About EPHA

EPHA is a change agent – Europe’s leading NGO alliance advocating for better health. We are a dynamic member-led organisation, made up of public health civil society, patient groups, health professionals, and disease groups working together to improve health and strengthen the voice of public health in Europe.

EPHA’s work on Antimicrobial Resistance

EPHA’s work on Global Public Health focuses on the leading health concerns: antimicrobial resistance (AMR) threatens human, animal and environmental health and, if left unchecked, poses an unprecedented risk to health systems and the economy. Our work therefore strives to ensure AMR remains high on the political agenda, under a One Health approach.

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Introduction: The Global Health Burden

Antimicrobial resistance (AMR) is a global public health concern, with the World Health Organization designating it a leading health threat. The 2022 GRAM Global Burden Report calculated bacterial AMR to be associated with 4.95 million deaths in 2019, including 1.27 million attributable deaths, placing AMR as a leading cause of mortality globally. This data updates the 2016 Jim O’Neil Report, which then estimated the yearly AMR attributable deaths to be 700 000. The Global Burden Report also presented regional AMR mortality, as well as the leading pathogens associated with resistance. Within the European Union (EU)/European Economic Area (EEA), a study using data from 2015, showed bacterial AMR to be responsible for 33 000 deaths that year.

The consequences are already being felt by health services, as patients with antimicrobial resistant infections are often hospitalised for longer, require more expensive medicine courses, and are more likely to have worse health outcomes, with some infections untreatable. Vulnerable groups, such as pre-term infants and the immunocompromised, have an additional risk due to their increased susceptibility to infections generally. AMR also threatens outcomes of surgical, medical, and dental treatments, putting patients at increased danger of serious complications, including disability and death, if they acquire antimicrobial-resistant infections during the treatment process.

Compounding the situation are issues including a lack of new antimicrobial medicines being developed, due to a lack of viable market; problems of access – financially and practically; and quality of existing antimicrobials. However, the direct replacement of antimicrobials only offers a short-term solution. The establishment of long-term preventative measures, under an inter-sectoral One Health approach – considering human, animal, plant, and environmental aspects – is essential to ending the crisis.

The following overview is designed to set the scene on AMR in a concise and accessible manner for those working across health, research, and policy, as well as the public, who are seeking to broaden their knowledge on this health threat and engage in dialogue and collaboration. It presents a scientific summary on antimicrobial resistance, current surveillance efforts, recent policy developments and areas of future action, with a focus on the global and EU level.

3 The Jim O’Neil Report acknowledged that their figure may be a low estimate given the scarcity of data then available, therefore these two statistics cannot be directly compared.
Microbes, Antimicrobials and AMR

Awareness of the scientific basis of AMR is key to understanding the issue, identifying surveillance targets, and developing evidence-based policy interventions. A summary of the topic is given below.

Microbes

Microorganisms, commonly referred to as microbes, are a collective term for bacteria, viruses, fungi, and protozoa. They can be found in water, soil, and air, as well as humans, animals, and plants – either in a commensal (non-disease causing) or pathogenic (infection causing) relationship.8

Antimicrobials

Antimicrobials kill or prevent the growth of microbes, and are used to treat infections in humans, animals, and plants.9 Each type of antimicrobial affects a particular anatomical characteristic or physiological process specific to its target microbe. Antimicrobials can either be broad – targeting a commonly shared trait within a group of microbes, or narrow – affecting a trait only present in a (few) species, within a group. Antimicrobials effective against one species/group are therefore ineffective when used against another species/group that do not share the targeted trait.10

Antimicrobial Resistance (AMR)

AMR is a naturally occurring process, which arises when a pathogenic microbe – pathogen – has a genetic mutation that significantly alters an aspect of its anatomy or physiology, allowing it to evade or resist the action of an antimicrobial medicine.11 For example, antibiotic resistance, also called bacterial AMR, occurs when bacteria become resistant to antibiotic medicine.12 The resistant strain therefore survives exposure to the antibiotic, where other strains without this mutation do not. The genetic advantage can then be passed on when the resistant microbe replicates and divides itself or, in some instances, between species through horizontal gene transfer.13 An infected individual or host – human, animal, or plant – can spread their anti-microbial resistant strain to others, via direct or indirect transmission, e.g. between animals and humans by direct contact, via food products or the environment.14 In time, the resistant strain becomes the most prevalent in the species, rendering the antimicrobial medicine widely ineffective. Multidrug resistance (MDR) arises when a microbe is resistant to multiple antimicrobial medicines that are normally effective against it.15

12 Antibiotic resistance is of particular concern, as many human infections are caused by bacteria, and many medical interventions carry a risk of infection, such as surgery and chemotherapy.
Example: *Mycobacterium tuberculosis* is a species of bacteria that is spread between humans through the air and causes the disease Tuberculosis (TB), which had 10 million cases and 1.5 million related deaths in 2020.\(^{16}\) There are antibiotics that can normally target *M. tuberculosis* and cure an infection, however drug-resistant strains have developed and spread, limiting treatment options and accounting for half a million infections annually.\(^ {17}\)

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**Drivers of AMR**

Whilst AMR is a naturally occurring process, certain human activities can hasten its occurrence.\(^ {18}\) Key drivers occur across the One Health interface including inappropriate, unregulated and overuse of antimicrobials; inadequate infection prevention and control measures; poor farming husbandry, food processing, and distribution practices; inadequate sewage and waste management, including in the production and disposal of antimicrobials.

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Surveillance and Monitoring

Up-to-date data on the AMR burden is necessary for evidence-based policy decision-making to target the areas of priority, considering the risk posed to public health and limited resources available – financial budget, capacity etc. Below lists periodic global and European AMR surveillance reports.

Access to Medicines Foundation (AMF)

- Antimicrobial Resistance Benchmark annual report evaluates antimicrobial producing pharmaceutical companies for their AMR limiting initiatives, including antimicrobial research and development, manufacturing, access, and stewardship.\(^\text{19}\)

European Centre of Disease Prevention and Control (ECDC)

- Annual Epidemiological Report provides data on human antimicrobial consumption in the EU/EEA.\(^\text{20}\)
- European Antimicrobial Resistance Surveillance Network (EARS-Net) annual report collects data on invasive microbes resistant to antimicrobials in humans.\(^\text{21}\)

European Food Safety Authority (EFSA) joint with ECDC, and EMA

- Antimicrobial Consumption and Resistance in Bacteria in Human and Animals (JIACRA) report series, monitors antimicrobials in humans and food producing animals the EU/EEA.\(^\text{22}\)

European Medicines Agency (EMA)

- European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) annual report for sales of veterinary antimicrobials in European countries.\(^\text{23}\)

World Health Organization (WHO)

- Antimicrobial Resistance Surveillance in Europe report series in collaboration with ECDC, provides data on the WHO European region, including EARS-Net countries.\(^\text{24}\)
- Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR) annual report provides information on coordination and surveillance of AMR in clinical settings and includes countries in the WHO European Region that are not covered by EARS-Net.\(^\text{25}\)
- Global Database for the Tripartite AMR Country Self-assessment Survey (TrACCSS), produced by the WHO, Food and Agriculture Organization of the United Nations (FAO) and OIE, is used to track nation level progress in addressing AMR, with results made available annually.\(^\text{26}\)

World Organisation for Animal Health (OIE)

- Annual Report on Antimicrobial Agents Intended for Use in Animals offers global and regional analysis of food-producing animals.\(^\text{27}\)

\(^{19}\) https://accessstomedicinefoundation.org/amr-benchmark


\(^{22}\) https://op.europa.eu/en/publication-detail/-/publication/5b831304-0ace-11ec-adb1-01aa75ed71a1


\(^{26}\) https://www.who.int/publications/m/item/tripartite-amr-country-self-assessment-survey-tracss-2020-2021

Policy Developments

The risk of AMR to public health has seen responses at all levels of society. This section will focus on global and European (EU) level policy developments, outlining key stakeholders and publications.

Global Developments

In 2015, World Health Assembly (WHA) adopted the Global Action Plan on AMR to address antimicrobial misuse and overuse in human medicine and food production and the risk of a post-antibiotic era. The five objectives are to improve awareness, evidence-base, reduce incidence, optimise antimicrobial use, and develop sustainable medical interventions.

A formal Tripartite partnership between the WHO, FAO, and OIE was made in 2018, to address AMR in a coordinated One Health approach, and published their Monitoring and Evaluation Report of the Global Action Plan the following year. The Tripartite became a Quadripartite in 2022, with the inclusion of the United Nations Environment Programme (UNEP), with a collective goal to “preserve antimicrobial efficacy and ensure sustainable and equitable access to antimicrobials for responsible and prudent use in human, animal and plant health.” In the same year, the UNEP published the Environmental Dimensions of AMR Report, with a focus on pollutants and a call to strengthen environmental action.

An ad hoc interagency coordination group (IACG) on AMR, comprised of representatives from the then Tripartite partnership, produced the No Time To Wait Report in 2019. At the request of UN member states, this document made a list of recommendations to respond to the global threat of AMR. One recommendation realised is the formation of the Global Leaders Group on AMR (GLG). This group brings together heads of state, current or former ministers and governmental officials, and intersectoral – foundations, civil society and private – experts in an advisory and advocacy role, working to promote political action on AMR. GLG’s AMR Priorities include sustained political action, transformation in all One Health areas, improved surveillance and monitoring, increased mobilisation of financial resources, increased medical innovation, and a better understanding of the role of the environment in transmission, and supports the mandates of the now Quadripartite.

Internationally, in 2021, G7 finance ministers agreed on Actions to Support Antibiotic Development. This saw a political commitment to prioritise their own national AMR Action Plans as well as help strengthen antibiotic research and development, to bring new drugs to market.

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European (EU) Developments

The European Commission (EC) adopted the One Health Action Plan against AMR in 2017, building upon the 2011 Action Plan and 2016 Council Conclusions on the Next Steps under a One Health Approach. Bi-yearly Progress Reports have since followed. The objectives were to make the EU a best practice region, including assisting Member States in the development of National Action Plans (NAPs), as agreed upon in the 2015 WHA; improve research, development, and innovation; and shape the global agenda. Political decisions that directly affect human health are predominantly the remit of Member States, therefore NAPs are essential to ensure AMR measures in this area.

EU policy developments on AMR have included the 2019 Strategic Approach to Pharmaceuticals in the Environment to address the potential impact of pharmaceuticals at all stages of their lifecycle on the environment. The 2020 Pharmaceutical Strategy indicates plans for AMR policy development around procurement of antimicrobials and their alternatives. In the same year, an Implementing Decision on Monitoring and Yearly Reporting of AMR in zoonotic (transferrable between animals and humans) and commensal bacteria was mandated for Member States. The adoption of the 2020 Farm to Fork Strategy had as its objective to reduce antimicrobial sales by 50% in animal farming and aquaculture by 2030. This was supported by two regulations on Veterinary Medicinal Products and Medicated Feed that came into force in 2022, which included data collection on antibiotic use in animal agriculture in Member States and foresees a list of antibiotics to be reserved for human use only. These two regulations also have implications for third countries, where animal-derived food products are being imported into the EU, including the banning of antibiotics being used as growth promoters and compliance with the list of reserved antibiotics.

During the 2022 One Health Ministerial Conference on AMR, the presidency trio of France, the Czech Republic and Sweden published a Declaration on AMR, indicating it as a continuing priority for their respective presidencies of the European Council, until June 2023. Participants at this event also included the ECDC, EFSA, WHO, FAO, OIE, and heads of EU Member State NAPs.

Areas for Future Action

The current burden of AMR and future implications on global public health, if not properly and timely addressed, are well established in literature. Surveillance and policy developments are underway, but there still remain gaps requiring attention, as well as emerging concerns that need to be considered to ensure AMR is addressed holistically. Below highlights areas for future action.

Surveillance Opportunities

One Health surveillance is necessary to prevent AMR build up in one area, which can in turn transmit to others.\(^48\) AMR surveillance systems and reporting for human and animal antimicrobial consumption are now established, though there are national and regional variances in implementation. However, surveillance of antimicrobial use in crops and AMR environmental monitoring are not yet at the same level.\(^49\) FAO’s plans for an AMR Monitoring (InFARM) System\(^50\) that presents global data on AMR in food and agriculture, including antimicrobial use in crop production, is a promising development. Environmentally, expansion of AMF’s antimicrobial production surveillance initiative and the development of standardised and systematic antimicrobial sewage and waste disposal surveillance at antimicrobial production plants, as well as at clinical, agri- and aquacultural sites would also assist in understanding the full scope and spread of AMR.\(^51\)

Regional surveillance is required, especially targeting areas where AMR burden is greatest. The Fleming Fund, a UK aid programme, is supporting AMR surveillance capacity building throughout Africa and Asia, utilising WHO’s Global Antimicrobial Resistance Surveillance System\(^52\) (GLASS). However, more international support and partnerships would ensure that such projects achieve their implementation, reach, output, and sustainability.

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Policy Opportunities

Addressing AMR drivers in a One Health approach: the 2021 G7 summit highlighted policy areas requiring development in human health, including education, infection control, appropriate antibiotic use and developing common indicators.53 Recent EU agricultural policy developments revolve around preventing inappropriate antimicrobial use, yet concerns have been raised regarding their effectiveness, given the widespread presence of high intensive livestock farming systems that sees excessive use of antibiotics.54 That said, the EC has committed to revising current animal welfare legislation by the end of 2023, regarding the keeping, transport and slaughter of agricultural animals.55 In light of the apparent lack of environmental surveillance initiatives and data currently available, policy developments for sewage and waste management throughout the antimicrobials life-cycle, from production to its use in human, animal and crops, also appears awaiting development.56

Emerging global public health issues: the COVID-19 pandemic has stimulated political attention regarding the need for robust frameworks to effectively respond, coordinate and manage global public health crises, as well as prevent future occurrences. These policy developments have seen initial discussions to involve AMR, including the development of a WHO-led international pandemic prevention, preparedness and response initiative,57 with the Global Leaders Group on AMR already signalling the need for AMR to be explicitly considered.58 At the EU level, the creation of the Health Emergency Response Authority (HERA)59 to respond to future health crises, has seen preparatory activity including tendering an AMR medical countermeasures study.60 Additionally, initial effects of COVID-19 on AMR drivers have already been observed, therefore, any wider pandemic countermeasures have the potential to co-benefit AMR.61

Research, development, and production of medical interventions is essential to protect population health, thereby providing an additional line of defence. These areas sees increasing policy interest, with new incentive models being proposed and trailed to stimulate pharmaceutical company engagement. Attention to other medical products, such as vaccinations, or rapid diagnostic tests is also necessary, new incentive models being proposed and trailed to stimulate pharmaceutical company engagement. Research, development, and production to co-benefit AMR.

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Professional user engagement is important in the decision-making process to ensure awareness and understanding of the issue, policy relevance and, in turn, implementation success. European level policy-making process currently allows for input through public consultations; however, this method tends to favor already aware and politically engaged professionals. Other avenues to develop interest and opportunities for continuous collaboration in policy development, realizing the expertise that health professionals, veterinarians, agri- and aquacultural farmers can provide, would help strengthen AMR policy, as well as encourage adherence.

Civil society engagement is invaluable to policy development as it can provide a collective voice for public, animal and/or environmental health. Moves to engage beyond public consultations sees the EC chaired EU AMR One Health Network, traditionally consisting of Commission experts, EU agencies, public and animal health representatives from Members States, planning to expand to include civil society organisations. Similar permanent developments at the global level could also prove beneficial to policy development. 63

Conclusions

Multiple areas still require attention in order to overcome the AMR public health crisis, including ensuring global surveillance coverage in all aspects of One Health; addressing every driver sufficiently, with attention given to the compounding effect of other global public health issues; supporting the research and development of both short- and long-term medical interventions; and developing further avenues for professional and civil society policy involvement.
