions.

1. Public health campaigns.
2. Interventions among HCPs.
3. Interventions on the health policy level.
4. EU interventions.

In this chapter, we provide a summary of the findings for each type of intervention.

6.2. Methods

The ARNA team organised a one-day expert meeting on 30 October 2015. It included 20 experts from around Europe. The objective of the meeting was to discuss and agree a set of interventions based on the literature review of reviews (Chapter 5), to complement that set with other policy measures and interventions that are based on expert opinion and to decide upon the interventions that are considered most feasible to be implemented in EU Member States.

A total of 16 experts were invited to participate in the meeting. Invitees were scientific experts and policy advisors with expertise in prudent use of antibiotics in outpatient care. Of the 16 invitees, three were not able to attend the meeting. Suitable replacements were searched for and an additional expert (from Spain) was proposed and invited. Eventually, apart from the research team, 15 experts from 11 European countries participated; the Netherlands (three), Switzerland (one), Norway (one), Hungary (one), Denmark (one), France (one), Italy (one), Poland (one), Spain (three), Belgium (one) and the United Kingdom (one).

The meeting included four sessions according to the levels of interventions (patient, professional, healthcare system, EU). Each session started with an introduction to the area and a presentation of the findings from the literature review, followed by a thorough discussion about the content of the presentation (e.g. used methods and generalisability to other countries) and the pros and cons of interventions to stimulate more prudent use of antibiotics in the outpatient setting.

At the end of the meeting a consensus statement was drafted and presented to the experts to agree upon. A consensus statement is defined as a comprehensive summary of the opinions of an independent panel of experts, usually multidisciplinary, about a particular scientific or medical issue^(bbb). Its aim is to advance the understanding of an issue and to provide guidance to healthcare professionals. After the meeting the consensus statement was circulated for approval to all experts.

Participating experts

External: Ria Benko (Hungary), Lars Bjerrum (Denmark), Robert Cohen (France), Céire Costelloe (United Kingdom), Cesar Hernandez García (Spain), Benedikt Huttner (Switzerland), Siri Jensen (Norway), Przemyslaw Kardas (Poland), Antonio López (Spain), Carl Llor (Spain), Wim Opstelten (the Netherlands), Annalisa Pantosti (Italy), Anja Schreijer (the Netherlands), Theo Verheij (the Netherlands), Jamie Wilkinson (Belgium).

ARNA team: Liset van Dijk (NIVEL), John Paget (NIVEL), Anna de Jong (NIVEL), Ann Versporten (University of Antwerpen), Dominique Lescure (NIVEL), Francois Schellevis (NIVEL, chair)

^(bbb) *Miller-Keane Encyclopedia & Dictionary of Medicine, Nursing, & Allied Health*, seventh edition, 2003; <http://medical-dictionary.thefreedictionary.com/consensus+statement>

6.3. Public health campaigns

Expert opinions – main conclusions

- Public health campaigns should be integrated into multifaceted interventions that are evaluated correctly.
- Interventions should be tailored to a country's specific profile and to specific target groups.
- Patients should be educated about when to consult their doctor or pharmacist and when an antibiotic is appropriate.
- People's health literacy should be taken into account. Messages should be framed in such a way that patients remember and learn the right information.
- Mass-media messages should be consistent with information and be supported by pharmacists and GPs.

A first set of interventions that was discussed during the expert meeting was aimed at the general public. More specifically, public health campaigns were discussed. The experts stressed the need to carefully select messages that are suitable for public health campaigns.

First and foremost, the experts stressed that public health campaigns in themselves are not sufficient and that a multifaceted approach is required in order to accomplish behavioural changes in patients. This means that public health campaigns should be combined with other interventions such as restrictive prescribing measures, working with HCPs and information on leftover antibiotics and on completing a treatment.

When combined with other strategies, the function of public health campaigns is to educate the general population on important issues such as when to consult their doctor or pharmacist. Patients also need to be educated, for example through a leaflet, about different aspects of antibiotic use, such as finishing their full course of antibiotics, what should be done with leftover antibiotics and the need to use antibiotics prudently. The experts underlined the importance of taking into account the notion of health literacy. For example, do people know the difference between antibiotics and other drugs? Maybe they do not know what their GP has prescribed them. Moreover, the experts agreed that public health campaigns should be specifically tailored to the culture and healthcare system of each country as, for example, the resources available, or the healthcare associations, will differ. The experts argued that the public health campaigns should be continued over a long period, while it is important that the messages are also communicated very carefully. The European Antibiotic Awareness Day was seen as a good example of a campaign that has continued over a long period and that can be used to communicate and build consistent public health messages. Campaigns should involve GPs, paediatricians and pharmacists as the public's trust in these professionals is high and their support for a campaign might convince patients of the messages the public health campaign communicate. Lastly, appropriate indicators are needed to measure the impact of public health campaigns.

6.4. Healthcare professionals

Expert opinions – main conclusions

- Attention should be paid to the skills needed to communicate properly with patients, taking into account their health literacy and supported by patient information.
- Collaboration between HCPs, and especially between GPs and pharmacists, should be promoted and strengthened.
- HCPs should be made familiar with guidelines for the prudent use of antibiotics.
- Rapid diagnostic tests could be of additional value but there is still no clear evidence regarding this point.

The second set of interventions that was discussed by the experts was aimed at HCPs. One topic the experts agreed on was the need for HCPs to have good communication skills adapted to the needs of their patients, taking into account patient literacy. The experts agreed that improvements in the general health literacy skills of patients will help improve communication between HCPs and patients. This is not only important for care delivered during office hours but also for out-of-office hours. The experts stressed that intervention to improve prudent use of antibiotics should include a focus on out-of-hours prescriptions – that is those issued when GP practices are closed and replaced by a GP on-call service. Such consultations result in a high proportion of antibiotic prescriptions for example in Denmark, where half of antibiotic prescriptions are made by telephone without the patient being physically seen or examined by the prescriber.

The experts agreed that HCPs need to be educated about antibiotics and also about treatment guidelines, as these are important to acquaint HCPs with good standards of care. The experts also mentioned that raising awareness and improving education is not enough. Targeted interventions are also needed in order to help change long established habits in antibiotic prescription. The World Health Organisation's regional office for Europe (WHO EURO) has developed the TAP (Tailoring Appropriate Antibiotic Use Programmes) tool. This includes a step-by-step approach to develop interventions targeted at changing behaviour regarding antibiotic use in both patients and professionals.

There was a general consensus that collaboration between HCPs is important, especially between GPs and pharmacists, for example to ensure consistent clear and uniform messages to patients. The objective for policymakers and professional organisations is to encourage a collaborative environment by providing HCPs with support, training and better tools to do their work.

Among the tools that can support HCPs are rapid diagnostic tests such as C-reactive protein (CRP) tests to detect an inflammation, or rapid strep tests (RST) for bacterial pharyngitis. There was no consensus amongst the experts about whether rapid diagnostic tests lead to an increase in the overall adherence of patients to taking antibiotics. There are also additional costs associated with rapid diagnostic tests. Training in the appropriate use of rapid diagnostic tests is also an important issue for HCPs. However, training is not available in several countries. It was felt that the rapid diagnostic tests need to support the diagnosis made by GPs. This is a critical point and needs to be properly evaluated before these tests are introduced more widely.

6.5. Policy options

Expert opinions — main conclusions

- National antibiotic plans or national plans to combat AMR should support activities in the field.
- Practices enforcing the refusal to provide antibiotics without a prescription should be encouraged.
- Sanctions, positive or negative, should be used to promote adequate use of antibiotics (positive incentives are preferable).
- Packages should be tailored to the course of the treatment.
- The length of time that antibiotic prescriptions are valid should be agreed and harmonised across all EU Member States.
- Surveillance is only useful if it includes quality indicators.
- Delayed prescribing should be encouraged.

The third intervention level discussed in the expert meeting was the policy level. The experts felt that national antibiotic plans or national plans to combat AMR can help establish policy objectives and targets that should include measurable indicators. These plans should aim to achieve cooperation between all stakeholders, such as ministries of health, ministries of agriculture and HCPs. This, in turn, can create important changes within an individual country. For example, in Spain, six ministries and 61 scientific societies have come together as part of its national antibiotic plan.

The experts stressed the importance of enforcing laws discouraging the provision of antibiotics without a prescription. With regard to the use of sanctions to promote appropriate use, the experts agreed that positive rewards, for those who are doing well, will work better than sanctions, although negative sanctions are sometimes needed or required. Sanctions should preferably be accompanied by educational support in order to encourage better behaviour.

The experts agreed that, in principle, tailor-made antibiotic dispensing — that is to give the exact number of pills needed for a course — is the right way forward. This would mean that incomplete packages might have to be dispensed. Thus, in many countries, it will require a number of regulatory modifications as the legal framework would need to be adapted or created. The experts from Spain and the Pharmaceutical Group of the European Union indicated that the manufacturers influence the size of the package that is available on the market. How this could be changed has been considered in detail in Spain and it would involve modifications to the delivery chain. Thus, in order to change the delivery chain safely, the manner in which the primary packages are produced needs to be changed, for example by producing packages in different sizes or through the delivery of large batches plus product instructions. There are also concerns from pharmacists that opening packages, cutting the blisters and adding product instructions can slow down the dispensing process. In addition, pharmacies do not receive reimbursement for printing the extra product leaflets, and some countries reported that pharmacies do not have the technology to print the product leaflets. There are also questions about whether patients would be entirely happy with incomplete packages; as such, patients will also need to be educated in order to persuade them that this is the best way forward.

There was a consensus among the experts that the validity of a prescription for an antibiotic should be shorter than for other medicines, for example for 2 weeks only. This might then help avoid the misuse of antibiotics. However, two types of prescriptions would then have to be considered, one for antibiotics and one for other medicines. This may be difficult to implement in practice. In France this approach was not a success, as

GPs did not like to use two forms. In Poland, however, prescriptions for antibiotics are, in any case, only valid for 7 days, and this does not cause any major problems for either patients or prescribers.

The experts indicated that delayed prescribing is a common practice in some countries, for example in the United Kingdom, and there is evidence that it reduces antibiotic use. A study in the Netherlands found that only one third of patients who were offered a delayed prescription actually ended up collecting their antibiotics. However, there does need to be good communication about these healthcare issues, as the patients need to be properly informed about how to use a delayed prescription.

According to the experts, there is a need to define quality indicators, meaning indicators that are tailored to a certain diagnosis, and to link these to clinical data, as 'total use' in a country does not offer sufficient detail as an indicator. For example, the average level of antibiotic use in a country may be moderate but it may differ across diseases. Finally, the experts discussed the need for pharmacists to be able to review the clinical diagnoses so that they can check the prescription properly. In some countries the information concerning diagnoses is not shared for reasons of privacy and this affects the ability of the pharmacists to check the appropriateness of the antibiotic when considering the diagnosis and the local guidelines.

6.6. EU interventions

Expert opinions – main conclusions

- Public health campaigns: the EU's European Antibiotic Awareness Day is an excellent initiative but needs to be complemented with activities or interventions on a national level to produce a sustainable change in behaviour.
- Benchmarking: this is a very effective approach, as countries in Europe want to do their best and it stimulates action.
- Benchmarking also helps improve transparency, which is important for governance and compliance.
- Benchmarking should be encouraged at a regional level in Member States.

The last set of interventions that were discussed were EU-level interventions. There was a general consensus among the experts that mass-media campaigns such as the European Antibiotic Awareness Day on 18 November are good initiatives, as they raise awareness across the whole EU and AMR is a problem that goes beyond borders. Moreover, the fact that the EAAD occurs every year is of value, as it is known that repetition is needed to get messages across. Moreover, by joining forces at the EU-level, Member States do not all have to develop their own campaigns but can learn from each other, which can save resources.

The EAAD and other public campaigns should be supported by other interventions (see also Section 6.2), as public campaigns in themselves are not sufficient to produce sustainable behavioural change.

Another intervention at the EU level that was discussed was the benchmarking of issues such as antibiotic prescription rates, AMR rates or policies to reduce antibiotic use between Member States. Benchmarking also helps to improve transparency, which is a good thing for governance and compliance. Benchmarking at the Member State level does not provide insight into regional differences within a country, and as such national overall figures might not provide the most valuable information. An example is the case of Italy, where there are clear differences between the north and the south parts of the country. Benchmarking of regional differences within countries thus should also be encouraged according to the experts.

6.7. The results of the expert meeting compared with the scientific evidence

In Chapter 5 we produced an overview of effective interventions on three levels based on scientific knowledge. These levels were those of the patient's health, the HCP and the healthcare system. In this section we compare the interventions based on scientific knowledge with the interventions formulated by the expert meeting to create a more elaborate overview of effective interventions.

The patient's health

The effectiveness of the public educational campaigns, as found by the literature review, was also underlined by the experts. Moreover, the experts stressed the need for multifaceted campaigns that include these public campaigns. This is also supported by the scientific evidence. Sustainable behavioural change can be achieved by activities on all levels.

The HCP

The experts agreed with the scientifically proven effectiveness of educational interventions and professional meetings to stimulate collaboration between different HCPs. In addition, the experts noted that these professionals should agree to the use of uniform messages and that, in order to do so, they need to obtain good, specific communication skills while taking into account patients' health literacy. Although the literature showed the positive effects of the use of rapid diagnostic tests, the experts were less certain about their effectiveness. Moreover, the use of rapid diagnostic tests will lead to additional costs and training for HCPs to ensure they are used appropriately.

The healthcare system

The literature showed that changes to the financial and healthcare system are effective in stimulating more prudent use of antibiotics. In addition, the experts suggested developing and implementing national antibiotic plans, the use of sanctions and the dispensing of exact dosages.

At the EU level

In contrast to the scientific evidence, the experts emphasised the need for mass-media campaigns at the EU level to raise awareness. In addition, the experts also considered benchmarking important. They believe it is a powerful tool as it triggers Member States to perform well and it improves transparency.

Table 6.1. List of effective interventions based on the literature review and the expert meeting consensus statement.

Interventions on the different levels	Scientific evidence based?	Expert opinion based?
Population		
▪ Educate patients (when to consult their doctor or pharmacist, when an antibiotic is appropriate)	X	X
HCP		
▪ Technological support tools	X	
▪ Initiatives to stimulate appropriate prescribing (physician reminders)	X	
▪ Antimicrobial prescribing guidelines (standards for good antibiotic use)	X	X
▪ Financial measures	X	
▪ (Continuous) education	X	X
▪ Rapid diagnostic tests (these tests could be of additional value but there is still no clear evidence regarding this point)	X	X
▪ Professional meetings/collaboration between HCPs needs to be promoted and strengthened, especially between GPs and pharmacists	X	X
Healthcare system		
▪ Financial/healthcare system changes	X	
▪ Delayed prescribing	X	X
▪ National antibiotic plans could be of help for supporting activities in the field		X
▪ Look at the legal framework for not providing antibiotics without prescription and how to enforce the framework in the field (investigate sanctions on pharmacists)		X
▪ Use of sanctions, positive or negative, to promote adequate use of antibiotics (positive sanctions are preferable)		X
▪ Packages should be tailored to the course of treatment		X
▪ The length of time antibiotic prescriptions are valid should be agreed (e.g. 2 weeks) and harmonised across all EU Member States		X
▪ Surveillance is only useful if it includes quality indicators		X
Multifaceted interventions to have an influence on different levels	X	X
EU		
▪ Public health campaigns: the EU European Antibiotic Awareness Day needs to be complemented with activities or interventions on a national level to produce sustainable behavioural change		X
▪ Benchmarking		X

6.8. Conclusions

The 1-day meeting brought together experts from across Europe to discuss policy options to reduce the use of antibiotics without a prescription. The experts complemented the work of the ARNA project as they could assess the evidence collected by the project, provide input on the different policy options, including new ones, and provide the latest developments in the field that might not yet have been published. In addition, the experts work for national and international bodies and so bring with them the latest knowledge regarding the different policy options. As seen above (see Table 6.1), many of the points raised by the experts were also supported by the scientific literature. However, the experts also proposed interventions that were not supported by the scientific literature. These included the use of incentives to promote adequate use of antibiotics or the use of benchmarking at the EU level. This probably reflects the fact that some interventions have not been evaluated or are difficult to evaluate, and supports the decision to use experts to complement the work of the ARNA team.

7. Policy measures to enhance more prudent use of antibiotics in six EU Member States

Main findings

The country-dialogue meetings resulted in six action plans for each Member State with various interventions on different levels. Each Member State has its own issues to be addressed but the action plans showed similarities. The most important interventions included in the action plans are summarised below.

- *Patient level.*
 - Educational campaigns on a large scale, with clear messages and focused on health literacy.
 - Increase the use and availability of rapid tests.
 - Stimulate better use of vaccinations to reduce infections.
- *HCP level.*
 - Education: lifelong learning, including the study of infectious-disease medicine in the curricula of HCPs.
 - Health literacy: improve the way HCPs communicate with patients.
 - Monitor practices and provide feedback.
 - Stimulate collaboration between HCPs, in particular GPs and pharmacists.
 - Increase the use of electronic tools.
 - Develop up-to-date guidelines that are local and easy to disseminate.
- *Healthcare-system level.*
 - Involve all important stakeholders, including patient organisations.
 - Stimulate collaboration between the community and hospital sectors and between the public and private sectors.
 - Produce good scientific evidence and data.
 - Develop a national plan to combat AMR.

7.1. Introduction

Six country-dialogue meetings were held in EU Member States where studies among GPs, pharmacists and the general population were performed by ARNA. The Member States involved were Cyprus, Greece, Hungary, Italy, Romania and Spain. There was no country-dialogue meeting in Estonia as the problem of non-prescribed antibiotic use was much lower than anticipated.

The aims of the country-dialogue meetings were:

- to obtain insight into the extent to which stakeholders in the six countries recognise the results of the ARNA analyses (see Chapter 4), while at the same time creating an awareness of the problem;
- to discuss policy options based on the results of the ARNA project and propose amendments and additions;
- to formulate recommendations specific to individual Member States in order to stimulate the prudent use of antibiotics.

This chapter describes the main results from each of the meetings, including a summary of the main discussion points and a list of action points. The chapter starts with a description of how the country-dialogue meetings were organised and then presents the main results per Member State. It then draws general and specific conclusions regarding them. Detailed information, including each of the country-dialogue meeting reports, can be found in a separate report.



7.2. Methods

A collaborating partner was identified in each of the six Member States who was able to organise the country-dialogue meeting. These were usually based at a national institute or at a university. They prepared the meeting together with the ARNA team. The ARNA team provided a factsheet for each Member State, with a summary of the findings of the analyses of the surveys (see Chapter 4) and a template for the meeting programme. Stakeholders were invited by the local organisers. The meetings were organised in 2016 and were attended by 13-30 stakeholders per Member State, including HCPs (GPs, pharmacists and paediatricians), consumer organisations, experts in the field of AMR and policymakers. Information on the local organiser, the date of the meeting, the number and type of participants and the programme can be found in Box 7.1.

All the meetings resulted in action plans that stakeholders considered important to enhance the prudent use of antibiotics in their Member State. The country-dialogue meeting report, which included the action plan, was then prepared by the ARNA team and returned to the collaborating partner to be revised and checked before being finalised.

Box 7.1. Details of country-dialogue meetings.

Cyprus	
Local organiser	National Antibiotics Committee of Cyprus (AMR national focus point) (Niki Paphitou)
Location and date	Nicosia, 23 April 2016
Participants	28 participants including microbiologists, specialists in infectious-disease medicine, paediatricians, GPs, pharmacists, representatives from the veterinary sector and infection-control practitioners
Programme	Presentation of the ARNA results Presentations by local stakeholders Group discussions on policy options Plenary presentation, recommendations and further steps
Greece	
Local organiser	The Committee of HCDCP for the Promotion of the Prudent use of Antimicrobials (Flora Kontopidou)
Location and date	Athens, 29 May 2016
Participants	15 participants representing national professional societies and public stakeholders
Programme	Presentation of ARNA results Presentations by local stakeholders Group discussions on policy options Plenary presentation, recommendations and further steps
Hungary	
Local organisers	University of Szeged (Ria Benkő, Mária Matuz, Gyöngyvér Soós), Hungarian Chamber of Pharmacists (Attila Horváth-Sziklai, Gabor Pongrácz)
Location and date	Budapest, 4 March 2016
Participants	13 participants from the National Institute for Health Development, the Hungarian Federation of Drug Companies and the Ministry of Health, Social and Family Affairs, doctors' and pharmacists' organisations, asthma and allergy patient organisation
Programme	Presentation ARNA results Presentations by local stakeholders and by experts from Sweden (Jenny Hellman, Public Health Agency) and Norway (Salvesen Blix, National Institute of Public Health) Group discussions on policy options Plenary presentation, recommendations and further steps
Italy	
Local organisers	Instituto Superiore de Sanità (Annalisa Pantosti)
Location and date	Rome, 15 April 2016
Participants	24 participants attended the meeting. Italian institutes and organisations were represented, such as the Agenzia Italiana Del Farmaco, Federazione Italiana Medici Pediatri, the Federazione Ordini Farmacist Italiani and a national consumer organisation
Programme	Presentation of Italian data Presentation of ARNA results Group discussions about interventions on regulatory and on professional and patient levels Recommendations and further steps

Romania	
Local organisers	Romanian Ministry of Health (Alexandru Rafila)
Location and date	Bucharest, 26 April 2016
Participants	19 participants from national stakeholders and focal points for the rational use of drugs in Romania, directors and professionals who prescribe and dispense antibiotics
Programme	Presentation of ARNA results Presentations by local stakeholders Group discussions on policy options Plenary presentation, recommendations and further steps
Spain	
Local organisers	AEMPS, the Spanish Agency for Medicines and Medical Devices (Antonio López and Eduardo Padilla)
Location and date	Madrid, 11 March 2016
Participants	29 participants attended the meeting. Various stakeholders were represented such as the AEP (the Spanish Association of Primary Care Paediatricians), SEFAC (the Spanish Society of Community Pharmacists) and SEMG (the Spanish Society of General and Family Medicine), plus the national consumer organisation
Programme	Presentation of ARNA results Presentations by local stakeholders Group discussions on policy options Plenary presentation, recommendations and further steps

7.3. Main results per Member State

This section summarises the main points of discussion and outcomes of the country-dialogue meetings in all Member States. It should be noted that in some Member States the stakeholders had discussed the subject of non-prudent use of antibiotics beforehand, whereas in others, such as Hungary and Italy, it was the first time the stakeholders had met each other. For some Member States it was also the first time consumer or patient organisations had been involved. What became clear during all meetings was that action to reduce the use of antibiotics without a medical prescription is considered as part of broader plans to combat AMR. Therefore, the discussions in all six Member States were not only focused on actions to reduce the use of antibiotics without a prescription but on potential interventions in general. These were summarised in a short action plan. Below we describe the main results of each country-dialogue meeting. As the focus of the ARNA project is on the use of antibiotics without a prescription, a box with proposed actions to reduce this use is included for each Member State. Section 7.4 contains a comparison of the main proposed interventions for all six Member States. As such, Section 7.4 includes more information on specific interventions.

Reports of the meetings for each Member State — with all actions — can be found in a report that has been published separately.

Cyprus

The national strategy was adopted in April 2013, and can be viewed as a national action plan with goals that are in various stages of implementation, including the following.

- Achieve an effective infection-control programme with feedback.
- Develop structured national guidelines on infection control.
- Develop national guidelines on appropriate antibiotic use.
- Develop an effective system for inappropriate antibiotic use restriction in both the public and the private sectors.

- Develop an audit tool to monitor compliance with guidelines in hospitals.
- Establish an antibiotic stewardship team/committee in each hospital to coordinate/audit programs as appropriate.
- Ensure continuous surveillance of hospital-associated infections and antimicrobial use in hospitals. The ECDC protocol is being employed.
- Strengthen education and awareness on appropriate antibiotic use among healthcare workers and the public.
- Ensure continued full and wide distribution of all promotional for the European Antibiotics Awareness Day materials to all stakeholders ^(ccc).

The main action proposed by Cypriot stakeholders was to implement a national action plan for improving antibiotic use in Cyprus through this Cyprus national strategy to combat AMR. This covers both the public and the private sectors, involving all stakeholders. Overall, Cypriot stakeholders agreed that there was a need for national guidelines on antibiotic use in outpatient care in order to establish a standardised educational background. Moreover, there is a need for better cooperation between the public and private sectors by, for example, improving the information technology systems and digitalising the prescription forms. At the moment, however, there is no national health system, which makes it difficult to implement strategies in primary care. This is especially true for the private sector, where there is a complete lack of control. Box 7.2 shows issues that were discussed on the use of antibiotics without a prescription.

Box 7.2. Examples of issues discussed on the use of antibiotics without a prescription in Cyprus.

Patient level

- Education of the public to increase awareness, for example by media campaigns, such as on the use of leftovers by district posters in the offices, or by using stickers on the boxes stating that you should not use leftovers.

HCP level

- Education of professionals on how to deal with leftover medication.
- Considering incentives (positive and negative) for pharmacists to comply with the law that antibiotics should only be dispensed with a prescription. There is a legal provision for a financial penalty upon non-compliance, however there is doubt that this is an effective measure.

Healthcare-system level

- Improve enforcement of the law by strengthening the team of inspectors at the Ministry of Health.
- Introduction of electronic prescriptions and dispensing so what the pharmacist dispenses can be controlled.
- Dispense the exact number of antibiotics.

Greece

Greece has updated guidelines for the prudent use of antibiotics and many educational activities for GPs across the country, along with a strong legal framework on antibiotic use, but enforcement of the law should be improved. Therefore, the Greek stakeholders agreed that there is a need for greater political interference. An important issue is pressure from patients who request antibiotics when they are not indicated. Policy options are needed to manage this pressure and to change the mentality within Greek society. Greece has a national antibiotic plan, which is mainly focused on antibiotic stewardship in healthcare facilities. The workshop acknowledged the need for a national

^(ccc) Cyprus has been a very active participant: distribution of leaflets to patients visiting the public health sector, infographics in hospitals, letters to GPs, TV videos, billboards on big highways, materials for the veterinary sector.

strategy for antibiotic use in the ambulatory care sector. This strategy should enhance the implementation of following aspects.

- *Education at all levels.* Pharmacies have mandatory courses, though not all pharmacy schools teach at the same standards. Moreover, physicians and pharmacists should go through lifelong learning and training constantly.
- *Raising public awareness.* Messages need to be communicated to the public in the simplest way.
- *Diagnostic tools.* The introduction of rapid diagnostic tests, which must be mandatory and performed by the clinicians at the bedside.
- *Communication and collaboration.* An improvement in the communication between professionals, such as doctors and pharmacists, through the introduction of an electronic prescription tool.
- *Monitoring of compliance.* Strict government monitoring of compliance with the OTC ban and other illegal sources of antibiotics.
- *Surveillance.* Improvement in the surveillance of antibiotic consumption and the evaluation of results to guide the design and implementation of specific targets.

Box 7.3 shows issues that were discussed on the use of antibiotics without a prescription.

Box 7.3. Examples of issues discussed on the use of antibiotics without a prescription in Greece.

Patient level

- Create a communication strategy reaching out to the public, for example by means of a public information campaign, in order to provide information to patients and raise awareness that an antibiotic is a special drug and should not be taken OTC and should not be requested or provided any more for every minor symptom. Include civil society in conveying the message.

HCP level

- Acknowledge the problem of leftovers: how should we decrease storage and usage, what factors can help, what is the role of healthcare professionals?
- Patients should have continuous and easy access to a medical prescription for antibiotics.

Healthcare-system level

- Establishment of a national strategy regarding the use of antibiotics in ambulatory sector.
- Promotion of the Health professionals training at graduate and postgraduate level.
- Enhancing the suitability of prescription through the promotion of rapid diagnostic tests to health professionals and their easy access to the national guidelines.

Hungary

In Hungary, the ARNA country-dialogue meeting was the first time for stakeholders to meet and discuss AMR. They mentioned different areas in Hungary that prevent more prudent use of antibiotics. These are as follows.

- The healthcare system lacks an antibiotic policy. Stakeholders are not supported in the collection and analysis of medical information.
- There are no clear guidelines. Although a number of guidelines have been published, many diseases and professions lack proper guidelines.
- There is limited financial support for public health programmes.
- There is a lack of feedback for HCPs. However, while feedback would be useful, it costs GPs time and, at the same time, receiving feedback on how badly they are performing will not motivate them to act in the right way.
- There are many older GPs, which makes change more difficult.

The stakeholders came up with a set of potential interventions (see Section 7.4). Most of these proposals were on the use of antibiotics in general. The experts did not feel that the use of antibiotics without a prescription was a large problem in Hungary as OTC dispensation is strictly regulated in Hungary. It was felt that there was a strong need to

better inform the public on the prudent use of antibiotics, including discouraging the use of leftover antibiotics without a prescription (see Box 7.4). Also, it was felt that the curriculum of healthcare professionals should pay more attention to infectious diseases and AMR. The stakeholders emphasised that the National Institute of Public Health and the Health Development Institute should take the lead with regard to an action plan to improve the prudent use of antibiotics.

Box 7.4. Examples of issues discussed on the use of antibiotics without a prescription in Hungary.

- Teach patients to bring back leftover antibiotics to the pharmacy and, as such, discourage the use of leftover antibiotics.
- Include communication experts in reaching patients with messages to improve their use of antibiotics so that patients react in a proper way.

Italy

In Italy, the participants of the country-dialogue meeting felt it was important that their Member State should develop a national plan to combat AMR. It should contain multifaceted interventions and should demonstrate the need for an increase in vaccinations to prevent the use of antibiotics. In addition, the participants discussed various problems that prevent the prudent use of antibiotics. These are as follows.

- A lower rate of vaccinations, resulting in an increased risk of disease and therefore increased antibiotic use.
- Insufficient attention to diagnostics, even though the technology to identify the cause of an infection is available in some cases, such as for a sore throat.
- Italian pharmacists are not allowed to give incomplete packages because of the reimbursement system. To change this practice would be expensive and difficult.
- Information about how to use antibiotics prudently is not widespread.
- Many antibiotics are bought out of pocket, which increases the amount of leftover antibiotics and makes it difficult to control whether the antibiotics are appropriate.
- There is a lack of new antibiotics. This increases the problem of antibiotic resistance to the current drugs available. This is a problem across the EU.
- There are difficulties in encouraging professional participation and thus strengthening the professional position.
- There is very little awareness of the problem due to a lack of national guidelines in Italy.
- Health literacy is low. This should be the main focus of campaigns.
- A systematic approach is lacking, such as towards interventions and guidelines.

In addition, there are some cultural aspects which play a role in the non-prudent use of antibiotics.

- There is a tradition of using leftover antibiotics.
- Antibiotics are often immediately prescribed in multiple, possibly excess, doses.
- In the south the misuse of antibiotics is a greater problem than in the northern part of Italy.

Based on this background, different interventions were proposed both for the use of antibiotics in general (see Section 7.4) and for the use of antibiotics without a prescription. The stakeholders stressed the need for commitment in order to ensure that the action plan formulated will be effective. Firstly, the commitment of the regions is needed as each regional government is responsible for local activities. Secondly, national and political commitment is needed to increase collaboration between all the different actors so that they use similar methods of measurement and agree on how aspects need to be measured.

Box 7.5. Examples of issues discussed on the use of antibiotics without a prescription in Italy.*Patient level*

- Introduce educational campaigns with simple and clear instructions to increase awareness about the consequences of non-prudent use of antibiotics and include doctors and pharmacists in educational campaigns to get the messages on prudent use across.

HCP level

- Strengthen patient-provider education by putting more emphasis on communication in university curricula.

Health-system level

- Change the regulatory environment in order to reduce the possibility to store antibiotics at home (leftover antibiotics).
- Put a limit on the number of packages of antibiotics for prescription.

Romania

In Romania, the stakeholders in the country-dialogue meeting stated that the problem of OTC use of antibiotics mainly lies within the lack of knowledge of the population and the pressure put on pharmacists to sell antibiotics over the counter, although this is not allowed. Many Romanians who cannot afford to visit a GP immediately go to the pharmacy and hope to get an antibiotic there. The Romanian stakeholders not only considered the use of antibiotics to be a problem, but also the fact that antibiotics are often prescribed when not needed. There was discussion about interventions to improve the use of antibiotics at the level of the general population, the HCPs and the healthcare system. The main findings and actions discussed were as follows.

- The need to ensure a multifaceted approach with representation and collaboration between all stakeholders.
- Developing and implementing a national AMR strategy.
- The need to provide knowledge and create awareness among the public regarding self-medication and antibiotic resistance through the organisation of national public information campaigns.
- Releasing funds for organising educational campaigns.
- Enforcing health authorities to adopt a 'prescription-only' policy for antibiotics.
- Dispensing the exact number of tablets.
- Developing national therapeutic antibiotic guidelines.
- Monitoring local AMR profiles and adapting local antibiotic prescribing guidelines to these results.
- Enhancing adherence to antibiotic guidelines through the application of a smartphone.
- Introducing electronic drug prescribing.
- Organising medical training among professional organisations.
- Developing a platform for online courses targeting professionals and the public.
- Extending existing programmes of surveillance and control of AMR and healthcare-associated infections.

All initiatives and ideas need to be combined in one antibiotic stewardship plan. The National Committee needs to make a long-term plan, in which the Institute of Public Health could take the lead.

Box 7.6 shows issues that were discussed on the use of antibiotics without a prescription.

Box 7.6. Examples of issues discussed on the use of antibiotics without a prescription in Romania.*Patient level*

- Educational campaigns for patients with the following as the main message: 'only use antibiotics that are prescribed by physicians'. Multiple media should be used to get this message across.

HCP level

- In Romania, psychiatric medicines are given out on special prescription. This should also be the case for antibiotics.

Healthcare-system level

- Providing the patient the exact number of antibiotics needed, not the whole package.
- There should be an administrative rule for pharmacists to never deliver antibiotics without a medical prescription. Bringing back leftovers to the pharmacy is assessed as not being feasible.

Spain

The main objective of the country-dialogue meeting was to formulate specific recommendations to encourage the prudent use of antibiotics, with a special emphasis on self-medication. To this end, the meeting was divided into two parts. In the first part, representatives of the ARNA group presented data on the use of antibiotics without a prescription in the European Union and the effectiveness of interventions to reduce this consumption based on scientific literature and expert opinions. Representatives of Spanish organisations also presented their work focusing on the prudent use of antibiotics. The second part of the meeting included a workshop where three working groups discussed and prioritised actions to further reduce the consumption of antibiotics without a prescription in Spain. Each working group had its own topic, as follows.

1. Measures to address the prescribing and dispensing of antibiotics when they are not indicated.
2. Measures to address the storage of antibiotics at home and the use of these leftover antibiotics (from previous prescriptions).
3. Measures to strengthen the position of health professionals to feel less pressured by patients in making decisions regarding the prescribing and dispensing of antibiotics.

In Spain the national antibiotic plan (NAP) was introduced in 2014, with its main aim being to enhance the prudent use of antibiotics using a One Health approach. As such, a lot of initiatives are already being developed in Spain. The NAP is coordinated by the Medicines Agency (AEMPS). The ARNA workshop fitted into processes that had already been initiated as part of the NAP. Stakeholders agreed during the meetings on how to combat the problem of AMR. The consensus document that was prepared as a result of the meeting was approved by all participants and will be used as part of the national strategy to improve the prudent use of antibiotics. Key elements of the consensus document included the following.

- Awareness-raising campaigns for patients including TV spots, brochures in pharmacies and primary care centres, all providing the same message.
- Information, education and training for HCPs.
- The implementation of guidelines.
- The implementation of support systems for prescribing.
- The development of a national surveillance network of antibiotic consumption and AMR.
- The implementation of a rapid diagnostic test.
- Delayed prescribing of antibiotics.

The AEMPS, as the coordinator of the NAP, has a leading role in the implementation of these actions, and cooperates with other stakeholders involved.

Box 7.7 shows issues that were discussed on the use of antibiotics without a prescription. This box differs from those of the other Member States as the Spanish report included not only actions but also information who would sponsor the action and which party would be the vehicle.

Box 7.7. Actions on the use of antibiotics without a prescription in Spain.

Action	Type	Sponsor	Vehicle
Awareness-raising campaigns			
General population: 'Importance and consequences of the inappropriate use of antibiotics'	TV spot	National action plan on antibiotic resistance (AEMPS)	Ministry of Health, Social Services and Equality
General population: 'Return of leftover antibiotics. Collection points Sigre'	Explanatory brochures in pharmacies	National action plan on antibiotic resistance (AEMPS)	General Council of Professional Associations of Pharmacists SEFAC
General population: 'Prohibition of dispensation of antibiotics without a medical prescription'	Informative brochures and posters in pharmacies	National action plan on antibiotic resistance (AEMPS)	General Council of Professional Associations of Pharmacists SEFAC
Information/education/training campaigns			
Healthcare professionals: 'Regulations on the prohibition of sale of antibiotics without a medical prescription'	Informative notes	National action plan on antibiotic resistance (AEMPS)	General Council of Professional Associations of Pharmacists SEFAC
Healthcare professionals: 'Prudent use of antibiotics'	Ongoing training courses	National action plan on antibiotic resistance (AEMPS)	General Council of Professional Associations of Pharmacists General Council of Professional Associations of Physicians Ministry of Education Ministry of Health, Social Services and Equality (Professional Regulation)
Health policy and legislation			
Healthcare professionals: Discussion forum on the compulsory nature of a registry of dispensation of antibiotics in pharmacies	Work meetings	National action plan on antibiotic resistance (AEMPS)	General Council of Professional Associations of Pharmacists SEFAC
National health system: Coordination between healthcare professionals from different health settings	Establishment of the programmes of Optimised Antibiotic Use (PROA) in Primary Care	National action plan on antibiotic resistance (AEMPS)	Autonomous communities

7.4. Actions proposed in multiple countries

All six Member States proposed to continue the collaboration that was started or encouraged by the ARNA project and the country-dialogue meetings.

Stakeholders in all six Member States discussed potential interventions and policy measures for their country. The action plans that were developed included ideas for interventions on different levels. The context of each Member State is crucial in defining what actions can be taken. Interventions that are feasible for one Member State might not have a similar effect in another. Moreover, some Member States have already done more than others. Nevertheless, a number of similarities can be observed in the action plans.

7.4.1. Patient level

Table 7.1 shows that all Member States consider education campaigns targeted at patients to be a crucial element in enhancing the prudent use of antibiotics. The actions they have proposed differ slightly, but one issue that was mentioned in several Member States was the wish to target a broader public while at the same time focusing on specific groups of patients who are more likely to use antibiotics non-prudently. Overall, the need to take the patient's health literacy into account was recognised. Related to this is the wish for simple and clear messages.

Another intervention which was frequently reported was an increase in the use and availability of rapid tests. These supporting decision-making about whether an antibiotic is indicated for a particular patient. Significantly, such interventions are made at the point where the patients and HCPs meet. A final intervention that was mentioned in multiple Member States was the need to stimulate better use of vaccines. Our study showed that influenza is a common reason for patients to use non-prescription antibiotics. Influenza vaccination lowers the incidence of flu and, as such, indirectly reduces the non-prudent use of antibiotics.

7.4.2. Professional level

Table 7.2 shows that all Member States consider the education of professionals to be a crucial element in enhancing the prudent use of antibiotics. AMR and antibiotic usage should be integrated into national training curricula, including continuous education programmes and lifelong learning. Professionals' communication skills are also important and must take into account the need to communicate with patients who have a low level of literacy. Surveillance and monitoring of the use of antibiotics are also considered important. Most Member States have a surveillance system in place (Chapter 3), and this could be used for benchmarking and providing feedback.

Improved collaboration in primary care, especially between GPs and pharmacists, is also considered to be important. Professionals can also have an important role in patient campaigns. A powerful instrument is the development and implementation of clinical guidelines to guide doctors in their prescribing and to support pharmacists in not dispensing OTC despite patient pressure. Finally, electronic recording and support of prescribing and dispensing is considered useful.

7.4.3. Healthcare-system level

The third level for which interventions were discussed was the healthcare-system level. First of all, national action plans and antimicrobial stewardship^(ddd) were mentioned. Both the WHO and the Commission have urged and agreed that countries formulate national action plans, including all aspects of antibiotic use, while applying a One Health approach. Four of the six Member States do not yet have an action plan, while Cyprus and Spain do have one (ARNA Ministry of Health Survey, June 2015).

The importance of guidelines was also stressed at the healthcare-system level. While guidelines need to be developed and used at the professional level, there is a need for coordination and support for implementation at the healthcare-system level by national stakeholders. Cooperation is not only considered important between HCPs in primary care but also by all stakeholders at regional and national levels (including patient and consumer organisations) in order to enhance the prudent use of antibiotics. Collaboration is also important between different sectors in the healthcare sector: primary and secondary care, private and public sectors. In order to enhance cooperation and actions

^(ddd) Antimicrobial stewardship is a coordinated programme that promotes the appropriate use of antimicrobials (including antibiotics), improves patient outcomes, reduces microbial resistance and decreases the spread of infections caused by multidrug-resistant organisms (<http://www.apic.org/Professional-Practice/Practice-Resources/Antimicrobial-Stewardship>).

taken by different stakeholders and professionals, coordination and leadership is necessary. In Spain, the Medicines Agency has a coordinating role in the national antibiotic plan. Other Member States felt that their ministries of health or their national institutes of public health could play such role.

7.4.4. Interventions that were mentioned in one Member State

There were many similarities between the Member States in the action plans they formulated, however, each had its own specific focus, and most Member States formulated specific ideas for interventions that were not mentioned by any of the others ^(eee).

Cyprus

In Cyprus, the participants in the country-dialogue meeting stressed that healthcare reforms are needed to stimulate more prudent use of antibiotics. Moreover, healthcare insurance needs to be reconsidered in order to limit the reimbursement of antibiotics. Another intervention, not mentioned in the other Member States, was to strengthen the regulation of medical representatives from the pharmaceutical industry covering such actions as offering free gifts. Official bodies and regulations are needed to regulate industry activities. The stakeholders from Cyprus also mentioned the importance of handling antibiotics for which the date for safe use has passed.

Greece

The internet is seen as an important upcoming source for obtaining antibiotics without a prescription. The stakeholders from Greece underlined the importance of banning illegal sources of antibiotics found on the internet. Another point that was raised in Greece was the availability of interventions in other Member States and the opportunity, therefore, of benefitting from the progress made elsewhere and to implement interventions that have proven to be effective in other Member States.

Italy

Unique action points from Italy included limiting the prescription of antibiotics, focusing on a global plan instead of single interventions and taking into consideration the role of industry in the national plan.

Spain

The Spanish stakeholders emphasised the important role of nurses in its action plan, which was elaborated upon in various interventions regarding public health campaigns, HCPs and health policy and regulation. Nurses could, for example, contribute to more prudent use of antibiotics by analysing the first aid cabinet in each household. In addition, GPs should then follow up with visits to the patient to make sure they comply with their treatment. Another point that was only mentioned in Spain was to encourage the sharing of patients' medical history in order to make this information accessible to HCPs.

^(eee) The main interventions mentioned in Hungary and Romania were also mentioned in other Member States.

**Table 7.1.** Interventions on the patient level suggested at country-dialogue meetings.*

	Cyprus	Greece	Hungary	Italy	Romania	Spain
Education	<ul style="list-style-type: none"> Educate the community; increase awareness, for example, by media campaigns, district posters in offices Scale up the campaigns Use of leaflets that are distributed by pharmacists More dramatic campaigns with striking pictures are needed 	<ul style="list-style-type: none"> Train patients, challenge their mentality and encourage them to comply There is a need for new communication channels with the public Communicate to a broader public Promotion to the public of understandable and simple messages regarding the avoidance of self-medication and the supply of antibiotics without a medical prescription 	<ul style="list-style-type: none"> Education of the public should be supported and start in early school years Health literacy should be improved for the adult population Use mass media Prevention of infections through education — washing hands Educational campaigns should be repeated over the years Use communication experts to ensure patients react in the proper way 	<ul style="list-style-type: none"> Educational campaigns Simple and clear instructions to increase awareness about the consequences of non-prudent use Health or e-health literacy Broaden the targeted public by using new media in the campaigns, such as Twitter and Facebook Not only a global focus but also a focus on specific groups as different groups need different approaches 	<ul style="list-style-type: none"> Educate the public regarding antibiotic use 	<ul style="list-style-type: none"> Educational campaigns on a large scale Directed at patients and those accompanying them, such as children, in primary care consultations All information provided to patients should come directly from HCPs; everyone should provide the same message
Rapid tests	<ul style="list-style-type: none"> Stimulate the use of point-of-care tests and differentiate between different infections 	<ul style="list-style-type: none"> Stimulate the use of rapid bacterial infection test tests Put the test on the shelves of the pharmacists or provide it through the government 		<ul style="list-style-type: none"> Increase the availability of rapid bacterial infection tests, stimulate its use and reassure parents of children 	<ul style="list-style-type: none"> Use rapid bacterial infection tests paid for by the patient 	<ul style="list-style-type: none"> Use of rapid diagnostic techniques in primary care centres Give legal character to rapid tests
Vaccinations		<ul style="list-style-type: none"> Focus on vaccinations. This year (2016) there was an extensive national campaign for promoting of influenza vaccination to public and healthcare professionals 	<ul style="list-style-type: none"> Stimulate better use of influenza vaccinations (30-40 % get destroyed) 	<ul style="list-style-type: none"> There is a lack of extensive vaccinations which might help reduce the demand for antibiotic use. Italy is not putting enough attention into diagnostics even though the technology is available 		

* More interventions are mentioned in each Member State; these can be found at www.nivel.nl/eu/arna

**Table 7.2.** Interventions on the professional level suggested at country-dialogue meetings.*

	Cyprus	Greece	Hungary	Italy	Romania	Spain
Education	<ul style="list-style-type: none"> ▪ Educate all HCPs involved early in their careers about AMR, in that they should not give antibiotics in packages and on how to communicate with patients ▪ Target specific subgroups such as GPs, paediatricians and pharmacists ▪ Educate through surveillance and online questionnaires 	<ul style="list-style-type: none"> ▪ Expand mandatory education of final-year medical students ▪ More training is needed on a postgraduate level ▪ Begin lifelong training of GPs ▪ Further improve the mandatory courses for pharmacists ▪ Infection and hygiene mandatory in nursing schools and for post graduates 	<ul style="list-style-type: none"> ▪ Increase awareness among professionals and include AMR/infectious-disease medicine as a topic in training 	<ul style="list-style-type: none"> ▪ Develop professional skills such as in the epidemiology of the field they work in ▪ Health or e-health literacy for professionals; priority for universities to teach professionals about patient communication ▪ Educational campaigns with simple and clear messages ▪ Focus too on the different approaches required for specific groups 	<ul style="list-style-type: none"> ▪ Provide information from the moment they finished their curricula 	<ul style="list-style-type: none"> ▪ Campaigns to make them aware of the legal regulations and the need to adapt therapeutic guidelines to the local epidemiology of antibiotic resistance ▪ Educational/training interventions through professional associations ▪ Focusing on joint training of HCPs ▪ Take the health literacy of patients into account when attempting to communicate
Surveillance/Monitoring	<ul style="list-style-type: none"> ▪ Strengthen the role of inspectors ▪ Monitoring and feedback ▪ Introduction of quality indicators ▪ Benchmarking 	<ul style="list-style-type: none"> ▪ Hygiene inspectors. There is a need for control and monitoring of the compliance with the regulations ▪ Improving the surveillance of antibiotic use using the electronic prescription database ▪ Improve feedback to HCPs 	<ul style="list-style-type: none"> ▪ Provide feedback to HCP (although this will take time) 	<ul style="list-style-type: none"> ▪ Stimulate GPs to review the data and provide feedback 		<ul style="list-style-type: none"> ▪ Establish surveillance system ▪ Obligation of registry of antibiotic dispensing



Collaboration	<ul style="list-style-type: none"> Stimulate collaboration between organisations and institutes by organising workshops and congresses 	<ul style="list-style-type: none"> Promote GP-pharmacist collaboration Meetings and distance monitoring platforms for pharmacists 	<ul style="list-style-type: none"> Stimulate collaboration between HCPs 	<ul style="list-style-type: none"> Raise awareness of the importance of mutual collaboration Increase cooperation and coordination between HCPs Coordinate therapeutic decisions between different professions 		
Campaigns		<ul style="list-style-type: none"> There is the need for a national campaign with simple and understandable messages to the public that come from all relevant stakeholders, including HCPs 	<ul style="list-style-type: none"> Include professionals in campaigns as they have greater contact with patients 	<ul style="list-style-type: none"> Active participation in the patient campaigns Provide consensual and coordinated training for all levels of healthcare. This should be oriented towards patient care according to their characteristics and also those of the infectious process 		
Guidelines	<ul style="list-style-type: none"> Prescribe the proper amount of antibiotics Develop guidelines that are easy to read, such as pocket guides that are easy to disseminate Adapt the existing guidelines and see if society at large adopts them Strengthen regulation 	<ul style="list-style-type: none"> Extensive dissemination of guidelines and their integration into the platform of electronic prescription Monitoring compliance with national guidelines using the electronic prescription database, for GPs and hospital prescribers 	<ul style="list-style-type: none"> Professional standards should be increased and promoted Inform about guidelines simply and practically, for example using pocketbook treatment guidelines 	<ul style="list-style-type: none"> Write specific guidelines for professionals, including dentists, provide them in a booklet or pocket-sized guide and ensure that they are implemented Regulate the prescription of antibiotics 	<ul style="list-style-type: none"> Application on the smartphone with regular guideline updates to enhance the adherence of guidelines Administrative rule for pharmacists to never deliver antibiotics without a prescription 	<ul style="list-style-type: none"> Compliance with the legal regulations Implementation of the guidelines for prescribing should be incorporated into the electronic prescription system
Electronic recording and support	<ul style="list-style-type: none"> Electronic recording and prescribing should be implemented Improve the IT system and digitise prescription forms 	<ul style="list-style-type: none"> Pharmacists should record prescriptions electronically Make e-platform/system more accessible Use of mobile device to prescribe 	<ul style="list-style-type: none"> Establishment of an antibiotics dispensing registry in pharmacies 			

* More interventions are mentioned in each Member State; these can be found at www.nivel.nl/eu/arna

**Table 7.3.** Interventions on a healthcare-system level suggested at country-dialogue meetings.*

	Cyprus	Greece	Hungary	Italy	Romania	Spain
National action plan/ stewardship	<ul style="list-style-type: none"> ▪ Cyprus has a national action plan 	<ul style="list-style-type: none"> ▪ The national plan for antibiotic use in the ambulatory sector is in process and is part of the national action plan to combat AMR 		<ul style="list-style-type: none"> ▪ Create a national antibiotic plan ▪ Check the current situation and monitor the results of the actions taken ▪ Establish a joint team involving various professionals to develop antibiotic stewardship 	<ul style="list-style-type: none"> ▪ Integrate all measures into one antibiotic stewardship plan 	<ul style="list-style-type: none"> ▪ The national plan for antibiotic resistance supports the different initiatives
Guidelines	<ul style="list-style-type: none"> ▪ The national guidelines should include specific protocols with regard to antibiotic prescribing ▪ Stricter and new regulations about safe use of antibiotics, which should be placed on the outside of packages ▪ Work with relevant societies so they can feel a sense of ownership with the guidelines 				<ul style="list-style-type: none"> ▪ Update the national guidelines 	<ul style="list-style-type: none"> ▪ Make implementation compulsory
Collaboration	<ul style="list-style-type: none"> ▪ Collaboration between the private and public sectors is needed ▪ Involve the scientific community and the public and private sectors in developing guidelines ▪ Inform all parties about decisions taken ▪ Involve patient organisations 	<ul style="list-style-type: none"> ▪ Collaboration between outpatient and inpatient setting ▪ There is need for instruments to exchange information ▪ Involve local associations ▪ Involve patient organisation 	<ul style="list-style-type: none"> ▪ Intersectoral approaches are needed which include the agriculture and human sectors ▪ Promote collaboration between public health services and the pharmaceutical sector ▪ Involve the patient organisations 	<ul style="list-style-type: none"> ▪ Involve all stakeholders and experts including patient organisations ▪ Create an alliance of patients and professionals ▪ stimulate collaboration between the community and hospitals 		<ul style="list-style-type: none"> ▪ It is important to have a coordinated attitude and shared methodology involving primary care units, emergency care units, hospitals, different professionals, societies and institutions
Coordination	<ul style="list-style-type: none"> ▪ Broaden the scope of the current committee in order to get medical associations, the society 	<ul style="list-style-type: none"> ▪ More committees are needed 		<ul style="list-style-type: none"> ▪ Promote networks at regional level ▪ Build up operational teams at local level 	<ul style="list-style-type: none"> ▪ Appoint coordinators for antibiotic stewardship 	



	of GPs, paediatricians, the scientific community and the public involved			who work in antibiotic stewardship	<ul style="list-style-type: none"> Establish committees in hospitals for controlling antibiotic use, including microbiologists 	
				<ul style="list-style-type: none"> Establish national objectives by the Ministry of Health to endorse agreement between the national and regional levels 		
Leadership	<ul style="list-style-type: none"> The Ministry of Health should take the lead 	<ul style="list-style-type: none"> The visibility of political leadership is needed The ministries need to be committed Promotion among politicians is needed Leadership and implementation of the law is needed 	<ul style="list-style-type: none"> The National Institute of Public Health and the Health Development Institute have to take the lead as they probably have the authority to apply for grants for antibiotic-related programmes 	<ul style="list-style-type: none"> The Ministry of Health should coordinate the different networks National and political commitment is needed to increase collaboration The commitment of the regions is needed 	<ul style="list-style-type: none"> The Institute of Public Health should establish a national committee The first task of the national committee is to make a plan 	<ul style="list-style-type: none"> The Medicines Agency has the lead
Dispensing system	<ul style="list-style-type: none"> Dispense the antibiotics in tablets 				<ul style="list-style-type: none"> Recommend adaptation of the formats to the duration of the dose and treatment 	
Research/data	<ul style="list-style-type: none"> Concrete data are needed 	<ul style="list-style-type: none"> There is need for studies that record good practices from pharmacists and GPs Stimulate the gathering of trend data Production of scientific knowledge in a simplified way 		<ul style="list-style-type: none"> Collect data on antibiotic use and resistance and make them freely available at and regional levels Participate in ECDC surveillance Collaborative research between academics and professions Support academic research Write and distribute periodic reports on AMR 	<ul style="list-style-type: none"> Share medical history; make information accessible 	

* More interventions are mentioned in each Member State; these can be found at www.nivel.nl/eu/arna

8. Consensus statement on the prudent use of antibiotics

A final conference was organised to conclude the ARNA project. Sixty people from 21 EU Member States attended the event, which was held at the Jaarbeurs conference centre in Utrecht, the Netherlands, on 17 June 2016. There were presentations by representatives from DG Health and Food Safety, the Dutch Ministry of Health, Welfare and Sport, the WHO Regional Office for Europe, the ECDC, the ARNA team, various experts in the field of antibiotics and representatives from the six EU Member States where the country-dialogue meetings had been held.

An ARNA conference statement was discussed during the conference and participants were asked to provide their comments and feedback in writing in the week following. The final conference statement (consensus statement) for the ARNA project is reproduced below. The full text can also be found on the ARNA website (<http://www.nivel.nl/eu/arna>).

Towards more prudent use of antibiotics in the European Union: ARNA Conference 2016

ARNA Utrecht conference statement, 17 June 2016

The conference reviewed what needs to be done to achieve more prudent and appropriate use of antibiotics in the Member States of the European Union (EU), with a special emphasis on non-prescription use.

1. Background

Antimicrobial resistance (AMR) is a public health threat for Europe and the world. The threat needs to be confronted through a comprehensive One Health approach, with action on more prudent and appropriate use of antibiotics in the human and animal sectors, the development of new antibiotics and the implementation of the WHO Global AMR Action Plan.

There is a need for clear leadership in all EU Member States by the development and implementation of national plans to combat AMR which should be in place before mid 2017.¹ Better collaboration is needed on a local, national, European and global level. The establishment of multidisciplinary professional networks, like the Strama in Sweden, Bapcoc in Belgium and the SWAB in the Netherlands, create important structures that support, coordinate and stimulate interventions in EU Member States.

Regarding the prudent use of antimicrobials in human medicine, multifaceted approaches are needed that target prescribers, the general public and healthcare as a whole. There is a need to combine interventions, for example restrictive antibiotic prescribing measures, patient education to improve health literacy and multi-/inter-professional collaboration. It is important to recognise that the prudent use of antimicrobials is a responsibility for all stakeholders.

2. General public

- Public health campaigns [Council of the EU ^(fff), 21.1.h] should be integrated into multifaceted interventions that are correctly evaluated.
- It is very important to help educate patients to understand and manage their conditions so that they do not self-medicate (When to consult a doctor or pharmacist? When is an antibiotic appropriate?).
- Messages and interventions need to take people's health literacy into account: the messages and support needs to be framed in such a way that patients remember and learn the right information.
- Innovative ways to educate the general public should be encouraged, for example, the implementation of campaigns in schools like the e-Bug project (<http://e-bug.eu>).
- Mass-media messages should be consistent with information provided by pharmacists and general practitioners (GPs).
- Mass-media messages need to be tailored to the country-specific profile and target groups in each EU Member State.

3. Healthcare workers

- Special attention should be paid to the communication skills of healthcare professionals towards their patients, taking into account the health literacy of patients and supported by patient information.
- Efforts need to be taken to promote and strengthen collaboration between healthcare professionals, and especially between GPs, paediatricians and pharmacists, such as through regular professional meetings.
- Healthcare professionals should also be familiar with treatment guidelines that recommend a prudent use of antibiotics.
- National treatment guidelines [Council of the EU, 22.5] need to be developed that are readily available to practising doctors such as through pocket handbooks. They should also be distributed to pharmacists who can then help to increase the number of prescriptions which adhere to such guidelines, if required.
- National treatment guidelines should be country specific, but to avoid duplication of efforts the evidence should be published in English and made available on a public website.
- The use of sanctions, positive or negative, to promote the adequate use of antibiotics should be encouraged. Positive incentives are preferable [Council of the EU, 21.1.g].
- The use of point-of-care tests to support clinical diagnoses should be explored, so that antibiotics are only used for bacterial infections.
- AMR and antibiotic usage should be integrated into national training curriculums, including continuous education programmes, for example postgraduate education, of HCPs (physicians, pharmacists, nurses).

4. Health system measures

- By mid 2017 all EU Member States [Council of the EU, 21.1] should have developed national plans to combat AMR that are aligned with the WHO Global Action Plan on Antimicrobial Resistance and with standards and guidelines established by intergovernmental bodies (http://www.who.int/drugresistance/global_action_plan/en).
- In EU Member States where antibiotics are available OTC without a prescription, the enforcement of existing laws should be strengthened.
- To avoid self-medication with leftover antibiotics, packages should be tailored to the course of the treatment.
- The surveillance of AMR resistance in primary and secondary care should be supported and strengthened [Council of the EU¹, 21.1.c].
- Surveillance of antibiotic treatments should be performed in primary care and quality indicators should be used [Council of the EU¹, 21.1.c].

^(fff) Council of the European Union conclusions of 17 June 2016 – The next steps under a One Health approach to combat antimicrobial resistance.

- The use of delayed prescribing should be encouraged.

5. EU policy measures

- EU-wide education initiatives such as the European Antibiotic Awareness Day should be supported and encouraged. These activities need to be complemented by interventions on a national or local level to produce sustainable behavioural changes.
- The length of time that antibiotic prescriptions are valid across the EU should be assessed. They currently range from 2 weeks to a full year.
- Benchmarking is a powerful tool in the EU, as countries want to do their best and benchmarking stimulates action. Benchmarking also helps improve transparency which is important for good governance and compliance in the EU [Council of the EU1, 22.1.g].

6. Other policy measures

- The scope of supervisory committees in the field of AMR should be broadened to include all relevant stakeholders, including patient organisations.
- Vaccination programmes, such as against influenza, should be stimulated and supported as these prevent infection and thereby the inappropriate use of antimicrobials.
- Regarding influenza vaccination, best practices should be shared between Member States relating to the delivery of influenza vaccination by other HCPs (nurses and pharmacists).
- Countries should produce and develop scientific evidence, for example the assessment of AMR rates, so that decisions are evidence based in all EU Member States.
- The use of electronic medical records should be increased to register the use of antibiotics and evaluate treatment patterns and outcomes better.
- The exchange of best practices between Member States concerning the use of electronic medical records should be supported, and in particular the use of shared medical records between HCPs. These practices can encourage the prudent use of antimicrobials in that they can prevent double dosing, interactions, adverse drug reactions and 'shopping around' different prescribers for multiple courses of antibiotics.
- EU Member States should integrate the use of targets into national plans to combat AMR, for example targets for antibiotic use measured in defined daily doses (DDD) per 1 000 000 inhabitants per day, or antibiotic prescribing quality indicators.
- A 'whole' healthcare approach should be taken to address the prudent use of antimicrobials, one that integrates both primary and secondary care.
- All EU Member States are encouraged to stimulate and develop antibiotic stewardship initiatives, in, for example, secondary and/or primary care.

9. Conclusions and discussion

This report describes the results of the ARNA project, which was commissioned by the European Commission (DG Health and Food Safety). The ARNA project aimed to:

1. identify key factors that drive the sales and non-prudent use of antibiotics in human medicine obtained without a prescription;
2. assess the level of enforcement of the legislation regarding 'prescription-only' use of antimicrobial agents in the EU;
3. document good practices aimed at strengthening more prudent use of antibiotics;
4. develop policy options for more prudent use of antibiotics.

The ARNA project resulted in the ARNA Utrecht meeting statement, which summarises the necessary actions to achieve more prudent use of antibiotics in the Member States of the European Union, with a special emphasis on non-prescription use. In this final chapter, we summarise and discuss the main findings of the ARNA study. We pay particular attention to the use of antibiotics without a prescription, as this was the main focus of the ARNA project. The findings will be discussed for each of the four aims. For each topic there will be a short discussion followed by a box with the main conclusions.

9.1. Identifying key factors that drive non-prescription use and level of reinforcement

Amount and sources of the use of antibiotics without a prescription

The first aim of the project was to identify key factors that drive sales and non-prudent use of antibiotics without a prescription in human medicine. Before identifying these drivers, the amount of and sources of the use of antibiotics without a prescription were analysed. Most antibiotics in the European Union are dispensed after a prescription by a medical practitioner. However, data from the 2013 and 2016 Eurobarometer surveys showed that the proportion of antibiotics in the EU that were used without a prescription increased from an average of 5 % of all antibiotics used in 2013 to 7 % in 2016.⁸ The highest rates were found in Greece, Romania and Cyprus in both 2013 and 2016. The Member State survey showed that OTC sales of antibiotics are illegal in all Member States, although there are some exceptions in a number of countries – for example creams or eye drops that contain antibiotics. Despite this legal framework, we found that illegal OTC sales occur in various Member States. In Member States such as Greece, Cyprus and Romania, antibiotic use without a prescription is driven by OTC sales in pharmacies. Between 80% and 100 % of all last courses of antibiotics without a prescription were bought in a pharmacy in these Member States. In other Member States, such as Italy, Hungary and Spain, the use of leftover antibiotics is (also) an important source of non-prescription use.

Conclusions

- Despite legal arrangements on antibiotics being prescription-only medicines, there is still use of antibiotics without a medical prescription in the EU.
- There is variation in the use of antibiotics without a prescription across EU Member States. Some Member States with a high level of non-prescription use also have a high level of prescription use, such as Greece and Cyprus, while others such as Hungary and Estonia have a relatively high level of non-prescription use but a lower level of non-prescription use.
- The two prevailing sources of antibiotics without a prescription are OTC sales in pharmacies and the use of leftover antibiotics. Buying antibiotics without a prescription via the internet did not prove to be a major source for antibiotic use without a prescription.

Based upon the results, it can be concluded that interventions and policies that simultaneously target patients and HCPs might be more effective than single-factor approaches. For both groups — patients and professionals — an increasing awareness and knowledge is needed in order to bring about behavioural change. Moreover, the enforcement of laws and regulations is necessary to ensure the sustainability of behavioural change. The studies included in this review paid little attention to the enforcement of laws, while in many European and Western countries obtaining antibiotics without a prescription is illegal. These insights were used in the expert meeting that was organised within the context of the ARNA project (see Chapter 6).

The review had some limitations. Despite our comprehensive search, it is possible that we did not find all the information about the non-prescription use of antibiotics due to publication bias. Still, we found a large variety of studies that did focus on this use. Another limitation is how far the studies we included can be compared. This is because of the different outcome measures they presented and the variety of study designs. Moreover, little information was found on the determinants on the healthcare-system level. On the pharmacy level, the majority of studies included — five out of the eight — were from Spain. Moreover, there was a limited number of studies focusing on the pharmacist, and no studies were found that took into account the prescriber's perspective. And yet, HCPs are key players in educating their patients about the proper use of medicines. As such, more research is needed on the perspective of HCPs. We will look at this again in Chapter 4 of this report. The same is true for the healthcare-system level. There is still much to be explored in the role of governments and other institutions in the prudent use of antibiotics, including the use of antibiotics without a prescription. Section 3.4 provides more insight into the efforts of EU Member States in this respect.

Factors driving the use of antibiotics without a prescription: a complex phenomenon

Patient level

The literature review showed that most evidence for drivers in previous studies was sought for at the patient level. Knowledge about antibiotics was found to be lower among patients who use antibiotics without a prescription compared to the general population (*Source: Eurobarometer analysis, Chapter 3*). Also, the review of the literature showed that knowledge is a crucial factor when it comes to the prudent use of antibiotics. A lack of knowledge is, for example, reflected in the main reasons why patients use an antibiotic without a prescription in the seven ARNA countries. Influenza, common cold, sore throat, cough, fever and headache are all common reasons given by patients for using antibiotics without a prescription, while these are conditions for which usually no antibiotic is needed.

HCPs

In the literature review we only found a limited number of studies focusing on the pharmacist, and no studies were found that took into account the prescriber's perspective. And yet, HCPs are key players in educating their patients about the proper use of medicines. The literature that was available showed that not only is patients' knowledge an important factor in reducing the non-prudent use of antibiotics, but also the knowledge and attitudes of pharmacists regarding antibiotics are critical. The better the knowledge, and the more reluctant the attitude of the pharmacist towards antibiotic use, the less likely he or she will dispense antibiotics without a prescription. Improving knowledge and attitudes should be accompanied by patient campaigns against the use of non-prescription antibiotics. This is important as both pharmacists and GPs in the seven ARNA countries mentioned pressure from patients requesting an antibiotic as a relevant factor. GPs and pharmacists do not always fulfil the requests from these patients, however some of them sometimes do prescribe or dispense an antibiotic when there is patient pressure or there is shared decision-making with the patient. Another reason to dispense an antibiotic in such situations was the fear on the part of pharmacists that patients would go to another pharmacy.

Healthcare system

OTC sales of antibiotics without a prescription are prohibited by law in all EU Member States, with the exception of some specific antibiotics in some countries. However, antibiotics are still being sold over the counter in some Member States. The highest rates of illegal sales of antibiotics without a prescription were found in Greece, Cyprus and Romania. It was found in the ARNA survey that patients in Greece and Cyprus were most convinced that they can easily obtain antibiotics without a prescription from the pharmacy. The literature lacked thorough analyses of the impact of the healthcare system on non-prescription use of antibiotics, yet experts and policymakers argued that the lack of enforcement of laws to prohibit OTC sales of antibiotics influences the use of antibiotics without a prescription. Another driver for the use of leftover antibiotics at the healthcare-system level is the dispensing of whole pre-packed packages of antibiotics.

Conclusions

Antibiotic use without a medical prescription is a complex phenomenon that can be explained on different levels.

Patient level

- At the patient level, knowledge about antibiotics is the most crucial factor to prevent the use of antibiotics without a prescription.
- Patient education on antibiotics should be improved, and special attention is needed for patients with low literacy skills.

HCP level

- At the HCP level, the knowledge and attitudes of pharmacists regarding antibiotics is critical to prevent the use of antibiotics without a prescription in the ARNA countries: the better the knowledge, and the more reluctant the attitude of the pharmacist towards antibiotic use, then the less likely he or she will dispense antibiotics without a prescription.
- HCPs should be educated about antibiotics and about guidelines on antibiotic use and their communication skills should be trained so that they can serve the needs of each individual patient and can handle patient pressure if needed.
- There is not much evidence in the literature on drivers of antibiotic use without a prescription at the HCP level and studies only focused on the pharmacist. HCPs are key players in educating their patients about the proper use of antibiotics. As such, more research is needed on the perspective of HCPs.

Healthcare-system level

- The lack of enforcement of laws to prohibit OTC sales of antibiotics influences the use of antibiotics without a prescription, and enforcement should be improved, for example by a system of rewards and sanctions.
- Dispensing whole pre-packed packages of antibiotics enhances the use of leftover antibiotics, but changing this may require changes in the legal framework or may involve modifications.
- There is not much evidence in the literature review on drivers of antibiotic use without a prescription at the healthcare-system level.

9.2. Good practices

Another aim of the ARNA project was to document good practices aimed at strengthening the prudent use of antibiotics. While the study focused on non-prescription use of antibiotics, this part included practices to increase prudent use of antibiotics in outpatient care in general. Good practices were identified that targeted patients, healthcare professionals and the healthcare system. Examples of good practices include the following.

- Patient level:
 - information campaigns to increase the knowledge of patients on prudent use of antibiotics, such as online campaigns.
- HCP level:
 - educational interventions such as practical training in antimicrobial stewardship or academic detailing;
 - technological support tools such as clinical-decision-support systems;
 - professional meetings such as peer group meetings of general practitioners and pharmacists and feedback on prescribing patterns (e.g. the Netherlands, Sweden);
 - guidelines for rational prescribing;
 - surveillance of antibiotic consumption.
- Healthcare-system level:
 - the European Antibiotics Awareness Day, which also acts as a trigger for attracting attention for prudent use of antibiotics in EU Member States at both the patient and the HCP level;
 - antimicrobial stewardship programmes.
- Multilevel:
 - multifaceted campaigns with consistent information about prudent use of antibiotics targeting the general population and healthcare professionals.

From the review of the literature, the expert meeting and the country-dialogue meetings it became clear that, given the complex of factors that induce the use of antibiotics without a prescription, interventions and policies that simultaneously target patients and HCPs will be more effective than approaches targeting just one of them. An increasing awareness and knowledge is needed from both groups — patients and professionals — in order to induce behavioural change. Targeted interventions are needed too in order to change long-established habits in antibiotic prescription. The World Health Organisation's regional office for Europe (WHO EURO) has developed the TAP (Tailoring Appropriate Antibiotic Use Programmes) tool. This includes a step-by-step approach to develop interventions targeted at changing behaviour regarding antibiotic use in both patients and professionals. Moreover, the sustainability of behavioural change should be ensured.

Still, it should be noted that as many of the interventions so far have not been properly evaluated, especially those on a healthcare-system level, it is difficult to be sure whether all interventions will be effective. This is an area that requires further attention.

Conclusions

- A wide variety of good practices to enhance prudent use of antibiotics exist with a strong focus on healthcare professionals (see above).
- Multifaceted targeted interventions that simultaneously target patients and HCPs will be more effective than approaches targeting just one of them.
- Proper evaluation of the effectiveness of interventions requires further attention as for many interventions.

9.3. Policy options for more prudent use of antibiotics

The last aim of the ARNA project was to develop policy options. During the expert meeting, the country-dialogue meetings and the final conference numerous policy options were discussed at different levels. These focused on both non-prescription and prescription use of antibiotics. This section does not include conclusions but lists the major policy options mentioned at different stages of the ARNA project.

Policy options with regard to sources of non-prescription use

It is important to distinguish between the different sources of non-prescription use of antibiotics as they partly ask for different solutions. In the expert meeting and the country-dialogue meetings, different policy options were mentioned to combat both types of non-prudent use.

Policy options to discourage OTC selling of antibiotics include:

- where OTC sales are occurring in EU Member States, legal enforcement practices need to be strengthened, for example by strengthening the team of inspectors;
- incentives for pharmacists not to sell OTC;
- creating awareness among healthcare professionals, including pharmacists, on non-prudent use of antibiotics and the role of OTC sales;
- creating awareness in the general public that antibiotics should only be used after a prescription from a medical practitioner.

Policy options to discourage the use of leftover antibiotics include:

- delivering the exact number of antibiotics needed and prescribed instead of delivering whole packages;
- avoiding over-prescription by doctors so that the chance of having leftover antibiotics is reduced;
- educating the public to increase awareness on not to use leftover antibiotics and to return leftover antibiotics to the pharmacy, for example by using posters in the offices or by stickers on medication boxes stating that leftovers should not be used;
- educating professionals on how to deal with leftover medication.

Policy options aimed at the public

In the ARNA expert meeting and in the country-dialogue meetings the lack of knowledge on antibiotics and the importance of education of the public were discussed, and it was agreed that the knowledge of the public should be improved. Special attention should be given to patients with low literacy skills, and communication should be adapted in such a way that it is understandable for this target group as well. The following policy options were distinguished to improve knowledge of the public.

- Media campaigns: patients should be educated about when to consult their doctor or pharmacist and when an antibiotic is appropriate. People's health literacy should be taken into account. Messages should be framed in such a way that patients remember and learn the right information and consistency is needed in the information provided by mass media to the general population and by healthcare professionals to patients.
- Encourage innovative ways to educate the general public, for example the implementation of campaigns in schools like the e-Bug project (<http://e-bug.eu>).
- Mass-media messages should be consistent with information provided by pharmacists and GPs. As such, campaign activities aimed at the population and patients should be synchronised with activities aimed at healthcare professionals.

Policy options aimed at HCPs

During the expert meeting it was agreed that professionals need to have good communication skills adapted to the needs of their patients. The expert meeting agreed that HCPs need to be educated about antibiotics and treatment guidelines and that they need to collaborate. An environment should be created that supports HCPs and does not penalise them when, for example, they do not follow the treatment guidelines. The objective should be to encourage a collaborative environment by providing support, training and better tools to do their work. The following main policy options were distinguished.

- Training of skills to communicate properly with patients, taking into account their health literacy, should be started at university. Messages should be framed in such a way that patients remember and learn the right information.
- Promotion of collaboration between HCPs, and especially between GPs and pharmacists, in jointly taking responsibility for prudent prescribing and prudent use of antibiotics, for example through regular professional meetings.
- Integration of AMR and antibiotic usage into national training curricula, including continuous education programmes, for example postgraduate education of HCPs (physicians, pharmacists, nurses), including awareness of non-prescription use of antibiotics.

Policy options at the healthcare-system level

Experts and the country-dialogue meetings in the ARNA countries highlighted the importance of enforcing laws that prohibit the provision of antibiotics without a prescription. The experts agreed that positive rewards for those who are doing well will work better than negative sanctions for those who are not complying. However, it was stated that negative sanctions are sometimes needed or required. Sanctions should be integrated into an educational spirit in order to encourage better behaviour. During the expert meeting and most of the country-dialogue meetings it was also argued that it should be possible to dispense incomplete packages or to adjust the sizes of packages. However, this may require changes in the legal framework in some countries or would involve modifications to the medication delivery chain, which may in turn pose risks to public health such as opening the packages or cutting the blister packs. Thus, in order to change the delivery chain safely, the manner in which the primary packages are produced needs to be changed, for example by producing packages in different sizes or through the delivery of large batches plus product instructions. To summarise, policy options at the healthcare-system level include the following.

- In EU Member States where antibiotics are available OTC without a prescription, the enforcement of existing laws should be strengthened, accompanied by media campaigns to explain the relevance of this law.
- Legislation should be initiated to allow and facilitate dispensing of the exact amount of antibiotics prescribed to avoid leftovers, although this option is not easy to implement.
- Policymakers should work with GP and pharmacist associations to implement different interventions to encourage prudent use of antibiotics.
- Complement the European Antibiotic Awareness Day with activities and/or interventions at national level in order to realise sustainable behavioural change.



9.4. ARNA conference statement

The ARNA project was concluded with the ARNA conference statement, which was formulated during the final conference on 17 June 2016. The conference reviewed what needs to be done to achieve more prudent and appropriate use of antibiotics in the Member States of the European Union. It was concluded that the threats caused by AMR should be confronted through a comprehensive One Health approach, with action on more prudent and appropriate use of antibiotics in the human and animal sectors, the development of new antibiotics and the implementation of the WHO Global AMR Action Plan. Important conditions to achieve this include clear leadership and better collaboration at the local, national, European and global levels. Regarding the prudent use of antimicrobials in human medicine, multifaceted approaches are needed that target prescribers, the general public and healthcare as a whole. There is a need to combine interventions, for example restrictive antibiotic prescribing measures, patient education to improve health literacy and multi-/inter-professional collaboration. Most of all, it is important to recognise that the prudent use of antimicrobials is a responsibility for all stakeholders.

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Appendix A. Questionnaire Member State survey

Survey – Non-prudent use of antibiotics in Europe: public health measures and legislation

The survey has 32 questions. You can stop completing the survey at any moment and you will return to the last question you completed via the URL link.

We understand that you may not be able to answer all of the questions; please skip these questions and continue the survey.

Non-prudent use of antibiotics means antibiotics that are used in insufficient dosages or when patients receive or consume incorrect or unnecessary antibiotics.

Please complete the survey in English.

Please identify yourself

NB: We are collecting this information so that we can contact you if we have any questions regarding your responses to the survey. We will not report names in our Report (only institution names) and once data collection is complete we will only work with an anonymous database.

Name and surname*: _____

Email address*: _____

Institution: _____

Your position: _____

Your area(s) of expertise: _____

**Obligatory*

Type of organisation that you work for:

- Ministry of Health
- National Health Insurance Board
- Institute for the Rational Use of Medicines
- National Public Health Institute
- Professional organisation
- Patient organisation
- Other: _____



National Antibiotic Plan

1. Is there a National Antibiotic Plan document that sets out activities regarding the promotion of appropriate use of antibiotics, responsibilities, budget and timeline in your country?
 Yes
 No (please skip to question 4)
 Don't know
2. If yes, is the National Antibiotic Plan publicly available?
 Yes, please provide a reference, link or attach the Plan: _____
 No, it is a draft version
 No, other reason: _____
 Don't know
3. Is there a national framework or institution that is responsible for assessing, monitoring and evaluating the National Antibiotic Plan?
 Yes, namely: _____
 No
 Don't know

National measures to enhance the prudent use of antibiotics

NATIONAL LAWS AND LEGAL REGULATIONS

NB: In this section we are only interested in national laws and regulations. The next section (questions 9-16) covers national policy measures.

4. We would like to know if there are any national laws or legal regulations for ambulatory (outpatient) care to reduce the non-prudent use of antibiotics in your country concerning the following areas (multiple responses are possible):
 Restrictive prescribing
 Use of delayed medical prescriptions*
 Unused antibiotics
 Preventive medical strategies
 Use of prices and economic incentives
 Statutory/legal guidelines on antibiotic usage
 Other, please specify: _____

*A delayed medical prescription means the antibiotic is prescribed without an immediate delivery of the antibiotic: the patient is advised to use the prescription only when the natural course of the illness develops differently than expected or



foreseen, or when specific criteria are met as indicated by the prescriber. They are also known as 'back-pocket', 'back-up' or 'as needed' prescriptions.

5. Could you describe the national laws or legal regulations which aim to reduce the non-prudent use of antibiotics in your country?

Explanation: If possible, we would like to receive the link for websites or another source (e.g. report) where we can find more information about the laws and regulations. If the text is translated into English, please provide the link.

National laws or regulations	Year	Source

- Don't know

6. Is there any legislation in your country aimed specifically at prohibiting self-medication?

Explanation: When using the term self-medication, we mean individuals who use antibiotics without a medical prescription to self-administer treatment. Individuals can use the following sources to obtain antibiotics without a prescription: (1) Left-overs from a previous treatment that they have stored at home; (2) At the pharmacy without a prescription ('over-the-counter'); (3) Online shopping/e-pharmacies.

- Yes
 No
 Don't know

7. Please briefly describe the content of this legislation?

- Not known

8. Are the laws and regulations to enhance the prudent use of antibiotics being enforced and monitored in your country?

- Yes, by who: _____
 Partly, by who: _____
 No
 Don't know

NATIONAL POLICY MEASURES

9. Are there any national policy measures in your country to enhance the prudent use of antibiotics in ambulatory (outpatient) care (including national campaigns and interventions)?

- Yes, already started
- Yes, in the (near) future
- No
- Don't know

10. What kind of national policy measures are implemented to enhance the prudent use of antibiotics?

NB: Multiple responses are possible

- National media campaigns to raise awareness among the general public
- Surveillance of antibiotic resistance and antibiotic use
- Educational interventions
- Promote research and development of alternative products
- Restrictive/conservative/appropriate prescribing policies
- Prevent self-medication from other sources (e.g. internet)
- Strengthen pharmacy regulations
- Campaigns to manage antibiotic waste (medicine-waste-collection services to avoid misuse of antibiotics)
- Promote collaboration between healthcare professionals (e.g. general practitioners and pharmacists)
- Using healthcare professionals (e.g. general practitioners and pharmacists) in campaigns to promote and conduct awareness on the use of antibiotics
- Training healthcare professions (e.g. general practitioners, pharmacists and pharmacy students) in antimicrobial resistance and antimicrobial resistance-related issues
- Providing antibiotic stewardship in primary care settings
- Other, please specify: _____
- There are no current national measures concerning antibiotic prescribing/dispensing
- Don't know

11. Are there results/evidence for the effectiveness of the above-mentioned national measures?

Explanation: If possible, we would like to receive the link for the website or another source where we can find more information about the effectiveness of these measures. Multiple responses are possible.

- Yes, see the following websites: _____
- Yes, see the following publications: _____
- Current, there is an evaluation of the following policy measures: _____
- No
- Don't know



12. Could you provide us with a Report or URL link that describes the content of national measures aimed at reducing the non-prudent use of antibiotics in your country?

National policy measures	Year

Don't know

13. Do healthcare professionals (e.g. physicians and pharmacists) receive training on good practices regarding the prescription of antibiotics?

Yes, please specify what training: _____

No

Don't know

14. Is there a professional body in your country that publishes treatment guidelines regarding the prescription of antibiotics for the management of infectious diseases?

Yes, see the following websites: _____

No

Don't know

15. Can you give us examples of good-practice projects that have been implemented to encourage more prudent use of antimicrobial agents in your country, including good practices to reduce/mitigate the consumption of antimicrobial use without a prescription?

NB: Multiple responses are possible

Yes, see the following websites: _____

Yes, see the attached report/publication: _____

Yes, please describe: _____

No

Don't know

16. Can you give us the contact details of persons, research groups or organisations in your country that we can contact to obtain more information about these good-practice activities?

Yes, contact details: _____

Don't know

SURVEILLANCE AND AUDITING

17. Does a surveillance or audit procedure exist in your country among healthcare professionals which targets antibiotic prescribing practices in ambulatory care?

- Yes
- No, there is no surveillance system (please skip to question 21)
- There are intentions to start a surveillance among GPs targeting their antibiotic prescribing practice
- Don't know

18. What type of surveillance system exists or are planned for the following healthcare professionals? You can tick all the relevant answer categories (more answers per discipline are possible).

	<i>Obligatory surveillance system</i>	<i>Voluntary surveillance system</i>	<i>Electronic surveillance system</i>	<i>Surveillance system on paper</i>	<i>Covers all antibiotics</i>	<i>Covers certain antibiotics</i>	<i>There is no surveillance system for this discipline</i>
General practitioner	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Paediatrician	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Dentist	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Pharmacist	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Nurse	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Other, specify	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

19. Do healthcare professionals receive feedback of the results of the surveillance procedure?

NB: Multiple responses are possible

- Yes, personal feedback
- Yes, feedback with a benchmark
- Yes, feedback provides conclusions and/or recommendations
- Yes, feedback incorporates eventual implications
- No
- Don't know

20. Does another national or regional system to the one described above exist to report and survey the following issues?

NB: Multiple responses are possible

	Yes	No
Side-effects of antibiotics	<input type="checkbox"/>	<input type="checkbox"/>
Misuse of antibiotics by citizens	<input type="checkbox"/>	<input type="checkbox"/>
Incidents with antibiotics	<input type="checkbox"/>	<input type="checkbox"/>
Over-the-counter antibiotic sales	<input type="checkbox"/>	<input type="checkbox"/>
Other, specify	<input type="checkbox"/>	<input type="checkbox"/>



Legal provisions for the prescription of antibiotics in your country

LAWS AND REGULATIONS REGARDING AMBULATORY (OUTPATIENT) CARE

21. Is it required by law that antibiotics are prescribed by a medical prescription?

- Yes, all antibiotics (for systemic and topical use)
- Yes, all antibiotics except for topical use (e.g. creams and eye drops)
- Some antibiotics require a medical prescription and some do not, please specify: _____
- No
- Other, please specify: _____
- Don't know

22. Do regional (provincial or other) differences exist in the legal provisions within your country?

- Yes, please specify: _____
- No
- Don't know

23. Are there healthcare professionals other than a medical doctor (general practitioner, paediatrician, etc.) or dentist who can prescribe an antibiotic prescription?

NB: Multiple responses are possible

- Pharmacist
- Nurse
- Non-practising clinician (e.g. medical doctor involved in research lab, clinician involved in politics....)
- Other medical / healthcare worker (e.g. veterinarian), specify: _____
- Other, please specify: _____
- No-one else than a practising medical doctor or dentist can prescribe antibiotics
- Don't know

24. Do pharmacists in your country have to dispense the exact prescribed amount of antibiotic pharmaceutical forms (pills, tablets, vials or other)?

- Yes
- No
- No, but there are specific margins specifying how many more or less a pharmacist can dispense
Please specify amount or %: _____
- No, please specify: _____
- Don't know



25. Can pharmacists dispense incomplete packages of antibiotics in your country?

NB: Multiple responses are possible

- Yes, antibiotics can be sold by individual blister
- Yes, antibiotics can be sold by reconstitute pack
- Yes, antibiotics can be sold by number of pills/items/flacons
- No, all antibiotics are dispensed by a 'complete package'
- Don't know

26. Are general practitioners allowed to prescribe antibiotics with a delayed medical prescription?

- Yes
- No, forbidden by law
- No, but a general practitioner / general practitioners might deliver antibiotics on delayed prescription
- Other, please specify: _____
- Don't know

OVER-THE-COUNTER ANTIBIOTICS

Over-the-counter (OTC) antibiotics are antibiotics that can be purchased at the pharmacy without a medical prescription from the general practitioner.

27. Is it possible for pharmacists to sell antibiotics over-the-counter in your country?

- No, it is forbidden by law
- It is not allowed, but in some pharmacies it can be common practice
- Yes, for specific antibiotics, please specify: _____
- Yes, it is allowed
- Other, please specify: _____
- Don't know

28. Can you give an estimate of the percentage of pharmacists in your country who sell antibiotics over-the-counter?

29. Are there any other (illegal) ways patients can obtain antibiotics in your country? (e.g. online shopping, internet pharmacies, with a prescription from another country)

- Yes, please specify: _____
- No
- Don't know



30. Is it possible to buy antibiotics:

a) Online with a prescription from your country?

- Yes
- No
- Don't know

b) Online without a prescription from your country?

- Yes
- No
- Don't know

c) Online with a prescription from another country?

- Yes
- No
- Don't know

d) Online without a prescription from another country?

- Yes
- No
- Don't know

e) Somewhere else than a pharmacy in your country?

- Yes
- No
- Don't know

In this last section of the questionnaire, it is possible to make any final statements that you find relevant with respect to the regularisation of antibiotics in your country.

31. Is there any other statement you wish to make with respect to the regularisation of antibiotics in your country / region. Please feel free to specify below:

32. In case you have ticked several times '**don't know**'. Could you please provide us a link to any other organisation, institution or person who would be able to further complete this questionnaire. Please specify:

Thank you very much for completing this questionnaire!



Appendix B. Questionnaire surveys in seven EU Member States

B.1. Patient questionnaire

Name of survey

ARNA patient questionnaire NIVEL

This questionnaire was written according to TNS quality procedures

checked by

TNS Company	TNS
Repeating study (if this survey has been previously conducted)	
Name of survey	ARNA patient questionnaire NIVEL
Version	3
Contact	
Panel	
Duration of questionnaire	0
Sample size	gross: 0 net: 0
Sample description	
Quota	
If several countries: indicate the countries	
If several targets	
Check-in site	www.tns-nipo.com
Comments	

T1:**Text**

Dear

sir/madam,

You are invited to participate in a research study about the use of antibiotics. With this study we want to gain knowledge about the amount of people in Europe using antibiotics and the reasons for doing this. This is important to know to improve consumer information on antibiotics.

This research project is being conducted by NIVEL (Netherlands Institute for Health Services Research), TNS/Kantar Health and the University of Antwerp. The project is funded by the European Commission.

The interview will require approximately 15 minutes to complete. Your answers will be entirely anonymous. Participation is strictly voluntary and you may choose not to participate at any time.

Your participation in the study is greatly appreciated!

B1: Screener and introductory questions**Begin block****T2:****Text**

We would like to start with some questions relating to the use of antibiotics.

Q1: v1oral**Single coded**

Have you or your child orally taken any antibiotics such as tablets, powder or syrup in the last 18 months?

Instruction for the interviewer: We only want to include respondents that used oral antibiotics. When someone used other forms of antibiotics (e.g. injections, crèmes or eye drops) they are excluded. With children we mean your children (all ages) that are living in your household.

- 1 Yes, I have
- 2 Yes, my child(ren) have
- 3 Yes, my children and I have
- 4 No
- ↙ [GO TO Q101](#)
- 99 Don't know/Don't remember/Refuse
- ↙ [GO TO Q3301](#)

Position fixed*ASK ONLY IF Q1 = 4****Q101: v2oral****Single coded**

Has any other person in your household orally taken any antibiotics such as tablets, powder or syrup in the last 18 months?

Instruction for the interviewer: We only want to include respondents that used oral antibiotics. When someone used other forms of antibiotics (e.g. injections, crèmes or eye drops) they are excluded.

- 1 Yes
- ↙ [GO TO Q102](#)
- 2 No
- ↙ [GO TO Q3301](#)
- 3 Don't know/Don't remember/Refuse
- ↙ [GO TO Q3301](#)



ASK ONLY IF Q101 = 1

Q102: V3oral

Single coded

Can I speak to that person in your household?

Instruction for the interviewer: if the person is home and willing to participate you have to ask Q1 again. Otherwise you can make an appointment to call back,

- 1 Yes, he/she will come at the phone and participate in the research
- 2 No, make an appointment to call back
- 3 No, this person does not want to participate
↩ GO TO Q3301

Q2: v2source

Multi coded

How did you obtain these courses of antibiotics in the last 18 months?

Read the different answer categories

Explanation: *If you used antibiotics for yourself and for your children, the answers should be given for all joint antibiotic courses.*

Explanation code 3: With leftovers we mean antibiotics that you have stored at home or that you received from family/friends

- 1 From a medical prescription
↩ GO TO Q3301
- 2 Administered by a medical practitioner
↩ GO TO Q3301
- 3 You had some left over from a previous course
- 4 Without prescription from a pharmacy
- 5 Online shopping/e-pharmacies
- 6 Without prescription from a pharmacy during my vacation in my own country
- 7 Without prescription from a pharmacy during my vacation in another country
- 8 Without prescription from my dentist/nurse/other healthcare professional
- 9 Without prescription from elsewhere

- 99 Don't know/Don't remember/Refuse
*Exclusive *Position fixed
↩ GO TO Q3301

T3:

Text

From now on, all questions will be related to the use of antibiotics that you received without a medical prescription from your doctor or another healthcare professional. By this we mean antibiotics you have bought or received at the pharmacy, on the internet or somewhere else. Besides, we mean antibiotics that you may have left over from a previous course. These could have been antibiotics with or without a medical prescription.



ASK ONLY IF Q1 = 1

Q301: v3course

Single coded

During the last 18 months, how many courses of antibiotics without a medical prescription did you follow?

Explanation: We mean all joint courses of antibiotics that you obtained from the different sources.

- 1 1 course
- 2 2-3 courses
- 3 4 courses or more
- 99 Don't know/Refuse

*Position fixed

ASK ONLY IF Q1 = 2

Q302: v3course

Single coded

During the last 18 months, how many courses of antibiotics without a medical prescription did your child follow?

Explanation: We mean all joint courses of antibiotics that you obtained for your child from the different sources.

- 1 1 course
- 2 2-3 courses
- 3 4 courses or more
- 99 Don't know/Refuse

*Position fixed

ASK ONLY IF Q1 = 3

Q303: v3course

Single coded

During the last 18 months, how many courses of antibiotics without a medical prescription did you and your child follow?

Explanation: We mean all joint courses of antibiotics that you and your child obtained from the different sources.

- 1 1 course
- 2 2-3 courses
- 3 4 courses or more
- 99 Don't know/Refuse

*Position fixed

B1: Screener and introductory questions

End block

B2: Last course with antibiotics without medical prescription

Begin block

ASK ONLY IF Q1 = 1

T401:

Text

The following questions relate to the last time you used antibiotics without a medical prescription for yourself.

Explanation: Antibiotics without a medical prescription from your doctor can be antibiotics that you had left over from a previous course or antibiotics that you bought at the pharmacy, the internet or somewhere else.

ASK ONLY IF Q1 = 2

T402:

Text

The following questions relate to the last time your child used antibiotics without a medical prescription.

Explanation: Antibiotics without a medical prescription from your doctor can be antibiotics that you had left over from a previous course or antibiotics that you bought at the pharmacy, the internet or somewhere else.

ASK ONLY IF Q1 = 3

T403:

Text

The following question relates to the last time you or your child used antibiotics without a medical prescription.

Explanation: Antibiotics without a medical prescription from your doctor can be antibiotics that you had left over from a previous course or antibiotics that you bought at the pharmacy, the internet or somewhere else.

ASK ONLY IF Q1 = 3

Q4: v4who

Single coded

Was the last course with antibiotics that you received without a medical prescription for yourself or for (one of) your child(ren)?

Explanation: With the last course with antibiotics without a medical prescription we mean the last time you used antibiotics for one or more days in order to relieve the symptoms.

- 1 For myself
- 2 For (one of) my child(ren)
- 99 Don't know/Refuse

**Position fixed*

ASK ONLY IF Q4 = 1,99

T501:

Text

From now on, all questions are related to your last course with antibiotics that you received without a medical prescription!

ASK ONLY IF Q4 = 2

T502:

Text

From now on, all questions are related to your child's last course with antibiotics that you received without a medical prescription!

Q98: bepalen voor zelf of voor kind

Single coded

Dummy

Hulpvraag — wordt niet getoond aan de respondent

- 1 yourself
- 2 your child

Q99:

Single coded

Dummy

Hulpvraag — wordt niet getoond aan respondent

- 1 you
- 2 your child

Q5: v5last

Single coded

How did you obtain the last course of antibiotics without a medical prescription that <answer question 99> used in the last 18 months?

Read the different answer categories

Explanation code 1: With leftovers we mean antibiotics that you have stored at home

- 1 You had some left over from a previous course
- 2 Without prescription from a pharmacy
- 3 Online shopping/e-pharmacies
- 4 Without prescription from a pharmacy during my vacation in my own country
- 5 Without prescription from a pharmacy during my vacation in another country
- 6 Without prescription from my dentist/nurse/other healthcare professional
- 7 Without prescription from elsewhere
- 99 Don't know/Refuse

*Position fixed

ASK ONLY IF Q5 = 1

Q6: v5last

Single coded

Were those leftovers from a previous course you followed yourself or from somebody else?

- 1 They were from a previous course I followed
- 2 They were from a previous course my child followed
- 3 They were from my partner
- 4 They were from friends
- 5 They were from family
- 6 Other

99 Don't know/Refuse**Position fixed***B2: Last course with antibiotics without medical prescription**

End block

B3: Type of antibiotics used + reason for using antibiotics without a medical prescription

Begin block

T6:

Text

The following questions also relate to the last course of antibiotics that <answer question 99> received without a medical prescription. The questions are about the type of antibiotics you used and the reason for needing them.

Q7: v7time

Single coded

When was the last time <answer question 99> used antibiotics without a medical prescription?

- 1 A week ago
- 2 A month ago
- 3 A half year ago
- 4 More than a half year ago
- 99 Don't know/Refuse

**Position fixed*

Q8: v8reason**Single coded**

What was the reason for using antibiotics without a medical prescription for <answer question 98>?

- 1 Pneumonia (an infection causing an inflammation of one or both lungs)
- 2 Bronchitis (the swelling of the airways that lead to the lungs. It often starts the same way as the flu or common cold. Yet, bronchitis is characterised by a painful and severe cough)
- 3 Flu/common cold/sore throat/cough/fever/headache
- 4 Diarrhea
- 5 Urinary tract infection
- 6 Skin or wound infection
- 7 Other
- 99 Don't know/Refuse

Position fixed*Q9: v9disp****Single coded**

How were the antibiotics dispensed?

- 1 Tablets
- 2 Capsules
- 3 Syrup for oral use
- 4 Powder
- 5 Other
- 99 Don't know/Refuse

Position fixed*Q10: v10dur****Single coded**

How many days did <answer question 99> use the last course of antibiotics without a medical prescription?

- 1 1 – 3 days
- 2 4 – 7 days
- 3 More than a week (more than 7 days)
- 99 Don't know/Refuse

Position fixed*Q11: v11use****Single coded**

Did <answer question 99> use all the antibiotics that were dispensed?

- 1 Yes, I used all of them
- 2 No, I had some leftover antibiotics
- 3 Other
- 99 Don't know/Refuse

**Position fixed*

Q12: v12moti**Multi coded**

What was your motivation to use this last course of antibiotics without a medical prescription for <answer question 98>?

Read the different answer categories

Explanation code 3: When the respondent has experience with the antibiotic (for previous courses) and is satisfied with that experience.

Explanation code 6: E.g. when the respondent had some leftovers, did not see the doctor or prefers cheaper antibiotics

Explanation code 7: E.g. because the respondent has a busy working schedule

- 1 Previously prescribed by qualified doctor
- 2 Previously given by pharmacist/medical store personnel without prescription
- 3 You have your own motivation as you like this/these antibiotics
- 4 My doctor is reluctant to prescribe antibiotics
- 5 Previously given/told by friend/family during any illness
- 6 Cost saving
- 7 Saving time instead of first going to the doctor
- 8 Triviality of the symptoms/ mild illness that does not merit seeing a physician
- 9 Quick relief
- 10 Other
- 99 Don't know/Refuse

**Exclusive *Position fixed*

Q13: v13reim**Single coded**

Were the costs of this last course of antibiotics without a medical prescription reimbursed by your health insurance?

Explanation: with health insurance we mean both public and private health insurances

- 1 Complete reimbursement
- 2 Patient co-payment
- 3 No reimbursement
- 4 I am not insured/have no health insurance
- 99 Don't know/Refuse

**Position fixed*

B3: Type of antibiotics used + reason for using antibiotics without a medical prescription**End block****B4: Experienced (side) effects****Begin block****T7:****Text**

The following questions relate to experienced positive or negative effects of the last course of antibiotics without medical prescription <answer question 98>.

Q14: v14better**Single coded**

When <answer question 99> last used antibiotics without a medical prescription, did they help?

- 1 Yes
- 2 No
- 99 Don't know/Refuse

**Position fixed*

Q15: v15ad**Single coded**

During the last course of antibiotics without a medical prescription, did <answer question 99> encounter any adverse side effects?

- 1 Yes
- 2 No
- 99 Don't know/Refuse

Position fixed*ASK ONLY IF Q15 = 1****Q16: v16ef****Multi coded**

Which side effects did <answer question 99> experience during the last course with antibiotics without a medical prescription?

Explanation code 3: the inappropriate use of antibiotics can mask the correct diagnosis and delay appropriate therapy.

- 1 Diarrhea
- 2 Rash
- 3 Masked diagnosis of infectious disease
- 4 Renal failure
- 5 Allergic reactions
- 6 Upset stomach
- 7 Other
- 99 Don't know/Refuse

Exclusive *Position fixed*B4: Experienced (side) effects****End block****B5: Information about prudent use****Begin block****T8:****Text**

The following questions are related to the last used course of antibiotics for <answer question 98> that you received without a medical prescription. We would like to know whether you received information about how to use these antibiotics.

Q17: v17advice**Single coded**

Did you receive advice or information about how to use the antibiotics without a medical prescription for <answer question 98>?

Explanation: We mean information or advice from the source where you obtained the antibiotics.

- 1 Yes
- 2 No
- 99 Don't know/Refuse

**Position fixed*

ASK ONLY IF Q17 = 1

Q18: v18where

Multi coded

From whom or where did you obtain this information about how to use the antibiotics properly?

- 1 Pharmacy staff
- 2 General practitioner (doctor)
- 3 Other healthcare professional
- 4 Internet
- 5 National campaign
- 6 Other media (than the internet/national campaign)
- 7 Other
- 99 Don't know/Refuse

**Exclusive *Position fixed*

ASK ONLY IF Q17 = 1

Q19: v19info

Multi coded

What information did you obtain about the use and side-effects of antibiotics without a medical prescription?

read the different answer categories

- 1 Complete the full course of antibiotics
- 2 Only take the antibiotics over the prescribed period at the correct dose
- 3 Do not give your antibiotics to anyone else
- 4 Return outdated or unused antibiotic (leftovers) to the pharmacy
- 5 Advise about how to act if the condition persists or if the infection becomes worse
- 6 Information about conditions under which the antibiotics should not be taken
- 7 Information about possible medical allergies
- 8 Information about side-effects (like soft stools, diarrhea, mild stomach upset)
- 9 Information about drug interaction
- 10 Other
- 99 Don't know/Refuse

Exclusive *Position fixed*B5: Information about prudent use**

End block

B6: Other person's use of antibiotics without a medical prescription

Begin block

T9:

Text

The next question is about other person's use of antibiotics without a medical prescription.

Q20: v20envi

Single coded

Are there people around you (i.e. partner and/or family) who use any antibiotic without a medical prescription?

- 1 Yes
- 2 No
- 99 Don't know/Refuse

**Position fixed*

ASK ONLY IF Q20 = 1

Q21: v21person
Multi coded

Can you tell us which persons in your near environment take antibiotics without a medical prescription?

Read the different answer categories

- | | | | |
|----|--------------------------|------------|--------|
| 1 | <input type="checkbox"/> | Partner | |
| 2 | <input type="checkbox"/> | Extended | family |
| 3 | <input type="checkbox"/> | Neighbours | |
| 4 | <input type="checkbox"/> | Friends | |
| 5 | <input type="checkbox"/> | Other | |
| 99 | <input type="radio"/> | Don't know | |
| 88 | <input type="checkbox"/> | Refuse | |
- *Exclusive *Position fixed*

B6: Other person's use of antibiotics without a medical prescription
End block
B7: Knowledge and attitudes about antibiotics in general
Begin block
T10:
Text

Contrary to the previous questions, the following questions are not only related to the last course of antibiotics used that you received without a medical prescription. These questions are about the use of antibiotics in general over the last 18 months. These questions relate to your knowledge and attitude about antibiotics in general.

Q22: v22knowa-f
Matrix

For each of the following statements, please tell me whether you agree or disagree.

	Strongly Disagree	Disagree	Neither agree/ nor disagree	Agree	Strongly Agree	Not sure	Refuse
Antibiotics kill viruses	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Antibiotics are effective against a cold and the flu	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Taking antibiotics often has side-effects such as diarrhea	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
If antibiotics have been prescribed before, they will be required again for similar symptoms in the future	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
A prescription for antibiotics for minor ailments is not necessary	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Unnecessary use of antibiotics make them become ineffective	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Q23: v23stata-d
Matrix

Think about the last 18 months. To what extent do you agree or disagree with the following statements:

	Strongly Disagree	Disagree	Neither agree/ nor disagree	Agree	Strongly Agree	Not sure/ not applicable	Refuse
I can easily convince my GP to prescribe me antibiotics	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
I can easily get antibiotics from my pharmacist without a medical prescription	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
I can easily get antibiotics from the internet without a medical prescription	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
I can easily get antibiotics from my family, friends or neighbours	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Q24: v24bron
Multi coded

Just imagine you have bronchitis and you think you need antibiotics. In which of the following situations do you believe it is appropriate to get antibiotics without a medical prescription?

Read the different answer categories

Interviewer instruction: Read the different answer categories and ask if it is appropriate to receive antibiotics without prescription in the view of the respondent. In case the respondent answers 'yes' then mark/tick/check off this answer category. In case the respondent answers 'no' then leave the square empty.

Explanation: Bronchitis is the swelling of the airways that lead to the lungs. It often starts the same way as the flu or common cold. Yet, bronchitis is characterised by a painful and severe cough.

Explanation code 1: Do you think it is appropriate to get antibiotics without prescription for your bronchitis when you have no other symptoms/illnesses and it is a normal work/living week without important events. You have the time to go to your regular practitioner for a diagnosis.

Explanation code 2: Do you think it is appropriate to get antibiotics without prescription for your bronchitis when you are on your holiday (you cannot see your own general practitioner) and there is an important event coming up that requires a lot of your energy.

- 1 During the week in a normal situation
- 2 During the week with an important event coming up or holiday abroad
- 3 You have no time to go to the doctor
- 4 When the doctor has no time to see you immediately
- 5 When a consultation with a doctor is too expensive

 9999999

Don't know

 88 Refuse

B7: Knowledge and attitudes about antibiotics in general
End block
B8: Background
Begin block

T11:**Text**

The last section of the questionnaire refers to background or biographical information. Although we are aware of the sensitivity of the questions in this section, the information is anonymous and allow us to compare groups of respondents.

Q25: v25area**Single coded**

Which of the following best describes the area you live in?

Read the different answer categories

- 1 Urban
- 2 Suburban
- 3 Rural
- 99 Don't know/Refuse

Position fixed*Q26: v26edu****Single coded**

What is the highest educational level you have completed?

- 1 Low
- 2 Medium
- 3 High
- 99 Don't know/Refuse

Position fixed*Q27: v27job****Single coded**

Which of the following categories best describes your primary area of employment?

Read the different answer categories

- 1 Self-employed
- 2 Employee at a company/business
- 3 Government employee
- 4 Incapacitated, unfit for work
- 5 Out of work and/or looking for work
- 6 Retired
- 7 A student
- 8 A housewife/houseman
- 9 Other
- 99 Don't know/Refuse

Position fixed*Q28: v28ins****Multi coded**

Do you have health insurance?

Explanation: with national health insurance we mean a public insurance. With a community/social insurance we mean an health insurance provided by an employer or organisation.

- 1 Yes, I am covered by the national (public) health insurance
- 2 Yes, I am covered by private health insurance
- 3 Yes, I am covered by a community/social healthcare insurance
- 4 Other
- 5 No, I am not insured
- 8888888 Don't know/Refuse

Exclusive *Position fixed*Exclusive *Position fixed*

**Q29: v29doc****Single coded**

Do you usually visit the same general practitioner (doctor) or the same practice (including a primary centre)?

- 1 Yes
- 2 No
- 3 Other
- 99 Don't know/Refuse

Position fixed*Q30: v30smoke****Single coded**

Do you currently smoke?

- 1 Yes
- 2 No
- 99 Don't know/Refuse

**Position fixed*

ASK ONLY IF Q98 = 1

Q3101: v31health**Single coded**

How is your health in general at the moment?

- 1 Excellent
- 2 Good
- 3 Fair
- 4 Bad
- 5 Very
- 99 Don't know/Refuse

bad

**Position fixed*

ASK ONLY IF Q98 = 2

Q3102: v31health**Single coded**

How is the health of your child in general at the moment?

- 1 Excellent
- 2 Good
- 3 Fair
- 4 Bad
- 5 Very
- 99 Don't know/Refuse

bad

**Position fixed*



ASK ONLY IF Q98 = 1

Q3201: v32chro

Multi coded

Do you suffer from any long-standing respiratory illness or condition or another long-standing illness or condition?

- 1 Yes, asthma
- 2 Yes, chronic obstructive pulmonary disease
- 3 Yes, emphysema
- 4 Yes, diabetes mellitus
- 5 Yes, cardiovascular disease
- 6 Yes, hypertension
- 7 Yes, other
- 8 No
- 99 Don't know/Refuse

**Exclusive *Position fixed*

ASK ONLY IF Q98 = 2

Q3202: v32chro

Multi coded

Does your child suffer from any long-standing respiratory illness or condition or another long-standing illness or condition?

- 1 Yes, asthma
- 2 Yes, chronic obstructive pulmonary disease
- 3 Yes, emphysema
- 4 Yes, diabetes mellitus
- 5 Yes, cardiovascular disease
- 6 Yes, hypertension
- 7 Yes, other
- 8 No
- 99 Don't know/Refuse

**Exclusive *Position fixed*

Q3301: v33age

Numeric

Max 100

What is your age?

Scripter notes: insert a 'refuse' button

ASK ONLY IF Q98 = 2

Q3302: v33age

Numeric

Max 100

What is the age of your child?

Scripter notes: insert a 'refuse' button



Q3401: v34sexe

Single coded

What is your gender?

Instruction interviewer: Only ask if you are not sure and if the question is about the respondent him-/herself!

- 1 Male
- 2 Female
- 88 Refuse

ASK ONLY IF Q98 = 2

Q3402: v34sexe

Single coded

What is the gender of your child?

- 1 Male
- 2 Female
- 88 Refuse

B8: Background

End block



B.2. GP questionnaire

Name of survey

ARNA GP questionnaire NIVEL

Client name

Author(s)

Tim van de Voorn

This questionnaire was written according to TNS quality procedures

checked by

TNS Company	TNS
Repeating study (if this survey has been previously conducted)	
Name of survey	ARNA GP questionnaire NIVEL
Version	2
Author(s)	Tim van de Voorn
Contact	
Panel	
Duration of questionnaire	0
Sample size	gross: 0 net: 0
Sample description	
Quota	
If several countries: indicate the countries	
If several targets	
Check-in site	www.tns-nipo.com
Comments	

T1:**Text**

Dear

sir/madam,

You are invited to participate in a research study about the use of antibiotics, with a specific focus on the use of antibiotics without a medical prescription. We would like to obtain more insight into the role general practitioners have in the use of antibiotics without a medical prescription. When patients use antibiotics without medical prescription from their healthcare professional, we call this self-medication. They can obtain the antibiotics without medical prescription at the pharmacy in your own country or in another European country. Moreover, patients can use antibiotics they had left over from a previous course. Information about this subject is necessary because patients who use antibiotics without a medical prescription don't always do this adequately. As a possible result, antibiotics may become ineffective.

This research project is being conducted by NIVEL (Netherlands Institute for Health Services Research), TNS/Kantar Health and the University of Antwerp. The project is funded by the European Commission.

The interview will require approximately 10 minutes to complete. Your answers will be entirely anonymous. Participation is strictly voluntary and you may refuse to participate at any time. Moreover, it is possible for you to indicate when a specific question is not applicable for your country.

Your participation in the study will be highly appreciated!

B1: Do patients use antibiotics without a medical prescription?**Begin block****T2:****Text**

We will begin with some questions about patients who use antibiotics without a medical prescription. These patients use antibiotics to self-administer treatment for often unmanaged, undiagnosed physical ailments. They obtained or purchased the antibiotics without medical prescription for example at the pharmacy in their own country or on vacation or on the internet. Besides they could have used leftover antibiotics from a previous course from themselves or from their friends, family.

Q1: v1aware**Single coded**

During the last 12 months, were you aware of patients who use oral antibiotics without a medical prescription?

1 Yes2 No↵ **GO TO Q8**3 Not sure↵ **GO TO Q8**

7777777

Not applicable

↵ **GO TO Q8**

9999999

Don't know/Refuse

↵ **GO TO Q8****Position fixed***Position fixed*



ASK ONLY IF Q1 = 1

Q2: v2ask

Numeric

Max 1000

During one month, how many patients on average, request oral antibiotics for reasons you would not prescribe an antibiotic (e.g. for minor ailments/viruses) in your practice?

Instructions interviewer: we would like to receive an absolute number from the respondent. If the respondent gives an percentage, ask if the respondent could try to give an absolute number.

In case the respondent don't know → Can you give an estimation of the number of patients that ask for antibiotics for reasons you would not prescribe an antibiotic in your practice (e.g. for minor ailments or viruses)?

Scripter notes: Please add a 'Don't know/Refuse' button with code 9999999
And a 'Not applicable' button with code 7777777

Also, the title of this don't know answer is v2b (instead of v2ask)

Q3: v5reason

Multi coded

Do you know what the reasons are for your patients to use oral antibiotics without a medical prescription?

Read the different answer categories

Explanation: *By antibiotics without a medical prescription, we mean e.g. antibiotics purchased at the pharmacy without medical prescription, leftovers from previous courses or antibiotics purchased online.*
Explanation code 4: *E.g. when the patient had some leftovers, did not see the doctor or prefers cheaper antibiotics*

Explanation code 5: *E.g. because of busy working schedules*

- 1 Patients have their own motivations because a qualified doctor has previously prescribed this/antibiotics to them in the past
- 2 Patients have their own motivations because they were previously given by pharmacist/medical store personnel without a prescription
- 3 Previously given/told by friend/family of the patient during any illness
- 4 Cost savings
- 5 Saving time instead of going to the doctor first
- 6 Mild illness that does not merit seeing a physician or quick relief
- 7 Other

9999999

Don't know/Refuse



*Exclusive *Position fixed

Q4: v6react

Single coded

How do you usually react to patients who demand for antibiotics when these are not indicated?

Explanation: For instance for minor ailments or a viral infection.

- 1 I refer them to the pharmacy with an antibiotic prescription
 - 2 Sometimes I give a prescription for the antibiotics, sometimes I refuse to give a prescription for antibiotics
 - 3 I always refuse to give them an antibiotic prescription
 - 4 I refer them to the pharmacy without an antibiotic prescription
 - 5 I advise them to wait and come back when the symptoms persist/become worse
 - 6 Other
- 9999999
Don't know/Refuse *Position fixed

ASK ONLY IF Q4 = 1,2

Q5: v7sel

Multi coded

What are your main reasons to prescribe antibiotics for complaints which not require an antibiotic course (e.g. minor ailments/viral infections)?

Read the different answer categories

- 1 Pressure from the patient (verbal patients and/or frequent consultation)
 - 2 Social or current vulnerable status of the patient (e.g. homeless)
 - 3 Shared decision-making with the patient
 - 4 Pressure from the pharmacist to sell antibiotics
 - 5 Threat to lose the business
 - 6 Fear that patients will go to another general practitioner, where they would probably get a prescription for antibiotics
 - 7 Competition from the internet
 - 8 Lack of national guidelines and regulations
 - 9 When patients are ill, I prescribe them antibiotics
 - 10 I end up prescribing an antibiotic because I have no time to spend explaining why an antibiotic for him/her is not needed
 - 11 Other
- 9999999
Don't know/Refuse *Exclusive *Position fixed

Q6: v10pres

Single coded

Do you sometimes feel pressured to prescribe antibiotics when they are not indicated (e.g. for minor ailments)?

Explanation:

- Do you have the feeling that you sometimes prescribe antibiotics only because the patient requests these antibiotics, even when an antibiotic course is not necessary?
- Do you have the feeling you do anything to please your patients?
- Do you find it difficult to refuse to prescribe antibiotics to (some of) your patients?

- 1 Yes
 - 2 No
- 9999999
Don't know/Refuse *Position fixed



ASK ONLY IF Q6 = 1

Q7: v11presex

Multi coded

What is or are the reason(s) for feeling this pressure?

Read the different answer categories

- 1 Diagnostic uncertainty
- 2 Verbal patients
- 3 Financial losses
- 4 Threat to lose the business
- 5 Pressure from pharmacist companies/enterprises
- 6 Fear that patients will go to another general practitioner
- 7 Competition from the internet
- 8 Other
- 9999999
- Don't know/Refuse

Q8: v8guide

Single coded

Do you have the feeling that general practitioners in your country follow the national guidelines for the appropriate way of prescribing antibiotics?

- 1 Always
- 2 For the major part
- 3 In the minority of cases
- 4 Not at all
- 5 Not sure
- 6 There are no national guidelines
- 9999999
- Don't know **Position fixed*
- 8888888
- Refuse **Position fixed*

B1: Do patients use antibiotics without a medical prescription?

End block

B2: Misconceptions among patients

Begin block

T3:

Text

The following question is about common misconceptions from patients about antibiotics. Therefore we would like to ask you if you can put yourself in the place of the regular patient and think about what their conceptions are. Also, think of questions patients often ask that indicate a lack of knowledge about antibiotics.

Q9: v18custa – f
Matrix

We would like to know to what extent you agree or disagree with the following statements about the conceptions of patients:

Read the different answer categories

	Strongly Disagree	Disagree	Neither agree/ nor disagree	Agree	Strongly Agree	Not sure	Refuse
Patients believe that antibiotics kill viruses	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Patients believe that antibiotics are effective against a cold and the flu	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Patients believe that antibiotics do not have side effects	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Patients believe that if antibiotics have been prescribed before, they will be required again for similar symptoms in the future	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Patients believe that a prescription for antibiotics for minor ailments is not necessary	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Patients believe that they can stop taking the antibiotics when the symptoms are over	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

B2: Misconceptions among patients
End block
B3: Do pharmacists sell antibiotics without a medical prescription?
Begin block
T4:
Text

The following questions relate to pharmacists in your country who sell antibiotics without a medical prescription.

Q10: v19other
Single coded

Do you personally know pharmacists in your country who sell antibiotics without a medical prescription?

 1 Yes

 2 No

 7777777

 Not applicable

 9999999

 Don't know

 8888888

 Refuse *Position fixed

*Position fixed

*Position fixed



Q11: v20perc

Numeric

Max 10000

We also would like to know if you think there are (other) pharmacists in your country who sell antibiotics without a medical prescription. In general, can you give an estimation of the percentage of pharmacists in your country doing this?

Instructions interviewer: we would like to receive an percentage from the respondent. If the respondent gives an absolute number, ask if the respondent could try to give a percentage.

Scripter notes: Please add a don't know and refuse button with codes 9999999 and 8888888 respectively

B3: Do pharmacists sell antibiotics without a medical prescription?

End block

B4: Do pharmacists sell antibiotics without a medical prescription?

Begin block

T5:

Text

The following question relates to your opinion on the use of antibiotics without a medical prescription.

Q12: v21stata – e
Matrix

We would like to know to what extent you agree or disagree with the following statements:

Read the different answer categories

	Strongly disagree	Disagree	Neither agree/nor disagree	Agree	Strongly agree	Not sure	Refuse
The use of antibiotics without a medical prescription increases the risk of antibiotic resistance	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The use of antibiotics without a medical prescription is a problem in the treatment of respiratory infections	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The use of antibiotics without a medical prescription is not an issue among the population visiting my own medical practice	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The use of antibiotics without a medical prescription is a significant problem in my country	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The use of antibiotics without a medical prescription is a significant problem in other countries within Europe	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

B4: Do pharmacists sell antibiotics without a medical prescription?

End block

B5: Possible solution(s) to diminish the use of antibiotics without a medical prescription

Begin block

T6:

Text

The next few questions are about possible solutions to diminish the use of antibiotics without a medical prescription. This means that the questions are only about non-prescribed antibiotics.

Q13: v22red**Single coded**

Do you think that the amount of antibiotics patients are taking without a medical prescription should be reduced?

Explanation: We mean the antibiotics patients receive without medical prescription from their general practitioner or from another healthcare professional.

- 1 Yes
↙ GO TO Q14
- 2 No
↙ GO TO Q17
- 7777777
Not applicable **Position fixed*
- 9999999
Not sure/Refuse **Position fixed*
↙ GO TO Q17

Q14: v23achieve**Multi coded**

How could this be achieved?

Read the different answer categories

Instructions interviewer: Only tick the answer category 'Other' if the respondent spontaneously gives an answer that doesn't resembles any of the existing answer categories.

- 1 Public education (national media campaigns) to reduce misconceptions about the use of antibiotics for minor ailments
- 2 Enforcement of the laws regulating the sale of antibiotics
- 3 Dispensing regulation: dispensing exact numbers of antibiotic tablets
- 4 Education for healthcare professionals
- 5 More restrictive/conservative/appropriate prescribing by general practitioners
- 6 Preventing of self-medication from other sources (e.g. internet)
- 7 Strengthening pharmacy regulations
- 8 Informing the medical guidelines more often
- 9 Providing more information on local resistance patterns
- 10 Other
- 9999999
Don't know/Refuse **Exclusive *Position fixed*

Q15: v24lim**Single coded**

Do you feel limited in what you can do as healthcare professional against the use of antibiotics without a medical prescription?

- 1 Yes
- 2 No
- 7777777
Not applicable **Position fixed*
- 9999999
Don't know/Refuse **Position fixed*

ASK ONLY IF Q15 = 1

Q16: v25expl

Multi coded

Could you explain why?

Read the different answer categories

Explanation code 3: if the patient repeatedly ask for antibiotics and tries to convince you to sell the antibiotics

Explanation code 8: *selling antibiotics over-the-counter by pharmacists*

- 1 You feel you have to do everything possible to cure the patient
- 2 Costs
- 3 Patient pressure
- 4 Legal issues
- 5 Company/enterprise pressures
- 6 Public health considerations
- 7 Cooperation of all pharmacists/general practitioners
- 8 OTC by pharmacists
- 9 Other

9999999

Don't know/Refuse

Exclusive *Position fixed*Q17: v26cam**

Single coded

Are there any national campaigns to reduce the use of antibiotics without a medical prescription that you are aware of?

- 1 Yes
- 2 No

7777777

Not applicable

9999999

Don't know/Refuse

Position fixed*Position fixed***Q18: v27prof**

Multi coded

Are there any professional meetings about the use of antibiotics in your country that you have participated in?

Explanation: With professional meetings we mean meetings between general practitioners and/or pharmacists and general practitioners that discuss problems concerning the use of antibiotics (for example PTAMs (Pharmaco Therapy Audit Meetings)).

- 1 Yes, between general practitioners
- 2 Yes, between pharmacists and general practitioners
- 3 Yes, between general practitioners and other healthcare professionals
- 4 No
- 5 Other

9999999

Don't know/Refuse

**Exclusive *Position fixed*

Q19: v28suf

Single coded

Do you receive sufficient information about the use of antibiotics without a medical prescription in your community?

1 Yes2 No7777777 Not applicable 9999999 Don't know/Refuse

*Position fixed

*Position fixed

B5: Possible solution(s) to diminish the use of antibiotics without a medical prescription

End block

B6: Background

Begin block

T7:

Text

The last section of the questionnaire refers to your (professional) background situation. Although we are aware of the sensitivity of the questions in this section, the information is anonymous and allow us to compare groups of respondents.

Q20: v29age

Numeric

Max 100

What is your age?

Scripter notes: Please add a 'Refuse' button with the code 9999999

Q21: v30type

Single coded

What is the type of your practice?

1 Public2 Private3 Group4 Other9999999

Refuse *Position fixed

practice

Q22: v31gra

Numeric

Min 1960 | Max 2014

In what year did you graduate?

Scripter notes: Please add a 'Refuse' button with code 9999999



Q23: v32sexe

Single coded

What is your gender?

Instruction interviewer: Only ask if you are not sure!

- 1 Male
- 2 Female
- 9999999
- Refuse **Position fixed*

B6: Background

End block



B.3. Pharmacist questionnaire

Name of survey

ARNA pharmacist questionnaire NIVEL

This questionnaire was written according to TNS quality procedures

TNS Company	TNS
Repeating study (if this survey has been previously conducted)	
Name of survey	ARNA pharmacist questionnaire NIVEL
Version	3
Contact	
Panel	
Duration of questionnaire	0
Sample size	gross: 0 net: 0
Sample description	
Quota	
If several countries: indicate the countries	
If several targets	
Check-in site	www.tns-nipo.com
Comments	



T1:

Text

Dear

sir/madam,

You are invited to participate in a research study about the use of antibiotics, with a specific focus on non-prescribed antibiotics. We would like to obtain more insight into the role of pharmacists in selling antibiotics over the counter without a medical prescription and to assess the issue of self-medication. Customers can obtain antibiotics for self-medication at the pharmacy in your own country or in another European country. Moreover, customers can use antibiotics they had left over from a previous course. Information about this subject is necessary as customers who use antibiotics without a medical prescription don't always do this adequately. As a possible result, antibiotics may become ineffective.

This research project is being conducted by NIVEL (Netherlands Institute for Health Services Research), TNS/Kantar Health and the University of Antwerp. The project is funded by the European Commission.

The interview will require approximately 15 minutes to complete. Your answers will be entirely anonymous. Participation is strictly voluntary and you may refuse to participate at any time. Moreover, it is possible for you to indicate when a specific question is not applicable for your country.

Your participation in the study will be highly appreciated!

B1: Do customers request antibiotics?

Begin block

T2:

Text

We will begin with some questions about customers who have requested antibiotics without a medical prescription from their general practitioner or another healthcare professional.



Q1: v1aware

Single coded

During the last 12 months, did customers in your pharmacy request for oral antibiotics without a medical prescription?

Instruction for the interviewer: We only want to know if the respondent was aware of the use of oral antibiotics among customers. When customers used other forms of antibiotics (e.g. injections, creams or eye drops) this means you should tick the answer category 'No'.

Explanation:

-With self-medication we mean individuals who use non-prescribed antibiotics for unmanaged and/or undiagnosed physical ailments.

-We also mean customers who asked for oral antibiotics without a medical prescription but did not receive them at your pharmacy.

- 1 Yes
- 2 No
↙ GO TO B3
- 3 Not sure
↙ GO TO B3
- 7777777 Not applicable
↙ GO TO B3 **Position fixed*
- 8888888 Refuse **Position fixed*
↙ GO TO B3

Q2: v2ask

Numeric

Max 1000

During one month, how many customers in your pharmacy, on average, ask for oral antibiotics without having a medical prescription?

Instructions interviewer: we would like to receive an absolute number from the respondent. If the respondent gives a percentage, ask if the respondent could try to give an absolute number.

In case the respondent doesn't know: Could you give an estimation of the number of customers that ask for antibiotics without a medical prescription?

Scripter notes: include a 'Don't know/Refuse' button with code 9999999

**Q3: v3otc****Single coded**

Can customers buy certain oral antibiotics at your pharmacy without a medical prescription?

1 Yes2 No↩ **GO****TO****B3**

7777777

Not applicable

*Position fixed

9999999

Don't know/Refuse

*Position fixed

↩ **GO TO B3****Q4: v4type****Multi coded**

During the last 12 months, which type of oral antibiotics did you sell without a medical prescription at least once? We are interested in the generic names of these oral antibiotics.

Instructions interviewer: Only read the different answer categories when the respondent cannot answer the question on his/her own (the answer categories are in alphabetical order).

1 Amoxicillin2 Amoxicillin and enzyme inhibitor3 Azithromycin4 Bacampicillin5 Benzathine phenoxymethylpenicillin6 Cefaclor7 Cefalexin8 Cefixime9 Cefpodoxime10 Ceftibuten11 Ceftriaxone12 Cefuroxime13 Ciprofloxacin14 Clarithromycin15 Clindamycin16 Doxycycline17 Flucloxacillin18 Fosfomicin19 Josamycin20 Levofloxacin21 Moxifloxacin22 Norfloxacin23 Phenoxymethylpenicillin24 Pivmecillinam25 Roxithromycin26 Sulfamethoxazole+trimethoprim27 Other

9999999

Don't know/Refuse



Q5: v5reason

Multi coded

Do you know what the reasons are for customers to buy antibiotics without a medical prescription at the pharmacy?

Read the different answer categories

Explanation code 4: E.g. when the customer had some leftovers, did not see the doctor or prefers cheaper antibiotics

Explanation code 5: E.g. because of the customer has a busy working schedule

NB: From now on, when we refer to 'antibiotics', we mean 'oral antibiotics'

- 1 Patients have their own motivations because a qualified doctor has previously prescribed this/antibiotics to them in the past. Patients have their own motivations because they were previously given antibiotics by a pharmacist/medical store personnel with
 - 2 Patients have their own motivations because they were previously given by pharmacist/medical store personnel without a prescription
 - 3 Previously given/told by friend/family of the customer during any illness
 - 4 Cost saving
 - 5 Saving time instead of going to the doctor first
 - 6 Mild illness that does not merit seeing a physician or quick relief
 - 7 Other
- 9999999
- Don't know/Refuse

Q6: v6react

Single coded

How do you usually react to customers who request antibiotics without a medical prescription?

- 1 I sell them antibiotics
 - 2 Sometimes I sell the antibiotics, sometimes I refuse to sell the antibiotics
 - 3 I always refuse to sell the antibiotics
 - 4 I give alternatives (like other drugs/treatments)
 - 5 I tell the customer to visit the physician first
 - 6 Other
- 9999999
- Don't know/Refuse



ASK ONLY IF Q6 = 1,2

Q7: v7sel

Multi coded

What are your main reasons for selling antibiotics without a medical prescription?

Read the different answer categories

- 1 Pressure from the customer (e.g. verbal customer)
 - 2 Social or current vulnerable status of the customer (e.g. homeless)
 - 3 Shared decision-making with the customer
 - 4 Pressure from the GP to sell antibiotics
 - 5 Threat to lose the business
 - 6 Fear that customers will go to another pharmacy, where they would probably get the antibiotics
 - 7 Competition from the internet
 - 8 Lack of national guidelines and regulations
 - 9 When patients are ill, I sell them antibiotics
 - 10 Other
- 9999999
- Don't know/Refuse

ASK ONLY IF Q6 = 1,2

Q8: v8why

Single coded

Do you ask customers why they request antibiotics without a medical prescription?

- 1 Yes, always
 - 2 Yes, sometimes
 - 3 Never
- 9999999
- Don't know/Refuse

ASK ONLY IF Q6 = 2,3,4,5

Q9: v9not

Multi coded

What are your main reasons for NOT selling antibiotics without a medical prescription?

Read the different answer categories

- 1 Administrative reasons
 - 2 Legal requirements
 - 3 Because of possible antibiotic resistance
 - 4 Risk for the customer for using the wrong antibiotics
 - 5 Risk for the customer for adverse antibiotic reactions
 - 6 Risk for the customer for a wrong diagnosis
 - 7 Risk for the customer for the wrong use of antibiotics
 - 8 Other
- 9999999
- Don't know/Refuse



Q10: v10pres

Single coded

Do you sometimes feel pressured to sell antibiotics without a medical prescription?

Explanation:
 -Do you have the feeling you sometimes sell antibiotics only because the customer requests these antibiotics, even when an antibiotic course is not necessary?
 -Do you have the feeling you do anything to please your customers?
 -Do you find it difficult to refuse the selling of antibiotics to (some of) your customers?

1 Yes

2 No

9999999

Don't know/Refuse

ASK ONLY IF Q10 = 1

Q11: v11presex

Multi coded

What are the reasons for feeling this pressure?

Read the different answer categories

1 GP pressures

2 Verbal customers

3 Financial losses

4 Threat to lose the business

5 Pressure from pharmaceutical companies/enterprises

6 Fear that customers will go to another pharmacy

7 Competition from the internet

8 Other

9999999

Don't know/Refuse

Q12: v12illa-e

Matrix

Could you tell me in which way you agree or disagree with any community pharmacist who sells antibiotics without a medical prescription for the following illnesses?

	Strongly disagree	Disagree	Neither agree/nor disagree	Agree	Strongly agree	Not sure/not applicable	Refuse
Urinary tract infection	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Sore throat	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Acute bronchitis	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Coughs	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Common cold	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

B1: Do customers request antibiotics?

End block

B2: Information provided to customers

Begin block



T4:

Text

The next set of questions is about the information you provide to customers who buy antibiotics without a medical prescription.

Q13: v13pro

Single coded

Do you provide information about the use and side-effects of antibiotics to customers who buy antibiotics without a medical prescription?

- 1 Yes, always
 - 2 Yes, sometimes
 - 3 No, never
- 9999999
Don't know/Refuse

Q14: v14how

Multi coded

In which way do you provide the information to the customer?

- 1 Orally
 - 2 Written
 - 3 With a standard leaflet
 - 4 Other
- 9999999
Don't know/Refuse

Q15: v15info

Multi coded

What kind of information do you provide these customers with about the use and side-effects of antibiotics?

Read the different answer categories

- 1 None *Exclusive
 - 2 Complete the full course of antibiotics
 - 3 Only take the antibiotics over the prescribed period at the correct dose
 - 4 Do not give your antibiotics to anyone else
 - 5 Return outdated or unused antibiotics (leftovers) to the pharmacy
 - 6 Advise about how to act if the condition persists/if the infection becomes worse
 - 7 Information about conditions under which the antibiotics should not be taken
 - 8 Information about possible medical allergies
 - 9 Information about side-effects (like soft stools, diarrhea, mild stomach upset)
 - 10 Information about drug interaction
 - 11 Other
- 9999999
Don't know/Refuse



Q16: v16que

Single coded

Do customers ask any questions about the use and side-effects of antibiotics they buy without a medical prescription?

- 1 Yes, always
- 2 Yes, sometimes
- 3 No, never
- 9999999
- Don't know/Refuse

ASK ONLY IF Q16 = 1,2

Q17: v17queco

Multi coded

In general, about which of the following subjects do customers ask questions?

Read the different answer categories

- 1 The appropriate way of intake
- 2 Duration of intake
- 3 Safety in combination with current medication
- 4 Side-effects
- 5 Adverse reactions
- 6 Miss a dose of antibiotics
- 7 Disposal of antibiotics
- 8 The effect of the antibiotic
- 9 The end of the antibiotic course
- 10 The use of leftover antibiotics
- 9999999
- Don't know/Refuse

B2: Information provided to customers

End block

B3: Misconceptions among customers

Begin block

T5:

Text

The following question is about common misconceptions from customers about antibiotics (with or without a medical prescription). Therefore we would like to ask you if you can put yourself in the place of the regular customer and think about what their misconceptions are. Also, think of questions costumers often ask that indicate a lack of knowledge about antibiotics.

**Q18: v18custa-f****Matrix**

We would like to know to what extent you agree or disagree with the following statements about the conceptions of customers:

	Strongly disagree	Disagree	Neither agree/nor disagree	Agree	Strongly agree	Not sure	Refuse
Customers believe that antibiotics kill viruses	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Customers believe that antibiotics are effective against a cold and the flu	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Customers believe that antibiotics do not have side effects	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Customers believe that if antibiotics have been prescribed before, they will be required again for similar symptoms in the future	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Customers believe that a prescription for antibiotics for minor ailments is not necessary	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Customers believe that they can stop taking the antibiotics when the symptoms are over	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

B3: Misconceptions among customers**End block****B4: Do (other) pharmacists sell without a medical prescription?****Begin block****T9:****Text**

The next questions relate to pharmacists in your country who sell antibiotics without a medical prescription.



Q19: v19other

Single coded

Do you personally know pharmacists in your country who sell antibiotics without a medical prescription?

1 Yes

2 No

9999999

Don't know

8888888

Refuse

Q20: v20perc

Numeric

Max 100

We also would like to know if you think there are (other) pharmacists in your country who sell antibiotics without a medical prescription. In general, can you give an estimation of the percentage of pharmacists in your country doing this?

Instructions interviewer: we would like to receive a percentage from the respondent. If the respondent gives an absolute number, ask if the respondent could try to give a percentage.

Scripter notes: include a 'Don't know' and a 'refuse' button

B4: Do (other) pharmacists sell without a medical prescription?

End block

B5: Opinion on the use of antibiotics without a medical prescription

Begin block

T6:

Text

The following question relates to your opinion on the use of antibiotics without a medical prescription.

**Q21: v21stata-e****Matrix**

We would like to know to what extent you agree or disagree with the following statements:
(matrix question)

	Strongly disagree	Disagree	Neither agree/nor disagree	Agree	Strongly agree	Not sure	Refuse
The use of antibiotics without a medical prescription increases the risk of antibiotic resistance	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The use of antibiotics without a medical prescription is a problem in the treatment of respiratory infections	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The use of antibiotics without a medical prescription is not an issue among the population visiting my pharmacy	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The use of antibiotics without a medical prescription is a significant problem in my country	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
The use of antibiotics without a medical prescription is a significant problem in other countries within Europe	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

B5: Opinion on the use of antibiotics without a medical prescription

End block

B6: Possible solution(s) to diminish the use of antibiotics without a medical prescription

Begin block

T7:

Text

The next few questions are about possible solutions — for your country or Europe — to diminish the use of antibiotics without a medical prescription.



Q22: v22red

Single coded

Do you think that the amount of antibiotics without a medical prescription that customers are using should be reduced?

Explanation: We mean the amount of antibiotics that customers receive without medical prescription from their general practitioner or from another healthcare professional.

1 Yes

2 No

↩ **GO TO Q26**

9999999

Don't know/Refuse

↩ **GO TO Q26**

Q23: v23achieve

Multi coded

How could this be achieved?

Read the different answer categories

Instructions interviewer: Only tick the answer category 'Other' if the respondent spontaneously gives an answer that doesn't resemble any of the given answer categories.

1 Public education (national media campaigns) to reduce misconceptions about the use of antibiotics for minor ailments

2 Enforcement of the laws regulating the sale of antibiotics

3 Dispensing regulation: dispensing exact numbers of antibiotic tablets

4 Education for healthcare professionals

5 More restrictive/conservative/appropriate prescribing by general practitioners

6 Self-medication from other sources should be prevented (e.g. internet)

7 Strengthening pharmacy regulations

8 Inform the medical guidelines more often

9 Provide more information on local resistance patterns

10 Other

9999999

Don't know/Refuse

Q24: v24lim

Single coded

Do you feel limited in what you can do as a healthcare professional against the use antibiotics without a medical prescription?

1 Yes

2 No

7777777

Not applicable

9999999

Don't know/Refuse

**Position fixed*

**Position fixed*



ASK ONLY IF Q24 = 1

Q25: v25expl

Multi coded

Could you explain why?

Read the different answer categories

Explanation code 3: if the customer repeatedly asks for antibiotics and tries to convince you to sell the antibiotics

- 1 You feel you have to do everything possible to cure the customer
- 2 Costs
- 3 Customer pressure
- 4 Legal issues
- 5 Pressure from company/enterprise
- 6 Public health considerations
- 7 Cooperation of all pharmacists/general practitioners
- 8 Inappropriate prescribing by general practitioners
- 9 Other

9999999

Don't know/Refuse



*Position fixed

Q26: v26cam

Single coded

Are there any national campaigns to reduce the use of antibiotics without a medical prescription that you are aware of?

- 1 Yes
- 2 No

7777777

Not applicable

9999999

Don't know/Refuse



*Position fixed



*Position fixed

Q27: v27prof

Multi coded

Are there any professional meetings about the use of antibiotics without a medical prescription in your country that you have participated in?

Explanation: With professional meetings we mean meetings between pharmacists and/or pharmacists and general practitioners that discuss problems concerning the use of antibiotics (for example PTAMs (Pharmaco Therapy Audit Meetings)).'

- 1 Yes, between pharmacists
- 2 Yes, between pharmacists and general practitioners
- 3 Yes, between pharmacists and other healthcare professionals
- 4 No
- 5 Other

9999999

Don't know/Refuse





Q28: v28suf

Single coded

Do you receive sufficient information about antibiotic use without a medical prescription from your professional community?

1 Yes

2 No

7777777

Not applicable

9999999

Don't know/Refuse

*Position fixed

*Position fixed

B6: Possible solution(s) to diminish the use of antibiotics without a medical prescription

End block

B7: Background

Begin block

Q33:: extra UA

Single coded

In general, when distributing antibiotics to your customers, do you usually deliver the antibiotics in:

Read the different answer categories

1 A whole package

2 A strip of pills

3 The precise number of required pills

9999999

Don't know/Refuse

*Position fixed

T8:

Text

The last section of the questionnaire refers to your (professional) background. Although we are aware of the sensitivity of the questions in this section, the information is anonymous and allows us to compare groups of respondents.

Q29: v29age

Numeric

Max 100

What is your age?

Scripter notes: include a 'refuse' button



Q30: v30type

Single coded

What is the type of pharmacy you work in?

- 1 Community pharmacy
- 2 Hospital pharmacy
- 3 Clinical pharmacy
- 4 Ambulatory care pharmacy
- 5 Consultant pharmacy
- 6 Other
- 7 Refuse

Q31: v31gra

Numeric

Min 1960 | Max 2014

In what year did you graduate?

Scripter notes: include a 'refuse' button

Q32: v32sexe

Single coded

What is your gender?

Instruction interviewer: Only ask if you are not sure!

- 1 Male
- 2 Female
- 8888888
- Refuse

B7: Background

End block

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