Closing the net on AMR: Prudent use of antimicrobials in human medicine

Antimicrobial Resistance Discussion Paper

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Introduction

Antimicrobial resistance (AMR) is becoming one of the biggest health threats to the human population worldwide. The ever-increasing resistance of diseases to antimicrobials is already costing 700,000 lives annually, and this number is expected to increase to 10 million by 2050.[1]

There is increasing concern that antimicrobials are declining in effectiveness through giving rise to drug-resistant microbes.[2] As a consequence of AMR, previously easily curable diseases could become complex cases involving mutated bacteria, requiring more expensive treatments for longer periods of time. Worse yet, fatalities related to AMR are expected to rise dramatically. The effects are not only affecting people, but also their productivity, healthcare expenditures and the wider global economy.

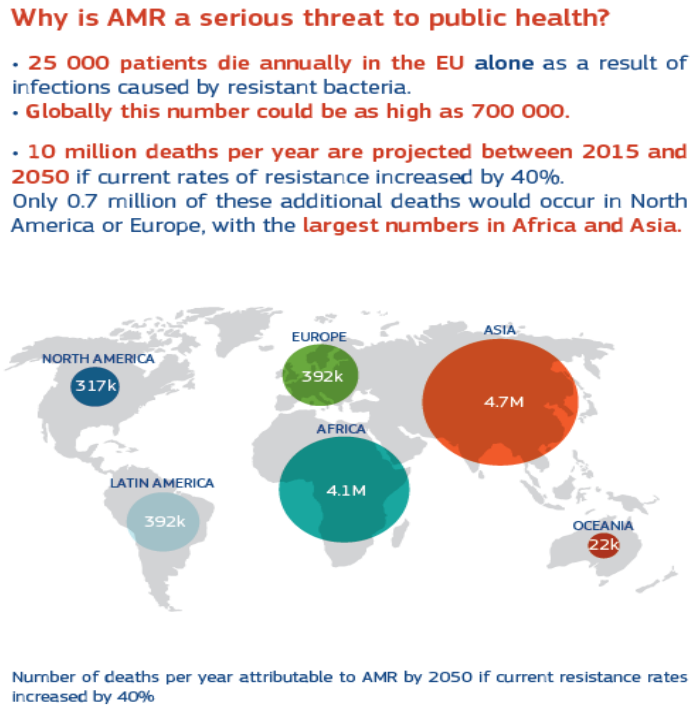


Fig. 1: AMR factsheet, ec.europa.eu/dgs/health_food-safety/docs/amr_factsheet_en.pdf

Human medicine is one of three main dimensions of the One Health approach to AMR, as highlighted in various documents including the 2016 Dutch Presidency's Council Conclusions,[3] the European Commission's Action Plan on AMR,[4] the World Health Organisation's (WHO) Global Action Plan,[5] and the Dutch national action plan.[6] According

to this approach, there is a need for strategies that take into account the interaction between the human, veterinary and environmental sectors.[7]

Excessive, unnecessary use of antimicrobials is one of the biggest contributors to resistance development; it exacerbates the biological process involved in creating drug-resistant microbes. This includes taking the wrong medication, using it for the wrong reason(s) and for longer or shorter periods than necessary. An example is the consumption of antimicrobials that should be kept in reserve, but that are taken anyway in case an infection is resistant to older medicines.[8]

In July 2016, the European Centre for Disease Prevention and Control (ECDC) presented draft guidelines providing 'generic elements of good practice on the prudent and appropriate use of antimicrobials in human medical practice'.[9] They contain a number of important principles and elements, pertaining to the roles and responsibilities of policymakers and stakeholders at all levels, which are hoped to stimulate the necessary system and behavioural changes. Such guidelines are indispensable because of the great variety of approaches towards prudent use in human medicine across Europe.

The premise of this **discussion paper** is that prudent use of antimicrobials in human medicine is an area where Europe must demonstrate its added value to avert a major public health crisis. It will focus on key drivers that influence human use, and analyse whether the issue is being sufficiently addressed and acted upon by the key stakeholders involved. Its scope will be limited to human medicine, i.e., veterinary uses, environmental concerns, research and development will not be touched upon.

The key message is that the complex, intangible, cross-border nature of AMR demands that all stakeholders need to work together effectively in order to close the net on it. AMR is a societal issue. It must be 'owned' by everybody.

Influences on human use

The human contribution to the development of AMR is significant. A number of factors influence whether antimicrobials are used prudently. Below, three of these are discussed; it will be explained why addressing them is important to motivate behavioural change.

Role of healthcare professionals

Apart from their responsibilities in the area of antimicrobial prescribing, healthcare professionals exert a big influence on patient behaviour. The 2016 Eurobarometer on AMR found that doctors are perceived to be the most trustworthy source of information about antibiotics[2], and similar relationships of trust are formed with other healthcare professionals[10]. Healthcare professionals are positioned at the base of the prudent use line – at the critical point where patients receive treatment and advice. Hence robust guidelines are needed to define their roles and responsibilities in meeting the antimicrobial resistance challenge. These include counselling and education, prescribing and dispensing.

Informing patients: Healthcare professionals can contribute in multiple ways to improving the knowledge of patients and the public. For example, at the moment of prescribing or dispensing antimicrobials, they should be supported to improve the provision of counselling on the correct way(s) to take them, as well as about adherence to prescribed drug regimens and about disposal.[11] This contact can thus be seized as an important teaching moment about prudent use and AMR.

As participants in national public awareness campaigns, healthcare professionals, including students, help to spread the campaign messages in various fora and with various methods, e.g. using off- and online tools. Many action plans on AMR stress public awareness as a vital point. In addition to the WHO and EU, the national action plans of Cyprus[12] and the Netherland[6] highlight the importance of media campaigns actively supported by healthcare professionals.

Prescribing behaviours: While General Practitioners (GPs) are key prescribers of antibiotics[13], the conduct of veterinarians, dentists, pharmacists and other prescribers (including nurse prescribers) is equally important.

According to a 2014 survey, 50% of British GPs are said to prescribe antibiotics unnecessarily.[14] This is often due to poor diagnostics, e.g. lack of access to effective diagnostic tools. A recent US study found that nearly one third of all prescriptions in human medicine are believed to be unnecessary.[15] Point of care testing not only brings opportunities for better prescribing but also for dialogue between patients and healthcare professionals.

In addition, various studies indicate that patients often pressure healthcare professionals to prescribe antimicrobials.[16,17,18] For example, GPs are induced to prescribe antibiotics for illnesses such as viral infections that do not benefit from antimicrobial drugs designed to combat bacterial and fungal diseases.

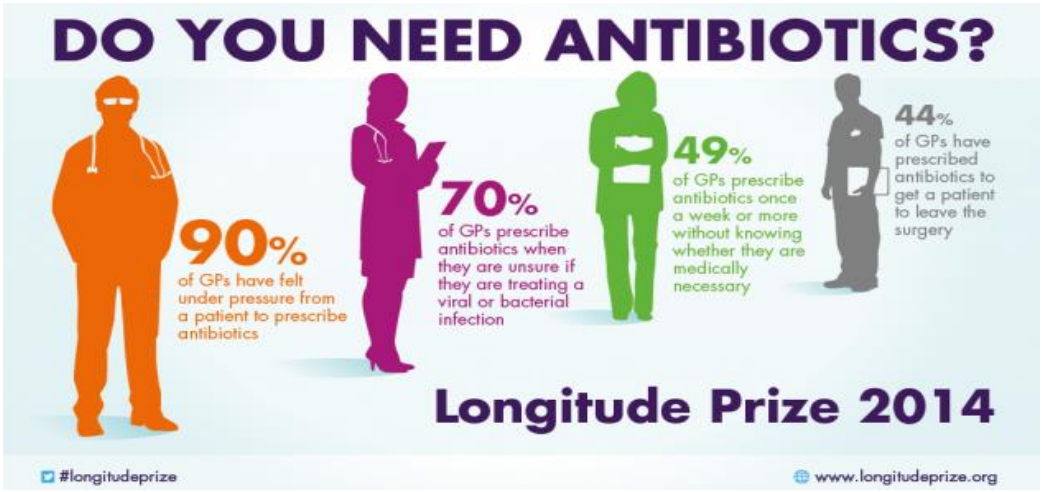


Fig. 2 - Source: https://longitudeprize.org/blog-post/balance-gps-patient-care-and-antibiotics

Education and training: The inclusion of AMR in professional curricula is crucial. Teaching the entire 'healthcare line', i.e. from veterinarians to doctors, dentists, nurses, pharmacists, and allied healthcare professionals creates awareness of how behaviours can reinforce or mitigate the problem and the benefits of collective action from a 'One Health' angle.

Providing opportunities for multidisciplinary learning can lead to better appreciation of other professional roles and responsibilities. Effective antimicrobial stewardship programmes rely on smooth collaboration of multidisciplinary teams.

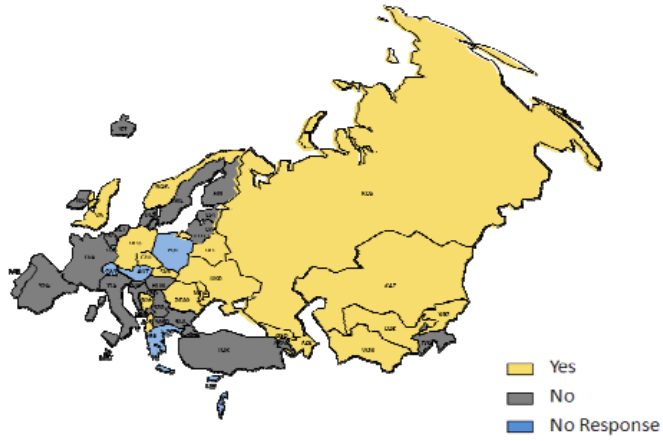
Over-the-counter and Internet medicines

According to a 2014 survey,[19] antimicrobials can be legally bought over the counter in 19 countries of the WHO European Region, including several EU countries.[20] Where this is permitted, it generally occurs under the supervision of a pharmacist who is responding to

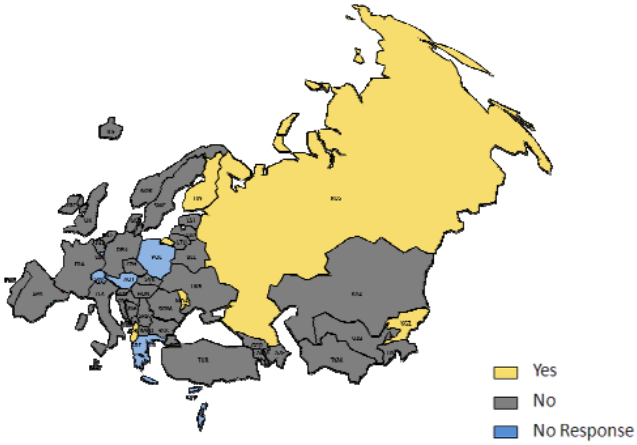
symptoms and following an established protocol under national regulatory, professional and ethical frameworks. However, lack of enforcement of national laws remains a challenge for the illegal sale of antibiotics, which means that obtaining them without diagnosis or prescription is still possible in some countries.

In a minority of countries it is also possible to purchase antibiotics over the Internet and from other sources than a pharmacy, e.g. retail outlets, veterinary clinics or the black market.

European countries in which antibiotics can be bought legally over the counter



European countries in which antibiotics canbe bought on the Internet without a prescription



European countries in which antibiotics can be bought somewhere other than pharmacies

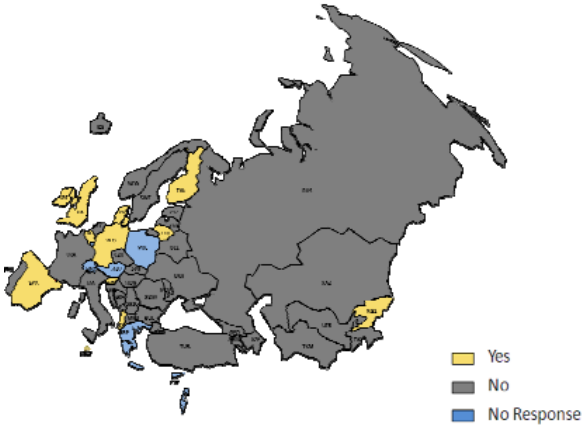


Fig. 3: Source: WHO Regional Office for Europe, http://www.euro.who.int/en/media-centre/sections/press-releases/2014/pharmacists-have-decisive-role-in-combating-antibiotic-resistance,-says-new-who-european-survey

There are various concerns regarding easy availability of antibiotics online and from other sources than a pharmacy. Firstly, when purchasing them in this way, healthcare professionals are usually not involved, i.e. no advice is given on use and dosage. This presents a problem for individuals with low health literacy,[21] often members of vulnerable groups, in terms of stimulating excessive use.

Secondly, the increase in non-pharmacy and online medicines is problematic because individuals may be tempted to stock up for future consumption; 'home supplies' are common even in countries where robust legislation supports prudent use. While such drugs enable self-care and potential cost savings, their utility hinges on prudent use.

Moreover, protecting patient safety and quality assurance has proven to be complicated.[22] The online market is said to be fragmented, and the regulatory and practical aspects of online pharmacy services are complex and difficult to implement.[23] There is also a risk that counterfeit medicines are purchased unknowingly by patients.

Population knowledge

Knowledge of antimicrobial use is still lacking despite growing awareness in many countries. Traditionally, many people in Europe have taken antibiotics for granted, and they readily consume them without giving them much thought. According to the latest ECDC survey examining the knowledge of the European population on AMR, only 24% of Europeans are aware that antibiotics do not kill viruses, that they do not work against colds and flu, that unnecessary use can make them ineffective, and that they often bring side effects.[23] On the other hand, people informed about prudent use and AMR were less likely to take antibiotics, attesting the value of public awareness campaigns.

There is a need for clear and accessible information through sustained health literacy campaigns to ensure that the general public becomes more aware of the risks of overconsuming antibiotics and the associated dangers. Hard to reach individuals, women, newborns, children, older people, migrants and chronically ill - are also more vulnerable to 'superbugs'.

Big differences remain in antibacterial consumption patterns across Europe, with much higher rates recorded in parts of Southern and Eastern Europe, where knowledge about antibiotics is also lower.

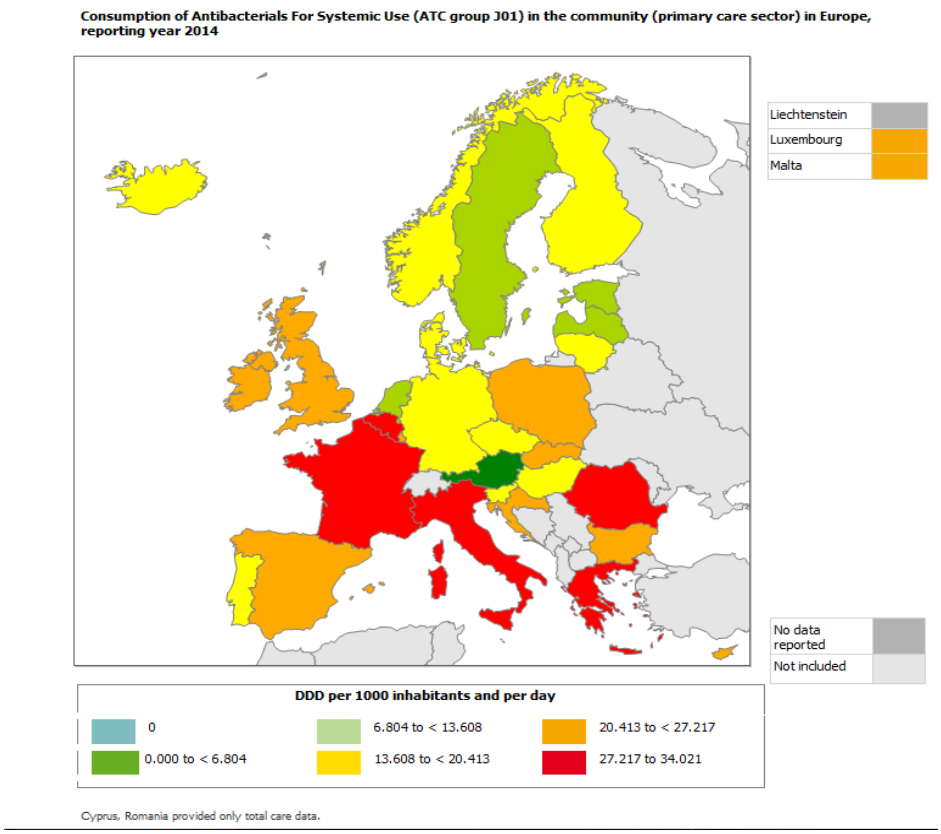


Fig. 4: Source: ECDC, http://ecdc.europa.eu/en/healthtopics/antimicrobial-resistance-and-consumption/antimicrobial-consumption/esac-net-database/Pages/geo-distribution-consumption.aspx

Keeping antimicrobials effective is everyone's responsibility. Responsible use helps prevent bacteria from becoming resistant, and thus supports tackling AMR.[24] Therefore, the entire population must be informed and engaged. The language used is important: a study commissioned by the Wellcome Trust reveals that the term 'AMR' is poorly understood compared to 'drug-resistant infections'.[25] Properly educating people about drug-resistant infections, their consequences, and how to prevent them from spreading further, is vital. For this reason, ECDC organises the annual European Antibiotics Awareness Day (EAAD), [26] tied in with national campaigns and World Antibiotics Awareness Week.[27]

Multi-level responsibilities

Prudent use in human medicine is only one side of a complex and pervasive threat. Therefore, responsibilities are split between many actors and levels. Generally speaking, we can distinguish four levels of responsibility: international, European, national and local.

International level

Among other activities, WHO has developed a Global Action Plan on AMR[5] and issued a manual for developing national action plans.[28] The plan acknowledges excessive human use as one of the main causes of AMR, and it highlights prescribing and dispensing as a tricky area due to the wide availability of antimicrobials.

The WHO Global Action Plan (GAP) lists improved use of antimicrobials as one of five goals. The recommended actions include, e.g. embedding of prudent use in school and teaching curricula to minimise misunderstandings; setting up public communication programmes targeting various population groups; and making AMR a core component of professional education.

WHO recommends undertaking behavioural and socioeconomic studies in order to better understand the reasons for imprudent use. The GAP also calls for **widespread recognition of antimicrobials as a public good**, to strengthen legislation on their use.

To improve prescribing, WHO recommends the implementation of rapid diagnostic tools (RDTs) in GP and pharmacy offices, including in low- and middle-income countries. While financial constraints pose a challenge, accurate diagnosis would reduce the need for antimicrobials. Regarding OTC and online drugs, WHO calls for strengthened legislation to limit their use (?) and ensure their quality.

Like the EU and its Member States, the USA has devised an AMR action plan[29] in which prudent use of antibiotics is mentioned in three out of five goals. The EU and US collaborate in a Transatlantic Taskforce on AMR[30] and in the wake of the reports by the UK Review team (see below), closer UK-US cooperation has been announced.[31,32]

European level

EU Institutions: At the EU level, various bodies and agencies are taking initiatives to combat AMR. In 2011, the European Commission published an EU-wide Action Plan[4] comprising twelve actions to be undertaken by the EU and its Member States, as well as proposals for local level actions. Prudent use in human medicine is included as a key area (action 1).

Over a decade ago, the first Council Recommendation on the prudent use of antimicrobial agents in human medicine (2002/77/EC) was released[33]. Subsequently AMR was highlighted in the 2008 Council Conclusions on Antimicrobial Resistance[34], which call upon the member states to ensure adequate resources for implementing the Council Recommendation and report on the state of implementation. More recently, AMR was the subject of Council Conclusions under the 2012 Danish[35] and 2016 Dutch Presidencies[3], underlining the One Health approach. Human prudent use is highlighted in several of the proposed actions.

Overall, the recommendations by the Council and Commission include enabling proactive collaboration between stakeholders involved in prudent use of human medicines, and further promotion of awareness campaigns (EU and national level). The amount of non-prescription medicines should be scrutinised and actions taken to mitigate the increasing AMR threat. The need for proper data collection and surveillance of antimicrobial use is underlined, as is education of healthcare professionals[4,43] and strengthening infection prevention and control. The EU Action Plan calls for an assessment of national efficiency in the implementation of national strategies and control, and improving the sustainability of national surveillance systems on AMR and antibiotic use.

EU agencies: As part of the programme on Antimicrobial Resistance and Healthcare-Associated Infections (ARHAI), ECDC has developed various documents that provide scientific advice (e.g. on surveillance and response), raise awareness and provide guidance and training on antimicrobials and AMR, aimed at different audiences.[36] Two interactive databases (EARS-Net and ESAC-Net) provide information on AMR and antimicrobial consumption in Europe. ECDC's draft guidelines on prudent use in human medicine, foreseen to be finalised in 2016, are discussed in more detail below.

The European Medicines Agency (EMA) website features an AMR section that outlines their work, EMA being "involved in the development of new medicines and treatment approaches, promoting of responsible use of existing antibiotics, and the collecting of consumption data to guide policy and research".[37] Moreover, EMA has published various documents, including a recommendation on the use of antibiotics in animals,[38] and a joint report on consumption data with ECDC and the European Food Safety Authority (EFSA).[39]

Other stakeholders: Developed to support the drafting of the Dutch Presidency's Council Conclusions on AMR, EPHA's *Recommendations for the Dutch Council Conclusions on Antimicrobial Resistance* include human-sector specific actions.[40] They confirmed the need for EU guidelines for prudent use of antimicrobials in human medicine, and call for investments in new technology to support treatment decisions. Furthermore, maintaining health as a way of prevention, and the role of ICT and the media in communicating AMR are highlighted.

In 2016, the European Health Parliament made eight recommendations on AMR, three of which relevant for human prudent use[41]. It recommends supporting the R&D sector in developing and implementing Rapid Diagnostic Tests (RDTs) in GP practices; including health literacy in educational programmes throughout childhood and adulthood; and setting up a European Health Semester to allow Member States to share best practices and report on the implementation of national plans and targets, e.g., unnecessary antibiotic use.

National level

National Action Plans: Many action plans on AMR[42] include member state-specific recommendations. They emphasise the wide spread of responsibility: most include a list of institutions, population groups and professions involved in implementing the actions. Some explicitly follow the One Health approach and cluster their actions accordingly.

One of the drawbacks of having many different action plans is their potential lack of alignment. Since AMR presents a serious cross-border healthcare threat, this is problematic: if actions are not coordinated across frontiers, they risk being implemented to varying degrees of security, and with different levels of ambition (e.g. legislation) - they could even be contradictory. On the other hand, national or regional plans can be adapted to specific conditions, e.g. in countries where antimicrobial use in agriculture is relatively high, the priority could be more towards the veterinary sector; in other places the focus could be more on the human or environmental side, or a clever combination (e.g. Norway).[43]

The AMR Next document[44] of the Dutch Council Presidency lists a number of good practices of prudent use in human medicine in various member states. The challenge is to find ways to adapt them to the specific situation, often shaped by economic and cultural factors, of another country or region.

Examples of national good practices include the following:

- In The **Netherlands**, a new treatment supervision system stipulates mandatory reviews by physicians and hospital pharmacists to alter, shorten, and reduce antimicrobial treatments; the discussions create effective learning moments. Moreover, RDTs to differentiate between acute bronchitis and pneumonia brought significant cost savings.
- In **Sweden**, early action on AMR – e.g., regulated sales of antibiotics and sound surveillance of prescriptions - has led to a total decline in antibiotic prescriptions of over 40% since the 1990s. Treatment recommendations for infections are regularly updated.
- In the **UK**, a new programme analyses behavioural indicators for prescribing, mainly at GP level. It provides insights into the drivers for imprudent behaviours and identifies regional differences, allowing targeted intervention strategies.
- In **France**, national media were heavily involved in public awareness campaigns on responsible use. Every hospital appointed a responsible person with specialist knowledge about AMR and available tools and guidelines to support prescribing.
- In **Spain**, consumption of antibiotics has significantly decreased in 2010-2014 by adjusting package sizes. An expert panel reviewed and adjusted packages according to the most common dosage and duration of treatment.
- In **Norway**, actions comprise regional infection control conferences, training healthcare professionals on prescription guidelines, enforcing vaccination coverage, strengthening infection monitoring and control, and international collaboration.

UK Review on AMR: In 2015-2016, the Review Team produced a number of reports for the UK Government. They contain recommendations that look beyond the national sphere towards action at the international level, e.g. political agreements of the UN and G20.

Its overview report[8] highlights that most practicing doctors use empirical diagnosis, i.e. they determine disease and treatment based on professional judgement. Viral infections are often misdiagnosed as bacterial infections and vice versa. This is where the importance of RDTs becomes clear: more refined tests will enable more precise prescribing, thereby reducing imprudent use.

Throughout its work, the Review team has stressed that all areas of AMR are interrelated. An example is the importance of vaccine coverage for improving prudent use. Where an infection can be prevented through vaccination, it no longer requires antibiotics. The same goes for improving infection prevention and maintaining health (e.g., many NCDs are preventable).

Similar to WHO, the UK Review calls for controlling unlicensed Internet and OTC sales by way of legislative measures, but also by Internet companies themselves and local authorities.

The **UK Review's final report**[1] sums up the team's recommendations for improving the AMR situation. Among those directly or indirectly relevant for prudent use in human medicine are the following:

- Implement a massive global public awareness campaign
- Improve infection prevention and control (including vaccination)
- Reduce use of antimicrobials in agriculture
- Promote the timely development and implementation of RDTs to enable informed and effective prescribing
- Raise the numbers, pay and recognition of people working in infectious diseases
- Ensure action is undertaken through a global coalition and pooling of funds.

Local level

At the local level, the responsibility lies with healthcare institutions to implement proper infection control measures; with healthcare professionals to adhere with prescription guidelines and to advise patients; with the local media to raise public awareness; and with the public for taking into account the threat AMR poses when taking antimicrobials.

Many of the national recommendations are applicable, but more specific guidance and adaptation is required. Personal contact between patients and healthcare professionals becomes particularly important: clear and easy to understand information must be delivered to patients on both prescription and non-prescription medicines.

Guidelines on prudent use of antimicrobials in human medicine

A number of improvements can be made when it comes to prudent use in human medicine; the examples highlighted above illustrate various ways to achieve results.

This section discusses in more detail the draft guidelines proposed by ECDC, which could bring more clarity to generate policy, system and behavioural changes at different political levels and for all stakeholders involved. Similar voluntary guidelines already exist for the veterinary sector.[45]

Summary of ECDC guidelines

In July 2016, upon request by the European Commission, the ECDC published a draft technical report[35] with proposals for EU guidelines on the prudent use of antimicrobials in human medicine. It outlines various principles for inclusion in the guidelines, each comprising effective elements for their application. They are directed at the international and national/regional level, as well as healthcare facilities, laboratories, prescribers, pharmacists, nurses, infection control practitioners, education and research, the public/patients and the pharmaceutical industry.

The international principle focuses on the collaboration of organisations, agencies and research institutes across borders, which is crucial given the impacts of migration and trade on AMR. The elements include ensuring market availability of essential

antimicrobials; encouraging the development of standards for selective microbiology reporting to optimise antimicrobial prescribing; fostering international collaboration to develop and implement antimicrobial stewardship programmes to support appropriate antimicrobial use, and sharing best practices on antimicrobial use at European level. Additionally, developing evidence-based guidelines on the use of RDT is highlighted.

Equally vital are the elements outlined for the national level: making available funding and developing national action plans for appropriate use in human medicine; setting qualitative and quantitative targets to improve prescribing; establishing a list of antimicrobials with restricted use; supporting national antibiotic awareness campaigns; reviewing antimicrobial availability over the Internet; exploring incentive systems for appropriate prescribing; establishing a feedback system on appropriate prescribing and appropriate use practices, considering behavioural interventions to reduce inappropriate prescribing and motivational approaches to optimise antimicrobial prescribing; and adapting pack sizes and distribution data to planned course duration and usage.

Correspondingly, the guidelines for healthcare facilities include the establishment and funding of antimicrobial stewardship programmes and promotion of RDTs. Additionally, they include clear documentation of patient treatment and introduction of electronic decision support systems to support prescribing practices.

For prescribers (including nurse prescribers), the guidelines are divided into three aspects: general prescribing practice, prescribing in the community and in hospitals. For the first, the most interesting elements include ensuring that prescribing occurs according to set guidelines; reassessing antimicrobial treatments after a certain period; informing patients about treatments and alternatives (if applicable); and ensuring attention is given to meeting patients' questions and expectations in the delivery of patient-centred care. At the community level, prescribers should ensure that the correct antimicrobials are prescribed for a given disease (e.g. antibiotics for bacterial infections, antivirals for viral infections), consider delayed antimicrobial prescribing, and evaluate symptoms systematically to guide the need for diagnostic testing. In hospital settings the guidelines stress the importance of giving thorough consideration to antimicrobial types and classes, and the appropriate way of administering them.

Pharmacists are addressed as gatekeepers to antimicrobials and as advisors for patients on their use. They are advised not to dispense antimicrobials without prescription - with the exception of specific provisions –, to ensure that patients understand the correct dosage and duration of treatments, and promote appropriate disposal of leftover antimicrobials.

Nurses are the healthcare professionals who have the most direct contact with patients, and thus the guidelines stress their responsibility for the correct administration and monitoring of antimicrobials' effects, and as members of clinical teams.

In support of infection control practitioners, the guidelines promote the "collaboration of antimicrobial stewardship programmes and infection prevention and control activities by highlighting the role of appropriate antimicrobial use in the prevention and control of healthcare-associated infections (HCAI)". High quality infection control is of primary importance to prevent the need for unnecessary antibiotic prescribing arising.

Ensuring regular training of all healthcare professionals on appropriate antimicrobial use, and including antimicrobials, AMR, prudent use, vaccination and hygiene in primary and secondary education, is also an element of the guidelines.

The guidelines also include research into assessing and comparing behavioural change interventions for antimicrobial prescribing that take into account cultural differences, as well as translational research into how antimicrobials are being used.

For the pharmaceutical industry, the focus lies on informing patients of the risks of using antimicrobials and of AMR, e.g. by including this information in the summaries of product characteristics and highlighting it in promotional activities. The guidelines propose adapting pack sizes and considering special labelling of packages to warn patients about the specific, time-limited use of antimicrobials.

Finally, they propose that patients and the public get informed about prudent use, AMR and adverse reactions, that they do not use antimicrobials without prescription, and that they do not use leftover antimicrobials.

EPHA assessment

The ECDC guidelines are comprehensive and its elements specifically address key stakeholders. This form of coordination is welcome given the multiplicity of approaches to prudent use in human medicine in Europe. The following gaps can nonetheless be identified, as also outlined in EPHA's consultation response.[46]

Stressing public health: The guidelines should stress more clearly the importance of public health as a driver of AMR and of keeping public health at the core of all proposed interventions, thus confirming antimicrobials as a public good and creating accountability for societal ownership of this issue. They are not only important to stimulate good practices and improve the AMR situation, but also to ensure that our 21st century healthcare services can continue to function normally, without reverting to a 'pre-antibiotic era' and the dramatic consequences this would entail.

Furthermore, other interrelated issues - e.g. promoting alternatives to antibiotics and maintaining physical and mental health as a way of prevention, and introducing mandatory check-up periods to change antimicrobial treatments where appropriate – could be addressed. It is important to do everything possible to prevent infectious illness and avoid the need for antimicrobials. The relationship between health and social/economic inequalities – leading to a higher potential need for antimicrobials in certain population groups – is not included either.

Strengthening the role of Europe & ECDC: The guidelines should highlight more strongly the EU added value: AMR is cross-border by nature. The EU should seize this as an opportunity, e.g. by creating an EU repository of transferable good practices to support target setting at national level, ensuring harmonised mandatory data reporting on antimicrobial consumption and AMR, developing common approaches to surveillance, and enabling common antimicrobial stewardship programmes on- and offline.

In the light of the growing crisis of AMR, consideration should be given to options for binding EU-wide legislation to ensure proper implementation of the (currently voluntary) guidelines and reinforce existing provisions against illegal practices.

The question of how to finance implementation and boosting capacities at national level – e.g., laboratory and technological (data collection and diagnostics) – looms large: will EU funding be made available to tackle AMR at national level, and will impetus be given to the ECDC to provide a pan-European coordinating role (i.e. to go beyond its current limited role in surveillance and monitoring)?

Global leadership: EU action is a chance to demonstrate leadership on practices that must be adopted beyond our borders. The WHO, G20 and the UN should ensure that actions are scaled up to the international level. What kinds of international collaborations are envisaged exactly, and will the EU initiate them?

In a global context, the issues of access to medicines versus excess use, as well as persistent shortages of antimicrobials[47] also demand consideration.

Enabling healthcare professionals: Additional recommendations for healthcare professions would provide more clarity on where they can add value, beginning with a better understanding of their potential to contribute to tackling AMR and encouraging prudent use, and supporting training and development of new services and infrastructures.

For example, the education, counselling and stewardship functions of pharmacists could be highlighted more strongly as an additional element in the guidelines. They are not only gatekeepers, but also experts in medicines, hence they can act as an important source of advice and information for patients on the safe, rational and effective use of antimicrobials (including on side effects, adherence, adverse reactions, cautions and contra-indications, storage, disposal and rationale for treatment.

The uptake and use of e-Prescribing systems and access to shared eHealth records / patient medication records / pharmaceutical records (depending on the country) should also be promoted as such infrastructure can highlight safety issues, interactions, overuse and abuse of medicines, as well as 'shopping around' at different prescribers and inappropriate prescribing practices (e.g. of consecutive broad spectrum antibiotics where a narrow spectrum product should have been prescribed), etc.

Moreover, in several European countries pharmacists administer the seasonal influenza vaccination in pharmacies following appropriate initial and refresher training. As such, they are able to increase population vaccination coverage and thus reduce inappropriate antibiotic seeking behaviour from those with flu symptoms.

Healthcare professionals must also be enabled to be actively involved in antimicrobial stewardship as part of multidisciplinary care teams, and they should be empowered to participate in local, regional or national public health campaigns concerning prudent use of antimicrobials.

Although traditionally seen as a 'medical' issue due to the emphasis on prescribing of antibiotics, other healthcare professionals have key roles to play in supporting and influencing this issue. Looking forward, the 'traditional roles' of clinicians such as nurses, can be strengthened and advanced through evaluating and redesigning specialist roles such as infection control to ensure that specialist expertise is utilised successfully and with maximum impact. This may require adjustments to changes to specialist training, building on work already undertaken through the ECDC competencies[48] with an additional

focus on a stewardship role, the interdisciplinary nature of AMR, and evolving responsibilities as both prescribers and specialists.

The expertise of infection control professionals goes beyond local HCAI and can benefit the national and international level. GPs and community healthcare services are not specifically addressed – which could however be beneficial given their close contact with patients at local level – and clinical microbiologists remain unmentioned.

Other healthcare professionals also play a role in maintaining good health and promoting prevention. Where appropriate, they can provide information about alternatives to antibiotics and about the potential impact of widespread antibiotic consumption on the human microbiome.

Empowering patients: The guidelines aimed at patients should include the importance of treatment adherence and proper disposal of antibiotics, as well as developing awareness of when antimicrobials are not needed e.g. for self-limiting infectious illnesses that will benefit from rest, fluids and good nutrition. It is important to ensure that all people, including individuals with low health literacy or experiencing access to healthcare problems, are targeted in public awareness campaigns.

Conclusion

Prudent use of antimicrobials in human medicine is a complex area shaped by many different actors and circumstances. Currently, levels of approach across Europe differ and this is hindering effective action on AMR, at EU level and globally. Robust guidelines outlining roles and responsibilities for all actors will contribute to better coordination in the fight against AMR.

Notwithstanding the potential need to introduce new legislation as a backup to the voluntary guidelines, Europe can add important value to the debate and action plan by enabling the identification and sharing of good practices, and by providing guidance on how they can best be implemented across Europe. Once finalised, ECDC's guidelines will provide practical support to the implementation of the European Action Plan on AMR, currently under revision, and the national action plans. The extent to which the guidelines are put into practice across the EU should be monitored. By taking a global leadership role, Europe can pave the way for a coordinated international effort to promote and implement prudent use of antimicrobials in human medicine.

EU member states have endorsed action on this topic through several sets of Council Conclusions. It is time to ensure words on international cooperation are converted into actions and positive outcomes. For this to happen, responsibility for implementation should be clearly and transparently assigned. EPHA suggests that the statutory remit (and funding) of the ECDC be enhanced to go beyond surveillance of antimicrobial resistance – to provide the necessary leadership in combating the crisis.

The WHO and EU action plans on AMR, the UK Review's Final Report and Recommendations, and EPHA's Recommendations for the Dutch Council Conclusions on Antimicrobial Resistance10 are all examples of documents that contain proposals for enabling prudent use in human and veterinary medicine; they also provide clear reasoning of the importance of the One Health approach. For future work in this area, it is recommended that these and other key documents will be consulted in order to ensure coherent, coordinated and binding action.

In addition to the points made in the previous section regarding the guidelines for prudent use of antimicrobials in human medicine, the EU must take the following steps to improve prudent use of antimicrobials in human medicine:

- Ensure that European policy actions, including the guidelines on prudent use of antibiotics in human medicine and the follow-up of the Action Plan, deliver on the WHO Global Action Plan; in addition, build close relationships and share knowledge with EU neighbours to ensure cross-border preparedness
- Focus on *implementation*: use available EU funds for national action plans and supporting prudent use, in addition to expanding the remit and funding of ECDC
- Ensure availability of comparable data, between Member States and regions, to better understand consumption and AMR trends (including better data on use of antimicrobials in hospitals and on prescribing behaviours)
- Explore available options for binding, EU-wide legislation to mitigate the AMR situation and support the proper implementation of (voluntary) guidelines; implement mandatory monitoring and provide incentives for healthcare professionals to encourage prudent prescribing
- Investigate illegal OTC, Internet and other availability of antibiotics in Europe, and support the enforcement of existing legislation on illegal practices
- Invest in laboratory infrastructure to support testing and surveillance
- Invest in education of all healthcare professionals on AMR including specialist infection control / hospital hygiene roles to support actions across health, public health and social care boundaries
- Set quantitative targets and indicators – 'you can't manage what you don't measure'

EPHA also calls on industry to act upon the guidelines by adapting pack sizes given that by law, in some countries pharmacists cannot provide fewer antibiotics than are contained in the pack.

Finally, further EU-level awareness-raising beyond the EAAD is necessary to ensure better accountability and societal ownership of the problem. While certain good practices may be hard to adopt in another country, others can be: AMR is also a test case for boosting solidarity and public health policy.

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About EPHA

EPHA is a change agent – Europe's leading NGO advocating for better health. We are a dynamic member-led organisation, made up of public health NGOs, patient groups, healthcare professionals, and disease groups working together to improve health and strengthen the voice of public health in Europe. EPHA is a member of, among others, the Social Platform, the Health and Environment Alliance (HEAL), and the Better Regulation Watchdog.
EPHA's Transparency register number is 18941013532-08.

Further reading

EPHA report on the Environmental Dimension of AMR
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