The Standing Committee of European Doctors (CPME) represents national medical associations across Europe. We are committed to contributing the medical profession's point of view to EU and European policy-making through pro-active cooperation on a wide range of health and healthcare related issues.

Policy on Antimicrobial Resistance

Main Messages:

1. Prudent prescribing of antibiotics is a responsibility of each practicing doctor in Europe and worldwide.
2. Doctors must prioritise the narrow-spectrum antibiotics while considering individual patient's needs.
3. Decisive political action is needed to ensure the prudent use of antibiotics and to improve infection prevention and control.
4. The European Union needs a common approach to antibiotic stewardship programmes, that will be adapted to healthcare delivery settings, local context and that will put emphasis on prescribing.
5. Each healthcare facility should be encouraged to establish and provide necessary funding and resources for AMR stewardship programmes.
6. Healthcare professionals must have access to fast and efficient point-of-care diagnostics to support prudent prescribing, and only in exceptional circumstances should antibiotics be prescribed without laboratory or point-of-care diagnostics.
7. Face-to-face consultations should remain a gold standard wherever possible. Telemedicine prescribing may be used as well as face-to-face providing proper diagnostic procedures have been followed.
8. Effective infection prevention and control (IPC) programmes must go hand in hand with adequate human and financial resources.
9. Hand hygiene should become a binding performance indicator for evaluating IPC practices in healthcare.
10. Cooperation between public health, veterinary and environmental sectors, rooted in the One Health approach, must be strengthened.

11. Prevention of overuse of antibiotics in agriculture and environmental contamination leading to antimicrobial resistance must be a priority.
12. Routine preventive use of antibiotics for healthy groups of animals must be banned. The use of critically important antimicrobials in agriculture and food production must be restricted.
13. Sale, including online, of over-the-counter antibiotics must be effectively banned in all Member States. European and national level controls must ensure compliance, adhering to current legislation.
14. Medical training curricula must be equipped with up to date and reliable information on the One Health approach, interprofessional cooperation and responsible prescribing practices, so that future doctors and other healthcare professionals have the appropriate knowledge and skills.
15. Doctors and medical students should be supported in developing skills to manage patient expectations regarding antibiotic prescribing. To support continued progress, it is vital that healthcare professionals have adequate time with patients to assess whether antibiotics are necessary.
16. The public should be informed about the correct use of antibiotics, their effectiveness, and the societal impact of misuse, as well as prevention of infections through increased hygiene.
17. Data on antibiotic use, prescriptions, prices, resistance patterns, and trade in all concerned sectors should be publicly available and accessible to the medical and scientific community.
18. Shortages of existing antibiotics pose a real challenge for doctors. To ensure stable supply of antibiotics, they should be considered a public good and certain public service obligations on marketing authorisation holders should be imposed.
19. Actions related to monitoring of availability and measures addressing root-causes of shortages of generic antibiotics are needed.
20. AMR needs to be re-approached with a new comprehensive alternative market model to ensure sustainable and equitable access to antibiotics.
21. An end-to-end approach to the development of new antibiotics is needed, supported by an innovative incentive model to decouple the revenue from the novel antibiotic from the quantity sold. Examples of such incentives are market entry rewards, guarantees for minimum turnover and milestone payments.
22. The European Union should regulate pharmaceutical production and ensure compliance with rules on pharmaceutical pollution monitoring and providing complete data to regulators.

1. Introduction

Antimicrobial resistance (AMR), particularly antibiotic resistance, is one of the greatest global health threats affecting the health of people across the world.

AMR occurs when bacteria, parasites, viruses and fungi evolve to resist treatment with antimicrobials. As a result, infections no longer respond to medicines making infections more difficult to treat.[1] This increases the risk of spread, severe illness and death.

This policy focuses on antibiotic resistance in bacteria, however CPME recognises increasing resistance in other pathogens.

According to the latest estimates of the European Centre for Disease Prevention and Control (ECDC), more than 35 000 people die from antibiotic-resistant infections in the EU/EEA each year.[2] The same study confirms a growing trend for this considerable health burden in the European region. Globally, AMR can be attributed to over 1.2 million deaths each year.[3]

Despite a decrease of 23% in total antimicrobial consumption in both the primary care and hospital sectors in the EU/EEA, between 2012-2021, AMR remains an unsolved challenge. Further and decisive action is needed to ensure the prudent use of antibiotics, especially in primary care, and to improve infection prevention and control, as well as to prevent the overuse of antibiotics in agriculture and environmental contamination leading to antimicrobial resistance.[4] It is equally important to ensure the availability and accessibility to effective generic as well as novel antibiotics.

CPME recognises that complacency, poor prescribing practice and the misuse of antibiotics are major factors in the emergence of AMR.[5] In a study on European doctors' knowledge and attitudes towards antibiotics and AMR, 80% of doctors acknowledged that they are aware of their individual prescribing's impact on the spread of the resistance.[6]

[1] World Health Organization, Antimicrobial Resistance Fact Sheet, 2021, https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance
[2] European Centre for Disease Prevention and Control, Assessing the health burden of infections with antibiotic-resistant bacteria in the EU/EEA (2016-2020), 2022, https://www.ecdc.europa.eu/en/publications-data/health-burden-infections-antibiotic-resistant-bacteria-2016-2020
[3] C. J. L., Murray, K. S. Ikuta, et al., Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis, The Lancet, 399(10325), 629–655, 2022, doi: 10.1016/s0140-6736(21)02724-0
[4] S., Reardon, Antibiotic use in farming set to soar despite drug-resistance fears. Nature, 614(7948), 397, 2023, doi:10.1038/d41586-023-00284-x
[5] The Standing Committee of European Doctors, Antibiotic Resistance: A CPME Position Paper, 2013.
[6] The Standing Committee of European Doctors, CPME report on European doctors' knowledge of and attitudes towards antibiotics and antibiotic resistance, 2020.

Prudent and evidence-based use of antibiotics must be a cardinal rule for all doctors. Guidelines on prescribing antibiotics should state that antibiotics should only be prescribed when necessary, and when prescribed should be in the dose appropriate for the infectious disease to be treated and as short as possible according to prevailing guidelines. A priority should be given to education and stewardship programmes. At the same time, authorities at all levels – local, regional, national and European – must facilitate and support this joint fight against AMR.

AMR reached the highest levels of political attention of leaders at G7 and G20.[7],[8] Yet, there is still a need for concerted action and implementation of plans.

2. One Health

AMR is far from being only a human health problem.[9] In fact, it is a challenge that binds together multiple sectors, disciplines and communities at varying levels of society. A One Health approach to combatting AMR brings together public health, veterinary and environmental sectors. WHO defines it as "an integrated, unifying approach to balance and optimise the health of people, animals and the environment".[10] An effective One Health approach is essential to minimise the unnecessary or inappropriate use of antibiotics and to prevent and control the transmission of resistance.[11] In practice, the implementation of the One Health approach includes elements of field epidemiology, sharing of laboratory resources and health information, the use of multi-sector teams and the use of assessment frameworks. The coordination mechanisms established between the public health, veterinary and environmental sectors are proving to be crucial in addressing issues related to food safety, management of disease emergencies and the impact of climate change on the emergence of diseases, as well as spreading of antimicrobial resistance.[12]

Developing solutions in the One Health approach may not be the easiest task to pursue, as it requires a high level of cooperation, communication and coordination, as well as political leadership.[13] One Health's High Level Expert Panel has identified a number of challenges to

[7] Declaration of the G7 Health Ministers 2015, 2015, http://www.g7.utoronto.ca/healthmins/2015-berlin.html.
[8] G20 Indonesia 2022, G20 Bali Leaders' Declaration 2022, 2022, https://www.consilium.europa.eu/media/60201/2022-11-16-g20-declaration-data.pdf?utm_source=dsms-auto&utm_medium=email&utm_campaign=G20+Bali+Leaders%e2%80%99+Declaration.
[9] United Nations Environment Programme, Bracing for Superbugs: Strengthening environmental action in the One Health response to antimicrobial resistance, 2023, https://www.unep.org/resources/superbugs/environmental-action.
[10] World Health Organization, Questions & Answers - One Health, 2017, https://www.who.int/news-room/questions-and-answers/item/one-health.
[11] Federation of Veterinarians of Europe, Using antimicrobials responsibly - Advice for Doctors, Dentists and Veterinarians, 2014.
[12] J. S., Mackenzie, M. C., McKinnon, & M. Jeggo, One Health: From Concept to Practice. Springer EBooks, 163–189, 2014, doi:10.1007/978-4-431-55120-1_8.
[13] J. S., Mackenzie, M. C., McKinnon, & M. Jeggo, One Health: From Concept to Practice. Springer EBooks, 163–189, 2014, doi:10.1007/978-4-431-55120-1_8.

achieving effective collaboration.[14] At the same time, it recognised that One Health's approach is the most promising and effective avenue in the fight against AMR. The European Union's institutions have on many occasions acknowledged the importance of the One Health approach. The latest Council Conclusions on AMR adopted in 2019 presented the One Health approach as a condition for success in the fight against AMR.[15] The European Parliament's Resolution on AMR placed One Health as a principle that should play a central role.[16] Finally, the European One Health Action Plan against AMR is built around the One Health approach.[17]

Cross-sectoral education and cooperation between doctors, veterinarians, dentists, pharmacists and other healthcare professionals, in line with the One Health approach, is particularly important in the context of antimicrobial resistance. As it has been estimated that over 70% of all antimicrobials sold globally are used in agriculture, actions in human health alone will not be enough.[18] The use in animal farming is even expected to grow.[19] It is recommended that the routine preventive use of antibiotics for healthy groups of animals is banned, as well as the use of critically important antimicrobials in agriculture and food production is restricted.[20] Instead, animal welfare should be increased.[21]

3. Prescribing and public health interventions

Stewardship interventions at all levels of care along with other legislative and technical steps are indispensable to fight the spread of AMR. Actions before, during and after prescribing are needed to guide prudent use of antibiotics. Stewardship should be preceded by a dedicated effort to prevent infections.

The Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU JAMRAI) identified a lack of efficient tools to influence the implementation of AMR stewardship

[14] World Health Organization, Questions & Answers - One Health, 2017 https://www.who.int/news-room/questions-and-answers/item/one-health.
[15] The Council of the European Union, Council conclusions on the next steps towards making the EU a best practice region in combatting antimicrobial resistance (2019/C 214/01), Official Journal of the European Union, 2019, https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52019XG0625(01)&from=EN
[16] European Parliament, European Parliament resolution of 13 September 2018 on a European One Health Action Plan against Antimicrobial Resistance (AMR), 2018, https://www.europarl.europa.eu/doceo/document/TA-8-2018-0354_EN.html.
[17] European Commission, A European One Health Action Plan against Antimicrobial Resistance (AMR), 2017, https://health.ec.europa.eu/system/files/2020-01/amr_2017_action-plan_0.pdf.
[18] K. Tiseo, L. R. Huber, et al., Global Trends in Antimicrobial Use in Food Animals from 2017 to 2030. Antibiotics, 9(12), 918., 2020, doi:10.3390/antibiotics9120918
[19] S. Reardon, Antibiotic use in farming set to soar despite drug-resistance fears, Nature, 614(7948), 397, 2023, doi:10.1038/d41586-023-00284-x
[20] World Health Organization, WHO guidelines on use of medically important antimicrobials in food-producing animals, 2017, CC BY-NC-SA 3.0 IGO, http://apps.who.int/iris/bitstream/handle/10665/258970/9789241550130-eng.pdf.
[21] Health Care Without Harm, Policy recommendations | Improve animal welfare to ensure responsible, 2022, https://noharm-europe.org/documents/policy-recommendations-improve-animal-welfare-ensure-responsible-use-antibiotics.

at both country and healthcare level in Europe.[22] EU JAMRAI also identified good leadership and clear lines of accountability as well as well-functioning IT as some of the success factors to roll-out effective stewardship programmes.[23] The EU Guidelines for the prudent use of antimicrobials recommend that each healthcare facility establishes and provides necessary funding and resources for AMR stewardship programmes.[24] The EU Guidelines further outline what is needed to achieve successful stewardship programmes.

There is a need to elaborate the core elements of European antibiotic stewardship programmes in order to translate them into practical and achievable policies at national and healthcare delivery level. They must reflect contextual complexities and put emphasis on prescribing. Existing resources are not fully adapted to the European Union context[25] but attempts to reach a consensus on the core elements of stewardship in human medicine have been made.[26] These key elements include senior leadership commitment, accountability and clear responsibilities, available expertise on infection management, education and practical training, actions aiming at responsible antimicrobial use, monitoring and surveillance, and finally reporting and feedback.

Doctors must prioritise the narrow-spectrum antibiotics while considering individual patient's needs. A decisive factor in ensuring prudent use of antimicrobials is access to fast and efficient diagnostics.[27] Studies show that by implementing point-of-care testing by doctors antibiotic consumption and AMR decreases.[28] This helps in decision-making between narrow and broad-spectrum antibiotics. Implementing prescription feedback system at healthcare or doctor level can also be helpful.

Infection prevention and control (IPC) is equally important as antibiotic stewardship. Along with extensive use of antibiotics, poor IPC is one of the main drivers of AMR.[29] 75% of the health burden of infections with bacteria resistant to antibiotics in Europe is due to healthcare-associated infections.[30] IPC measures can help reducing this burden, and hand hygiene was

[22] EU-JAMRAI, Appropriate use of Antibiotics in a One Health Perspective, 2021, https://eu-jamrai.eu/wp-content/uploads/2021/02/201020_EUJAMRAI_policy-brief_WP7_appropriate-use-of-antibiotics-one-health-perspective.pdf.
[23] EU-JAMRAI, Appropriate use of Antibiotics in a One Health Perspective, 2021, https://eu-jamrai.eu/wp-content/uploads/2021/02/201020_EUJAMRAI_policy-brief_WP7_appropriate-use-of-antibiotics-one-health-perspective.pdf.
[24] European Commission, Commission Notice EU - Guidelines for the prudent use of antimicrobials in human health (2017/C 212/01), Official Journal of the European Union, 2017, https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52017XC0701(01)&from=ET
[25] EU-JAMRAI, The Need to Develop Core Elements at the European Level on Antimicrobial Stewardship and Infection Prevention and Control, 2021, https://eu-jamrai.eu/wp-content/uploads/2021/03/201022_EUJAMRAI_policy-brief_WP4_core-elements.pdf.
[26] C. Pulcini, F. Binda, et al., Developing core elements and checklist items for global hospital antimicrobial stewardship programmes: a consensus approach. Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases, 25(1), 20–25, 2019, doi:10.1016/j.cmi.2018.03.033
[27] H. Admin, Lack of diagnostics helps fuel AMR. Health Action International, 2023, https://haiweb.org/lack-of-diagnostics-helps-fuel-amr/. .
[28] S. Singh, A. Numan, & S. Cinti, Point-of-Care for Evaluating Antimicrobial Resistance through the Adoption of Functional Materials. Analytical Chemistry, 94(1), 26–40, 2021, doi:10.1021/acs.analchem.1c03856
[29] EU-JAMRAI, The Need to Develop Core Elements at the European Level on Antimicrobial Stewardship and Infection Prevention and Control, 2021, https://eu-jamrai.eu/wp-content/uploads/2021/03/201022_EUJAMRAI_policy-brief_WP4_core-elements.pdf.
[30] European Antibiotic Awareness Day, SAVE LIVES: Clean Your Hands – ECDC supports World Hand Hygiene Day 2019, 2019, https://antibiotic.ecdc.europa.eu/en/news-events/save-lives-clean-your-hands-ecdc-supports-world-hand-hygiene-day-2019.

described by the World Health Organization as the "single most important measure" to prevent infections. Adequate human resources are critical for effective IPC. Successful IPC programmes may lead to a more than 30% reduction in healthcare associated infections, while hand hygiene practices can lead to a reduction of pathogen transmission in healthcare by at least 50%.[31] IPC programmes also support more effective implementation of antibiotic stewardship.[32] Hand hygiene should become a binding performance indicator for evaluating IPC practices in healthcare.

Another important angle to public health interventions in limiting AMR is enforcement of existing legal provisions to fully comply with a ban on antibiotics without prescription (OTC). 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 (Austria, Belgium, Bulgaria, Lithuania, Poland, Portugal, Netherlands, Greece, Hungary, Italy, Romania).[33],[34] Recent estimates show that in the European Union 8% of all antibiotics for human use are consumed without a prescription.[35] The World Health Organization surveyed EU neighbouring countries from the European region and estimated that as much as 1 in 3 people consume antibiotics without a medical prescription.[36] The main sources of obtaining antibiotics bypassing doctors are buying them without a prescription at home or abroad (despite the applicable law), using leftovers or obtaining them from friends and family.[37]

The availability of OTC antibiotics, including those for animals, on the Internet poses a major challenge in the fight against AMR. Recent research shows a scale of availability of antibiotics through direct-to-consumer online sale.[38]

Pharmaceutical promotion can negatively impact prescribing practices, including when it comes to antibiotics.[39] European and national level controls must be ensured to tackle the influence of industry marketing.

---

[31] World Health Organization, Hand hygiene improvement saves lives and fights antibiotic resistance, 2017, https://cdn.who.int/media/docs/default-source/integrated-health-services-(ihs)/clean-hands-2017/campaign_policymakers.pdf?sfvrsn=42c7df44_5&download=true.

[32] D. G. Baur, B. P. Gladstone, et al., Effect of antibiotic stewardship on the incidence of infection and colonisation with antibiotic-resistant bacteria and Clostridium difficile infection: a systematic review and meta-analysis. Lancet Infectious Diseases, 17(9), 990–1001, 2017. doi:10.1016/s1473-3099(17)30325-0

[33] European Union, Antimicrobial Resistance and causes of non-prudent use of antibiotics in human medicine in the EU, 2017. doi:10.2875/326847

[34] European Union, Antimicrobial Resistance and causes of non-prudent use of antibiotics in human medicine in the EU, 2017, Chapter 3. doi:10.2875/326847

[35] European Commission, Data on antimicrobial resistance (AMR): use of antibiotics in the EU decreases but more needs to be done, 2022, https://ec.europa.eu/commission/presscorner/detail/en/IP_22_6951.

[36] World Health Organization, 1 in 3 use antibiotics without prescription - WHO/Europe's study shows, 2022, https://www.who.int/europe/news/item/21-11-2022-1-in-3-use-antibiotics-without-prescription--who-europe-s-study-shows.

[37] European Union, Antimicrobial Resistance and causes of non-prudent use of antibiotics in human medicine in the EU, 2017. doi:10.2875/326847

[38] T. K. Mackey, A. K. Jarmusch, et al., Multifactor Quality and Safety Analysis of Antimicrobial Drugs Sold by Online Pharmacies That Do Not Require a Prescription: Multiphase Observational, Content Analysis, and Product Evaluation Study. JMIR Public Health and Surveillance, 8(12), e41834, 2022, doi:10.2196/41834

[39] A. Machowska, & C. S. Lundborg, Drivers of Irrational Use of Antibiotics in Europe. International Journal of Environmental Research and Public Health, 16(1), 27, 2018, doi:10.3390/ijerph16010027

4. Education and awareness raising

Understanding about AMR remains highly variable across European countries, and education and awareness raising have been one of the primary goals of many national action plans.[40]

Education and awareness-raising help to shape the competences, attitudes, and societal expectations to be more conducive to the responsible use of antibiotics and better antibiotic prescribing. For doctors, dedicated trainings and conferences are one of the most important sources of information on antibiotics, next to official guidelines issued by relevant authorities and scientific societies.[41]

In Europe, medical training curricula must be equipped with up to date and reliable information on One Health approach, interprofessional cooperation and responsible prescribing practices, so that future doctors and other healthcare professionals have the appropriate knowledge and skills. Well-developed skills of general practitioners can help facilitating prudent use of antibiotics. Doctors and medical students should be supported in developing skills to manage patient expectations regarding antibiotic prescribing. To support continued progress, it is vital that healthcare professionals have adequate time for clinical assessment with patients to assess whether antibiotics are necessary. Workforce shortages and heavy workloads across the health sector challenge this – workforce pressure is known to influence prescribing practices. Effective medical training as well as post-graduate education need adequate human resources – professionals in infectious diseases and medical microbiology.

The public should be informed about the correct use of antibiotics, their effectiveness, and the societal impact of misuse, as well as prevention of infections through increased hygiene.[42] While, the European Antibiotic Awareness Day is an important action, more is needed to be done, along with adequate funding for awareness raising activities in the European Union. The EU must raise awareness about the appropriate use of antimicrobials among healthcare professionals, veterinarians, the agricultural sector, and the public in a co-ordinated way.

[40] https://www.ecdc.europa.eu/en/publications-data/directory-guidance-prevention-and-control/prudent-use-antibiotics/antimicrobial
[41] The Standing Committee of European Doctors, CPME report on European doctors' knowledge of and attitudes towards antibiotics and antibiotic resistance, 2020.
[42] Health First Europe, 2021 Declaration of the European Patient Group on Antimicrobial Resistance, 2021, https://healthfirsteurope.eu/wp-content/uploads/2021/04/HFE-AMR-Patient-Group-Final-Declaration.pdf.

5. Digital health technologies

Digital health technologies offer a number of solutions that have a direct and indirect impact on AMR. From software and applications that allow better and more accurate monitoring of emerging resistance, through real-time signals and warnings in prescribing software, to technology that enables care to be delivered in the most remote locations, digitalisation in healthcare brings risks and benefits.[43]

The use of telemedicine[44] has been growing in recent years, accelerated by the COVID-19 pandemic. Telemedicine can be a useful tool in limited circumstances.[45] For example, it can promote antibiotic stewardship efforts in remote facilities by linking to professionals trained in infectious diseases. It does bring challenges and risks related to quality and cost effectiveness, confidentiality and security and accessibility.[46] In the context of AMR, it is important to note that rapid on-line consultations and quick prescriptions can result in over-prescribing of antibiotics and other drugs.[47],[48] Face-to-face consultations should remain a gold standard wherever possible. Telemedicine prescribing may be used as well as face-to-face providing proper diagnostic procedures have been followed. Relevant clinical and diagnostic examination should be performed before any treatment is initiated.[49]

Electronic health records can provide rapid access to diagnostic results and pretreatments, i.e., information that is highly relevant for decision making at the prescriber level. The availability and functionalities of electronic health records in human medicine should be further improved.

Digital technologies used in healthcare can support prudent prescribing decisions by providing easy point-of-care access to national country guidelines and tools.[50],[51],[52] Greater utilisation can be facilitated by clear evaluation, benefits communication and appropriate infrastructure and funding.

[43] The Standing Committee of European Doctors, CPME policy on telemedicine, 2021.
[44] Telemedicine is the practice of medicine over a distance, in which interventions, diagnoses, therapeutic decisions, and subsequent treatment recommendations are based on patient data, documents and other information transmitted through telecommunication systems.
[45] The Standing Committee of European Doctors, CPME policy on telemedicine, 2021.
[46] The Standing Committee of European Doctors, CPME policy on telemedicine, 2021.
[47] L. J. Peters, G. Greenfield, et al., The impact of private online video consulting in primary care. Journal of the Royal Society of Medicine, 111(5), 162–166, 2018, doi:10.1177/0141076818761383
[48] S. H. Subramanya, D. M. Czyż, et al., The potential impact of the COVID-19 pandemic on antimicrobial resistance and antibiotic stewardship. Virusdisease, 32(2), 330–337, 2021, doi:10.1007/s13337-021-00695-2
[49] The Standing Committee of European Doctors, Antibiotic Resistance: A CPME Position Paper, 2013.
[50] V. Carter, Blog: The role of Digital Health in combatting Antimicrobial Resistance - Commonwealth Pharmacists Association. Commonwealth Pharmacists Association, 2021. https://commonwealthpharmacy.org/blog-the-role-of-digital-health-in-combatting-antimicrobial-resistance/
[51] F. F. Tuon, J. Gasparetto, et al., Mobile health application to assist doctors in antibiotic prescription – an approach for antibiotic stewardship. Brazilian Journal of Infectious Diseases, 21(6), 660–664, 2017, doi:10.1016/j.bjid.2017.08.002
[52] B. A. Van Dort, J. E. Carland, et al., Digital interventions for antimicrobial prescribing and monitoring: a qualitative meta-synthesis of factors influencing user acceptance, Journal of the American Medical Informatics Association, Volume 29, Issue 10, Pages 1786–1796, 2022, doi:10.1093/jamia/ocac125

6. Antimicrobial resistance and use surveillance

Surveillance of antimicrobial resistance and use is an essential tool to inform policies and infection prevention and control actions.[53] Integrated surveillance of AMR that includes human and animal health, as well as food supply chains and environment has been recommended by a range of responsible international organisations. An example of such approach has been implemented in Canada since 2002 in a form of the Canadian Integrated Program for Antimicrobial Resistance Surveillance.[54],[55] In October 2022, the European Commission has proposed two Directives on a water protection framework and on urban wastewater treatment providing for the screening of surface and ground water, and of urban wastewater for antimicrobial resistant bacteria and their genes.

To ensure near-real time, effective and integrated monitoring of AMR and use trends and to improve global response a responsible data sharing an international, as well as interprofessional cooperation are needed.[56] Data on antibiotic use, prescriptions, prices, resistance patterns, and trade in all concerned sectors should be publicly available and accessible to the medical and scientific community. It is also important that collected data reflect local settings. Each region or hospital should establish a local surveillance system. The data should be stratified to support informed empirical antibiotic choice.

Surveillance mechanisms should monitor and track whether reductions in antibiotic prescribing are resulting in under prescription and adverse health consequences.

7. Development and access to antibiotics

Predictable access to life-saving antibiotics is a common global challenge. Countries in Europe and beyond, indicate shortages of existing antibiotics and struggle with working out an incentive scheme that would ensure sustainable access to both existing and novel antibiotics.[57] Shortages of existing antibiotics pose a real challenge for doctors and force them to prescribe antibiotics solely based on availability not suitability. It undermines efforts to fight AMR by using narrow-spectrum antibiotics as much as possible, and may result in worse patient outcomes, toxicity

[53] World Health Organization, Global Antimicrobial Resistance and Use Surveillance System (GLASS), 2015. https://www.who.int/initiatives/glass
[54] Health Canada, Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS), 2023, https://www.canada.ca/en/public-health/services/surveillance/canadian-integrated-program-antimicrobial-resistance-surveillance-cipars.html
[55] The objectives of this programme are to provide an integrated approach to trends monitoring in humans and animals and to facilitate the assessment of the public health impact of antimicrobials used in both sectors.
[56] M. E. Velazquez-Meza, M. Galarde-López, et al., Antimicrobial resistance: One Health approach. Veterinary World, 743–749, 2022, doi:10.14202/vetworld.2022.743-749
[57] H. Collis, Drug regulator probes EU-wide antibiotics shortage, 2022, https://pro.politico.eu/news/157847 (subscription required)

and accelerated resistance development. To ensure stable supply of antibiotics, they should be considered a public good and certain public service obligations on marketing authorisation holders should be imposed. More broadly, shortages must be managed by ensuring production independence and diversification of supply chains. Further actions related to monitoring of availability and measures addressing root-causes of shortages of generic antibiotics are needed. Notification requirements, safety stocks and deterring penalties for non-compliance are also of utmost importance.[58]

There is a consensus that both push and pull incentives are needed to stimulate antibiotic development.[59] Governments and international institutions worldwide have invested significant resources in pushing the research and development activities towards novel antibiotics, yet with very little effect. No new classes of antibiotics have been discovered since the 1980s.[60] The pharmaceutical industry argues for greater alignment of funding and pull incentive schemes with the actual scale of the threat.[61] The identified challenge with the antibiotics market is that they are unable to generate unit sale-based revenues large enough to sustain investments, while it is in the interest of everyone to administer as little as possible.[62]

A new approach is needed. AMR needs to be re-approached with a new comprehensive alternative market model to ensure sustainable and equitable access to antibiotics. While push incentives have been widely considered and implemented[63], the pull side is still very much being debated and piloted.

Transferable exclusivities (vouchers) represent another category of incentives that would allow for selling an extension of the market exclusivity period to another company. This extension would be obtained thanks to a successful development of a novel antibiotic meeting predefined criteria. The vouchers should be strongly opposed, as potential indirect costs for health systems (prolonged high prices of certain medicines) and ethical considerations seem to be outweighing its potential benefits.[64]

Due to the nature of the use of antibiotics (the less the better), the current market model is failing to support public health objectives. An innovative incentive is needed to decouple the

[58] The Standing Committee of European Doctors, CPME Policy on Medicine Shortages, 2020.
[59] C. Årdal, J. Røttingen, et al., Pull Incentives for Antibacterial Drug Development: An Analysis by the Transatlantic Task Force on Antimicrobial Resistance. Clinical Infectious Diseases, 65(8), 1378–1382, 2017, doi:10.1093/cid/cix526
[60] Wellcome Trust, Why is it so hard to develop new antibiotics?, 2020 https://wellcome.org/news/why-is-it-so-hard-develop-new-antibiotics
[61] Pfizer EU Policy, Committed to the fight against Antimicrobial Resistance (AMR) | Pfizer EU Policy, n.d., https://www.pfizereupolicy.eu/article/committed-fight-against-antimicrobial-resistance-amr
[62] EU-JAMRAI, Incentivizing Antibiotic Access and Innovation, 2021, https://eu-jamrai.eu/wp-content/uploads/2021/02/201211_EUjamrai_policy-brief_WP9_hub-incentives.pdf
[63] Carb-X, Home - Carb-X, 2023, https://carb-x.org/
[64] C. Årdal, E. Baraldi, et al., Transferable exclusivity voucher: a flawed incentive to stimulate antibiotic innovation. The Lancet, 2023, doi:10.1016/s0140-6736(23)00282-9

revenue from the new antibiotic from the quantity sold (delinkage). Examples of such incentives are market entry rewards, guarantees for minimum turnover[65] and milestone payments. These direct payments are paid to developers for bringing a product to the market or contributing to a certain stage of R&D, without linking it to the sale volume. As an example, in the past, the European Commission awarded Horizon prize for better use of antibiotics.[66] The added value of the prize system is, unlike patents, rewarding innovation that brings social value and address unmet medical need. In the fully delinked model, the payments are the main revenue for the antibiotic while units are sold at a contractually agreed price. Market entry rewards, if implemented correctly, promote stewardship and equitable access. Importantly, the prize system requires significant upfront public investments. However, through reallocation of resources that are already dedicated to encouraging innovation through the intellectual property rights system, this would not generate additional public spending.[67]

A number of initiatives have demonstrated the value and potential of such models e.g., DNDi, GARPD. The European Union should build on these examples and implement them broadly, also as non-legislative measures. The EU should also further explore the role of the Health Emergency and Preparedness and Response Authority (HERA) as a pipeline coordinator, to ensure an end-to-end approach to antibiotic R&D.[68] An end-to-end approach was also suggested by the European Parliament by creating of a European medicines public infrastructure that could provide a more sustainable way of producing necessary medicines, including antibiotics.[69]

8. Preventing pharmaceutical pollution contributing to AMR

Pharmaceutical effluent greatly contributes to AMR. Large amounts of pharmaceutical products (active pharmaceutical ingredients and finished pharmaceutical products) are discharged into the environment, as a by-product of technological processes leading to availability of these live saving medicines. The increase in antibiotic manufacturing, especially outside the European Union, has caused a consequent rise in the industry's pharmaceutical effluent.[70] However, this is not a non-EU problem. First, because of the global dependencies in the environment. Second,

[65] Folkhälsomyndigheten, Tillgänglighet till vissa antibiotika - En pilotstudie av en alternativ ersättningsmodel, 2023, https://cpme.eu/policies-and-projects/public-health-and-disease-prevention/alcohol-and-tobacco-control
[66] European Commission, Horizon Price for Better use of Antibiotics, 2017, https://research-and-innovation.ec.europa.eu/funding/funding-opportunities/prizes/horizon-prizes/better-use-antibiotics_en
[67] The Standing Committee of European Doctors, CPME Position Paper on the European Commission Pharmaceutical Strategy for Europe, 2021.
[68] C. Årdal, Y. Lacotte, & M. C. Ploy, Improving access to essential antibiotics, EU-JAMRAI, 2021, https://eu-jamrai.eu/wp-content/uploads/2021/07/1.3.1_Policy_brief_Improving_access_to_essential_antibiotic.pdf
[69] European Parliamentary Research Service & Panel for the Future of Science and Technology, European pharmaceutical research and development - Could public infrastructure overcome market failures?, European Parliamentary Research Service, 2021, https://www.europarl.europa.eu/RegData/etudes/STUD/2021/697197/EPRS_STU(2021)697197_EN.pdf
[70] A. Kotwani, J. Joshi, & D. Kaloni, Pharmaceutical effluent: a critical link in the interconnected ecosystem promoting antimicrobial resistance. Environmental Science and Pollution Research, 28(25), 32111–32124, 2021, doi:10.1007/s11356-021-14178-w

a study conducted in seven European countries confirmed the presence of 17 different antibiotics in European wastewater treatment plants.[71]

Globally, pharmaceutical manufacturing and the supply chain are guided by the intention to decrease costs and maximise profits, hence environmental standards are not prioritised.[72] Governments and regulators have a role in establishing evidence-based and enforceable targets for maximum levels of the pharmaceutical ingredients discharged into the environment. The European Union should regulate pharmaceutical production and ensure compliance with rules on pharmaceutical ingredients monitoring and providing complete data to regulators. A new strategic approach to pharmaceutical pollution is needed. The European Union should consider the impact of offshore pharmaceutical manufacturing on the spread of AMR, including in imports and trade agreements.

As individual disposal of medicines plays an important role, hence a need to adequately guide patients when it comes to safe disposal of medicines.[73]

[71] S. Rodríguez-Mozaz, I. Vaz-Moreira, et al., Antibiotic residues in final effluents of European wastewater treatment plants and their impact on the aquatic environment. Environment International, 140, 105733, 2020, doi:10.1016/j.envint.2020.105733

[72] E. Topp, D. G. J. Larsson, et al., Antimicrobial resistance and the environment: assessment of advances, gaps and recommendations for agriculture, aquaculture and pharmaceutical manufacturing. FEMS Microbiology Ecology, 94(3), 2018, doi:10.1093/femsec/fix185

[73] European Medicines Agency, Guideline on the Environmental Risk Assessment of Medicinal Products for Human Use, 2006, https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-environmental-risk-assessment-medicinal-products-human-use-first-version_en.pdf