



REPORT

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March 2018

**Publisher**Health Action International
Overtoom 60 (2) | 1054 HK Amsterdam
The Netherlands
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SUMMARY

The unnecessary use of antibiotics and associated rapid growth of antibiotic resistance is a widely acknowledged crisis and threat to global health, development and sustainability. While the underlying cause of antibiotic resistance is undoubtedly the overall volume of antibiotic use, in general, irrational antibiotic use, which is influenced by several interrelated factors, is a major contributor. The aim of this paper is to present and describe selected main drivers of irrational use of antibiotics in Europe, focussing on the general public and healthcare providers, and to propose a number of initiatives that, if implemented, can improve the current situation.

1. BACKGROUND

1.1 Current Antibiotic Use and Resistance in Europe and Worldwide

Antibiotics are one of the most cost-effective life-saving medical interventions and have contributed to an extended lifespan (1). Today, the effect of antibiotics is compromised by the rapid escalation of antibiotic resistance (ABR), which, combined with the lack of novel antibiotics in the pipeline, is considered a major global health threat (2). A key driver of ABR is the irrational use of antibiotics. According to the World Health Organization (WHO) definition, medicines are used 'rationally' (i.e., appropriately, properly, correctly, responsibly) when patients receive the appropriate medicines, for appropriate indications, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost both to them and society, and with appropriate information. 'Irrational' (i.e., inappropriate, improper, incorrect) or unnecessary use of medicines occurs when one or more of these conditions is not met (3).

ABR in common pathogens is consistently reported to be higher in countries that have higher antibiotic use (4). The European Surveillance of Antimicrobial Consumption

Network (ESAC-Net) showed that large variations in antibiotic use exist across Europe, with higher use in Southern Europe, and lower use in Northern Europe (5).

In 2015, antibiotic consumption for systemic use in the community (i.e., outside hospitals) in Greece was 36.1 defined daily doses (DDD) per 1,000 inhabitants per day (DDD/TID). Meanwhile, in the Netherlands, less than a third of this volume was used (10.7 DDD/TID). Between 2011 and 2015, a decreasing trend in antibiotic use was observed in Finland, The Netherlands and Sweden.

The health and economic consequences of ABR are severe. Today, drug-resistant infections lead to approximately 700,000 deaths globally per year. This is projected to increase to 10 million by 2050, with associated costs as high as US\$100 trillion worldwide if no action is taken (6). Each year, in the European Union (EU) alone, 25,000 patients die due to infections caused by multi-resistant bacteria, costing society approximately €1.5 billion annually. By 2050, expected cumulative losses due to multi-resistance will reach US\$2.9 trillion (7).

1.2 Spread of Resistant Bacteria

Bacteria may become resistant to antibiotics through de novo gene mutation, or by acquiring the genetic information that encodes resistance from other bacteria. The selective pressure imposed by the massive use of antibiotics makes bacteria carrying the resistance gene survive and grow (8). A special concern is the rapid spread of multi-resistant bacteria, reported in several countries, for some of which there is no available treatment. Data from the European Antimicrobial Resistance Surveillance Network (EARS-Net) showed substantial geographic differences in the proportion of resistance to various classes of antibiotics, with higher levels in Southern Europe, and lower levels in Northern Europe (4). From 2012 to 2015, the combined resistance to fluoroquinolones, third generation cephalosporins and aminoglycosides of *Klebsiella pneumoniae* isolates in Europe increased, on average, from 17.7 percent to 18.6 percent.

In 2015, 8.1 percent of *Klebsiella pneumoniae* isolates were identified as resistant to carbapenems, with variation across Europe from 0 percent in Denmark to 61.9 percent in Greece. At the same time, 13.1 percent of *Escherichia coli* isolates were identified as resistant to third generation cephalosporins, ranging from 1.7 percent in Iceland to 38.5 percent in Bulgaria. Methicillin-resistant *Staphylococcus aureus* (MRSA) invasive isolates reached a level of resistance of 16.8 percent, with large variations across Europe (0 percent in Iceland to 57.2 percent in Romania) (4).

2. DRIVERS OF IRRATIONAL HUMAN USE OF ANTIBIOTICS IN EUROPE

To adequately address the threat of ABR, it is essential to understand the main factors driving irrational antibiotic use in Europe. In this review, we aim to select and describe major drivers of irrational antibiotic use among the general public and healthcare practitioners (HCPs) in Europe. We will also discuss effective actions urgently required from international organisations, governments, researchers, and private and public sector clinicians to minimise ABR through improved use of antibiotics.

2.1 Drivers of Irrational Use of Antibiotics Among the General Public

2.1.1 Lack of Public Knowledge and Awareness

Public knowledge, attitudes and beliefs about antibiotics are strong determinants of irrational use of antibiotics. The latest Eurobarometer report showed that 34 percent of Europeans took antibiotics at least once during 2016 (9). There is a clear need to raise the awareness about antibiotic use and resistance among European populations. For example, 57 percent are unaware that antibiotics are ineffective against viruses, and 44 percent do not know that antibiotics have no effect against colds and influenza.

There are large differences between countries

and social groups. The use of antibiotics is shown to be higher among those with a lower level of education (39 percent compared with 32–33 percent) and those in worse economic circumstances (44 percent compared with 31 percent) (9). However, the opposite was shown in a study from southern Sweden, where socio-economic factors reflecting a privileged situation correlated positively with higher antibiotic use, especially among children aged 0–6 years (10). In districts with a high median family income and a high employment rate, the use of antibiotics was higher than in other districts. This suggests that antibiotic use among children may, in some cases, increase with the degree of parental affluence, but cannot be solely explained by economic factors.

People often have an incomplete understanding of—and misconceptions about—ABR. Many believe that they do not contribute to the development of ABR and do not understand that bacteria—and not humans—become resistant (11).

A comparative European study found the highest level of misconception contributing to inappropriate use was in Southern and Eastern Europe. The highest prevalence of ABR is found in countries where people have the lowest awareness about the issue. The underlying factor here is cultural differences in public attitudes, beliefs and knowledge about antibiotic use, resistance and self-medication (12).

A Lithuanian study showed that two-thirds of participants had an insufficient level of knowledge about antibiotics, and that participants tended to overestimate their knowledge, which may lead to increased non-adherence and self-medication (13). According to the Eurobarometer, sources of information about antibiotics vary across countries, but overall, only 32 percent of Europeans stated that they received information about correct use of antibiotics from doctors. When asked where, in the last 12 months, they had received information on the correct use of antibiotics, 10 percent of Europeans said it came from pharmacists, 27 percent from TV advertisements, 26 percent from TV news, 19 percent from newspapers, and 13 percent looked for information online (9).

2.1.2 Access to Antibiotics Without Prescription

Access to antibiotics without a prescription is a driving factor for irrational antibiotic use. This is due to a potential lack of access to proper diagnosis and diagnostic tools, eventually leading to the development and spread of ABR. Ninety-three percent of Europeans surveyed stated that they obtained their last course of antibiotics from a prescription or directly from a medical practitioner. However, despite the legal framework stating that antibiotics should only be dispensed with a medical prescription, and that over the counter (OTC) sales of antibiotics are illegal in all Member States (with some exceptions in a number of them—for example, creams or eye drops that contain antibiotics), 4 percent of Europeans reported obtaining their last course of antibiotics without a prescription (9).

In Greece, only 79 percent of respondents said they received antibiotics from a prescription or directly from a medical practitioner, whereas, in Sweden, that figure was 98 percent. (9). A survey from the Algarve region in Portugal showed that, of 1198 respondents, 7.5 percent answered that it was easy to buy antibiotics without a prescription (14).

The dispensing process greatly influences how antibiotics are used. In some countries, it is easier to buy antibiotics in community pharmacies without a prescription from a physician. A study from Catalonia, Spain (2009), showed that antibiotics were sold without a prescription in 55 out of 69 (79.7 percent) of studied pharmacies in which a simulated case of a urinary tract infection (UTI) was presented (15). However, it must be acknowledged that European countries have different approaches towards the treatment of uncomplicated UTI. In the United Kingdom (UK), UTIs are one of the most common acute medical conditions, accounting for 1–3 percent of all general practitioner (GP) consultations a year. To improve patient access to treatment—and decrease the number of consultations—in one area in Scotland, [pharmacists can now offer antibiotics](#) to treat uncomplicated UTIs.

To facilitate easier access to medicines, in some EU Member States, medicines can be authorised for sale or supply as OTC if it is safe to do so. The antibiotics available OTC are usually dispensed under the supervision of a pharmacist. A survey in 26 European Union countries and Norway identified 48 antibiotic formulations containing 20 different active substances available OTC. Most of these products are used mainly as topical preparations or eye drops in short treatment courses. Although this should not be confused with the illegal supply of antibiotics that require a prescription, the spread of ABR makes it important to limit the availability of licensed OTC antibiotics and to monitor their use (16).

The use of antibiotics without a prescription, obtained via the Internet or bought in another country, is considered to be a growing problem, as reflected in a European survey (17). There are numerous international online pharmacies operating illegally outside the EU that can supply European patients by post or courier. These online vendors are not authorised to operate in the EU, nor do they adhere to national practices and guidelines. For example, they offer antibiotics for sale without a prescription. To prevent this, all online pharmacies in the EU are currently required to display a [logo](#) that acts as a direct link enabling the checking of the legal status of the pharmacy via the Member State's official pharmacy regulator (18).

Another issue is the increasing access to Internet doctors (e.g., [Kry Doctor](#) in Sweden) who provide online consultations via video conference and prescribe antibiotics legally, without any medical examination. It is the lack of a proper examination and potential testing before the antibiotic is prescribed that leads to irrational use.

2.1.3 Leftover Antibiotics

Leftover (i.e., remaining) antibiotics from earlier prescriptions—when the patient did not adhere to the therapy, or the quantity of prescribed antibiotics exceeded the treatment duration—facilitate the practice of self-medication (19). According to Eurobarometer, 2 percent of

Europeans use antibiotics left over from previous courses (9). Data from a UK survey of 6,983 households showed that 19 percent of those surveyed had a leftover drug. Prescriptions for more than six days constituted 61 percent of leftover drugs, whereas prescriptions for less than three days constituted 6 percent of leftover drugs (19). Evidence shows that prolonged or repeated treatment with antibiotics provides a greater selective pressure on normal bacterial flora than a single course of treatment, favouring the emergence of resistant strains (20, 21).

2.3 Drivers of Irrational Use of Antibiotics Among Healthcare Providers

2.3.1 Knowledge, Attitude and Perception of Healthcare Providers Regarding Antibiotic Use and Resistance

Prescribers are ultimately responsible for making the decision to use antibiotics, and for the selection of the type of antibiotic. Their knowledge, attitudes, and how they perceive antibiotic use and resistance is likely to influence prescribing behaviour.

It has been suggested that the attitude and knowledge of physicians determines the quality of prescribing of antibiotics, as measured by indicators obtained from clinical practice. The results of a Spanish study indicated that fear of complications from infections, a complacent attitude towards patients, and insufficient knowledge regarding ABR, are factors related to the prescribing of antibiotics by GPs (22). Data from Sweden, however, shows that the reduced rate of antibiotic prescriptions in Sweden have not increased complications of the infections due to not treating with antibiotics. For example, the incidence of mastoiditis seems not to have increased in children despite a reduction in antibiotic prescriptions (23).

In a recent systematic review, it was shown that physicians generally believed that ABR was a serious problem, but not in their close proximity. The number of clinicians who believed it was a problem at the local, national or global level was

greater than the number who believed it was a problem at their practice level (24).

A qualitative study from Sweden showed that some GPs did not consider resistance as a problem they experienced in their everyday practice. Although some GPs were aware of the problem, this had a minor impact on their own practice, considering it a problem found in other countries, other parts of the country, or in hospitals. GPs' perceptions of ABR were mirrored in how they reported their treatment of UTI in practice (25).

2.3.2 Lack of Adequate Education for Healthcare Providers

Inadequate training on antibiotic prescribing during medical education and further on during the early stage of clinical practice, as well as inadequate continuing professional development throughout professional careers, can contribute to inappropriate antibiotic prescribing. The WHO recently highlighted the importance of undergraduate training in prudent prescribing behaviour (26). A survey among final year medical students at seven European medical schools showed that most students (74 percent) wanted more education on antibiotic therapy (27). A survey of five London hospitals, including 140 junior doctors, found that only 5–13 percent of participants thought their previous education on the use of antibiotics was sufficient. Sixty percent of those in their first-year post qualification reported wanting further education on antibiotic prescribing, rising to 74 percent among more experienced junior doctors (28).

2.3.3 Pharmaceutical Promotion

Pharmaceutical promotion is also believed to increase irrational prescribing. The EU rules on pharmaceutical promotion state that advertising must be consistent with the approved product information and cannot be misleading. It also states that Member States shall ensure that there are adequate and effective methods to monitor the advertising of medicinal products. However, it has been argued that, globally, even countries with adequate resources for regulatory oversight

vary greatly in the extent to which they effectively monitor pharmaceutical promotion and enforce laws with adequate sanctions (29).

Pharmaceutical promotion influences how healthcare professionals prescribe and dispense. Many studies included in a systematic review, published in 2010, showed that the exposure of physicians to information from pharmaceutical companies is associated with higher prescribing frequency, higher costs and lower prescribing quality. However, the heterogeneity of the included studies must be acknowledged (30).

An effective technique for developing relationships that influence prescribing behaviour is one-to-one contact between doctors and sales representatives. In fact, sales representatives are highly trained in persuasion and influencing skills. A 1992 United States study, looked at physician prescribing patterns for antibiotics made by pharmaceutical firms that offered all-expenses-paid trips to popular Sunbelt holiday sites to attend sponsored symposia. The study revealed a significant impact on physician prescribing patterns and an increased number of prescriptions once physicians returned from the symposia (31).

A study exploring the impact that sales representatives have on GPs in Brittany, France, revealed that those who met with sales representatives more frequently prescribed Tavanic[®]/Ketek[®]/Izilox[®] (lévofloxacin/moxifloxacin/télithromycine) more often than their peers when prescribing antibiotics (32). These three types of antibiotics have had a higher rate of consumption in France than in other countries, even at the expense of better therapeutic options. A recent study from Germany showed that doctors who frequently saw pharmaceutical sales representatives had a higher number of total prescriptions compared to doctors who were visited less frequently (33). In a qualitative study from Spain, focus group discussions among 33 physicians explored GPs' habits and knowledge with regard to antibiotics and aimed to identify factors that may influence prescribing. It was shown that

physicians attributed a very clear influence to pharmaceutical promotion and advertising when it came to choosing antibiotics. Some of the participants stated:

The influence of the pharmaceutical industry is so clear that, when they stop promoting a medication, then, in the long term, you, too, stop using it.

or,

We are constantly being bombarded by the pharmaceutical industry because they keep on saying that this is the latest cephalosporin, the best, the one that's recommended in all the guidelines for the treatment of increased expectoration in [chronic obstructive pulmonary disease], and it's a lie; and so that's what we have to fight against. (34).

2.3.4 Lack of Rapid and Sufficient Diagnostic Tests

A core problem behind the incorrect prescribing and use of antibiotics is the lack of sufficient diagnostic tests to rapidly identify the pathogen and its antibiotic susceptibility profile, guide antibiotic prescribing at the point of care, and reduce the need for broad spectrum antibiotics (35). Conventional culturing and susceptibility testing takes time, whereas, in most cases, empiric prescribing always precedes culture results. In all countries, empiric prescribing dominates, but the choice of antibiotics might be changed to less broad spectrum ones in situations where a culture is done and after culture results are available.

2.3.5 Patient-doctor Interaction

Many studies have shown the relevance of the doctor-patient relationship and communication for the prescribing of antibiotics. A qualitative study from UK showed that doctors overestimated patients' expectations for antibiotics, and prescribed antibiotics to maintain a good doctor-patient relationship (36). A survey of 1,000 GPs in the UK showed that 55 percent felt pressure to prescribe antibiotics, even if they

were not sure that they were necessary, and 44 percent admitted that they had prescribed antibiotics to get a patient to leave the surgery (37).

The consequences of misprescribing and/or overprescribing antibiotics are severe and have a major impact on the development of ABR, the medicalisation of patients' symptoms, and increasing healthcare costs (38). The vast majority of antibiotic prescriptions for systemic use in primary care, for both adults and children, is for respiratory tract infections (RTI) (39). The rate of unnecessary prescribing for RTIs, for which antibiotics are rarely indicated, ranges from 0.5 to 90 percent (40–42). A study from Poland showed overuse of antibiotics in primary care, where 50 percent of patients with a common cold received antibiotics (43). Only 10–20 percent of all antibiotics are used in hospitals, but the intensity of use is far higher than in the community. Hospitals are key locations in which final recourse antibiotics, such as carbapenems and polymyxins, are used (5, 44–46). For example, the ESAC-Net data showed a higher proportion of use of cephalosporins, other beta-lactams (including carbapenems), and other groups of antibiotics in hospitals compared to use in the community (5). The proportion of carbapenem-resistant invasive *Klebsiella pneumoniae* is strongly associated with carbapenem consumption. Therefore, data showing that more than 1 million carbapenem prescriptions are issued in Europe each year is a major concern.

2.3.6 Knowledge, Attitude and Perception of Pharmacists Regarding Antibiotic Use and Resistance

As part of the standard dispensing process, pharmacists in community and hospital settings provide counselling (advice, information and help) on the safe, effective and rational use of medicines (47). A study conducted by WHO showed that pharmacists are among the best positioned healthcare professional group to tackle ABR (48). Pharmacies are often the first point of contact with the healthcare system and are important in advising patients on symptomatic

self-care without antibiotics, or referring them to medical professionals for examination. In some countries, dispensing without a prescription is still a common practice. A study from Spain showed that pharmacists attributed the problem of antibiotics dispensed without a prescription—and its relationship to ABR—to external responsibility (doctors, dentists and the National Health Service), and acquiescence to customer demands and lack of continuing education for pharmacists (49). A study from Romania evaluating the perceptions and attitudes of pharmacists toward their role with respect to antibiotic consumption and resistance showed that pharmacists encounter many barriers in their activities related to antibiotic management, such as, seeing how the healthcare system impacts the patient's ability to seek medical care (50). The financial situation of a patient plays a major role in antibiotic consumption; this in turn impacts upon the role of the pharmacist.

3. RECOMMENDATIONS

3.1 Increase Public and Healthcare Professional Awareness about Antibiotic Resistance and Rational Use

1. Education and training at all levels (community, healthcare and individual) is essential to ensure rational use of antibiotics and to suppress the spread of ABR. Public education campaigns have been shown to be effective in changing attitudes and knowledge regarding antibiotic use and resistance and should be further targeted at Southern and Eastern European countries reporting the highest levels of resistance (51, 52). Since 2008, the European Centre for Disease Prevention and Control (ECDC) has coordinated “European Antibiotic Awareness Day”—an initiative that provides a platform for, and support of, national campaigns to raise awareness about the prudent use of antibiotics.
2. Improving education for healthcare professionals has recently been widely promoted as a potential method for optimising antibiotic use (39). Special emphasis should be put on antibiotic prescribing training for medical students

and junior doctors. Further, education on pharmaceutical promotion (including strategies used by companies, how they affect prescribing and dispensing, and practicing evidence-based medicine) should be adequately embedded in the curricula of medicine and pharmacy training.

3. Clinicians should support education of patients regarding antibiotic use and resistance. For example, they could use effective strategies, such as shared decision making, to alert people to the actual risk of acquiring antibiotic resistant bacteria following antibiotic use. Patients need to stay informed and receive independent information on antibiotics because better health literacy and a higher degree of knowledge and awareness about the appropriate use of antibiotics are associated with decreased consumption.

3.2 Optimise Antibiotic Use

1. Preventing leftovers from previous courses of antibiotics may be one effective way to prevent self-medication with antibiotics. This can be done through technical measures, such as promoting the dispensing of the exact number of tablets, or by educating patients not to use leftover medications.

2. Take-back programmes, including the return of unused or excess drugs to pharmacies, are recommended by WHO (53). Most people in Europe are able to return expired or unused medicines to their community pharmacy—encouraging this is crucial to preventing the inappropriate use or reuse of antibiotics (18).

3. Infection prevention and control measures are crucial in order to reduce the incidence of infections and, therefore, the potential use of antibiotics. This is included as one of the five objectives in the WHO Global Action Plan on Antimicrobial Resistance.

3.3 Strengthen the Data about Antibiotic Use and Resistance

1. Surveillance is one of the cornerstones of combating ABR. Lack of surveillance can lead to

misdirected and inefficient policies and waste of resources. It is essential to understand trends in antibiotic use and resistance, inform treatment guidelines, identify priorities for intervention, tailor and target interventions and monitor the impact of interventions. In a very recent draft opinion on ABR, developed by the European Parliament, it was emphasised that routine collection and submission of monitoring data at the EU level should be mandatory (54).

2. Mapping information regarding antibiotic use and resistance. The WHO has recently undertaken many initiatives to map information regarding antibiotic use and resistance. The implementation status of countries' action plans to address ABR across all sectors can be monitored via the WHO website (55). In Europe, networks such as ESAC-Net and EARS-Net have been providing information regarding antibiotic use and resistance for over 15 years. Recently, the Access to Medicine Foundation published the methodology for its [2018 Antimicrobial Resistance Benchmark](#). It is the first independently developed framework for assessing how pharmaceutical companies are taking action to limit ABR. Activities by 30 companies are being mapped to help identify obstacles and opportunities to tackle ABR (56). The first Antimicrobial Resistance Benchmark report showed that out of 28 antibiotics in the late stage of clinical development, only two have both access and stewardship plans in place, nearly half of companies are involved in ABR surveillance, and eight are setting limits on antibiotic wastewater discharge.

3.4 Support Public Health-driven Models of Innovation for the Development of Antibiotics

There is a shortage of coordinated priority setting in antibiotic research and development spending. The current pipeline demonstrates a lack of truly valuable new antibiotics, vaccines and diagnostics. Moreover, most publicly funded research and development initiatives in this area target the basic research phase. Much less funding is available for later stages of antibiotic development, which require continuous financial

support.

1. Focused research is needed to help develop new effective treatment principles. The pharmaceutical industry has an important role in the overall effort to ensure just and prudent use of antibiotics. Product development partnerships (PDPs) have the potential to address the lack of development of new antibiotics and to focus on unmet medical needs, and should always include stewardship principles of any treatments that result from collaboration.

2. Innovative, affordable and easy-to-use rapid diagnostic tests are needed to allow immediate identification of potentially infective organisms and to support doctors in deciding whether to initiate antibiotic therapy and, thereby, improve management of infectious diseases. It is also crucial to identify novel therapies that do not drive resistance. Numerous monoclonal antibodies have shown the potential to treat infectious diseases in preclinical evaluation, both in vitro and in animal models. As of November 2016, there were at least 38 monoclonal antibody products in active clinical development for 14 infectious diseases (57).

3. Research and development incentives based on the principle of delinkage should be applied in lieu of the traditional reward of market exclusivity (such as patents) to ensure the affordability of end products. The WHO and Drugs for Neglected Diseases initiative (DNDi) project on the Global Antibiotic Research and Development Partnership (GARDP) is a good example of an alternative, public health-driven model of innovation. More [stewardship from governments](#) regarding research and development agendas is needed.

3.5 Stronger Regulations Governing Pharmaceutical Promotion

1. Governments should ensure proactive and effective control of pharmaceutical promotion, taking into account the threat to public health of antibiotic overuse and misuse. At a minimum, all promotional material on antibiotics should undergo a system of pre-vetting.

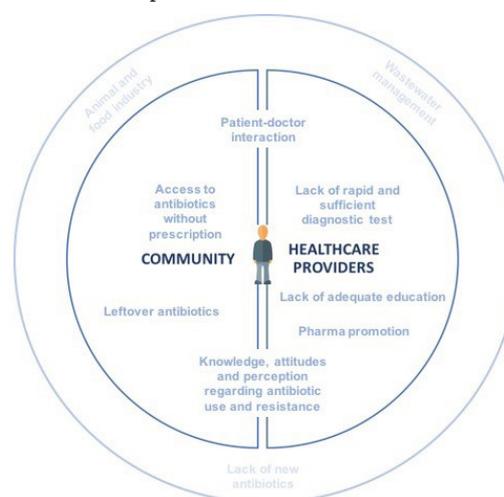
2. Pharmaceutical products with antibiotic components should only be available as prescription only, except where the healthcare system requires otherwise.

3.6. Policy Coherence and Adequate Implementation

Political will and coherence at the European level is needed to achieve an ambitious plan to reduce the emerging growth of ABR.

The European Commission has taken several actions to mitigate the growing problem of ABR in the EU. Following revision of its [EU Action Plan on Antimicrobial Resistance](#), implemented between 2011–2016, the Commission launched a more comprehensive European One Health Action Plan Against AMR on 29 June, 2017. It contains 75 actions aimed at supporting the EU and its Member States in delivering effective and sustainable responses to ABR.

Figure 1. Examples of drivers of irrational antibiotic use in Europe within community and healthcare providers.



The new European One Health Action Plan takes a multi-sectoral approach, links EU and international actors, and mentions the possibility of funding Member States' actions to combat ABR and to boost research and innovation. However, a number of shortcomings have been identified, such as the lack of a precise description of actions to support Member States and the engagement of various stakeholders that threaten this

ambitious EU goal. It must be acknowledged that, in order to achieve the common goal of reducing ABR, support for the development and implementation of national action plans and the allocation of adequate funds must be provided to the countries with the highest prevalence of ABR—and probably the lowest level of human and financial resources—and that strong national organisational structures are essential. The successful adoption and implementation of the European One Health Action Plan depends on the input of various actors—such as non-governmental organisations—which should be involved. The available and newly generated data should be used through the European One Health Action Plan as a benchmark for national reduction targets (58).

Today, due to increased visibility and the well-recognised severe health and economic consequences of ABR, the number of action plans, initiatives and actors working on ABR is immense. These include: the WHO's Global Action Plan on AMR; the EU's European One Health Action Plan on AMR; national action plans; EU guidelines on

prudent use of antimicrobials in human health (59); ECDC actions and initiatives, including ABR surveillance and drug use monitoring; the annual Eurobarometer survey; national surveys; the WHO's World Antibiotic Awareness week; and various reports released by the WHO, EU and Member States. It could be said that too many actors are involved in too elaborate descriptions of the problem, and with too few implemented actions. However, all these initiatives emphasise the importance of urgent action to combat ABR, the need for international and cross-sectorial collaboration, education of the public and healthcare professionals, and the foremost importance of a 'one health' approach. The use of antibiotics and their relation to the environment and other sectors—such as the animal and food industry—were outside of the scope of this review, which focused only on human antibiotic use, and selective main drivers of non-responsible use. However, humans, animals, the food chain, the environment, and the interconnectedness among them should be treated as one entity to enhance public and animal health, and to benefit European and national economies.

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