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Antimicrobial resistance (AMR): the loss of a major defence to the emerging challenge?

Executive summary

- Following the resolution on antimicrobial resistance (AMR) endorsed by the 39th Session of the FAO Conference in June 2015, FAO discussed progress on AMR activities at the 25th Session of the Committee on Agriculture (FAO. 2016a) An FAO Action Plan on AMR was adopted (FAO. 2016b). A thematic webpage on AMR gives an oversight of recent publications and activities.¹
- The potential impact of AMR on food security, nutrition and human health in general, is threatening the realization of FAO cross-cutting strategic objectives and several of the Sustainable Development Goals (for example 2, 3, 14 and 15).
- Drugs that defend livestock against infectious diseases are becoming less effective, due to growing AMR, thus compromising our ability to treat diseases. Increased antibiotic use in agriculture, particularly in intensive systems, is a contributor to AMR. Antimicrobial/antibiotic-resistant infections need to be limited through monitoring programmes, awareness-raising campaigns, altered management practices, optimal biosafety/biosecurity and the search for alternative medicines.
- Any AMR action plan must encompass prevention of infectious diseases (e.g. strengthening biosecurity, use of vaccination and improved husbandry), and the responsible usage of effective, safe and quality-assured drugs, avoiding their use as growth promoters or prophylactic treatments. Slowing the progression of AMR is a challenge which will require a One Health approach through cooperation between governments and organizations: stakeholders in industry; and ministries for public health, animal health and agriculture, resulting in policy changes and improved governance.

¹ www.fao.org/antimicrobial-resistance/en/



- Positive statements on tackling AMR have been delivered in the last two years by FAO as well as other international organizations (OIE, WHO), and the FAO Action Plan on AMR was adopted in 2015. FAO's Regional Office for Europe and Central Asia (REU) plays an active role in developing an AMR technical programme for the region and assists REU member countries in developing national action plans through normative and trust fund activities.

Guidance sought

The ECA is invited to:

- Endorse the policy recommendations for members as outlined in paragraph 18.
- Endorse the policy recommendations to FAO as outlined in paragraph 19.

I. Introduction

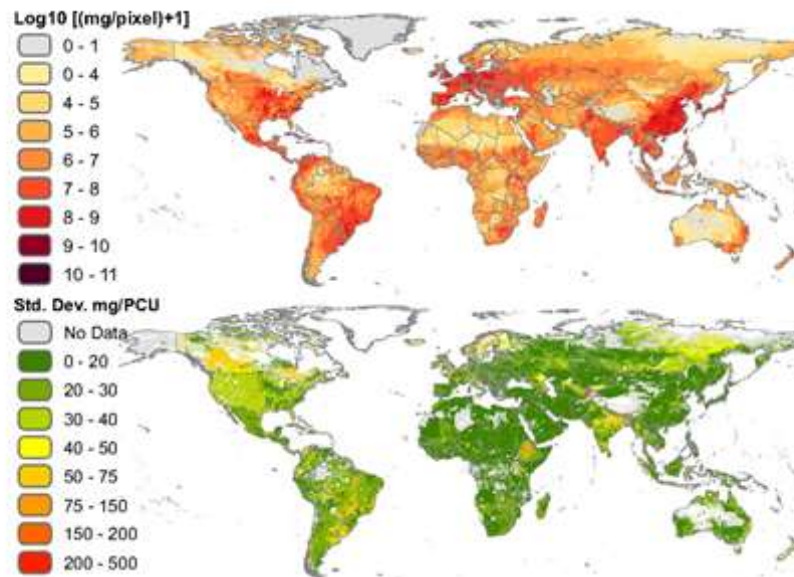
1. AMR occurs due to a combination of factors which may be driven by excessive and inappropriate use of antimicrobial drugs in humans and animals and poor hygiene or infection control practices, thus transforming AMR into a serious global threat with a heavy economic cost.

2. AMR is already associated with an estimated 700 000 human fatalities annually worldwide. Inaction is projected to cause millions of global deaths yearly and, by 2050, drug-resistant infections could cause global economic damage on a par with the 2008 financial crisis (World Bank, 2016).

3. The O'Neill report was commissioned in 2014 by the British Prime Minister and supported by the Wellcome Trust, in the light of positive statements from FAO, WHO and OIE, to make recommendations for actions to tackle AMR globally. It includes several papers on the economic impact of AMR, areas for immediate action against the slow rise in drug resistance, developing new antibiotic drugs for the future, improving diagnostics, the use of antibiotics in agriculture and the environment (O'Neill, 2015; O'Neill, 2016).

4. Estimates of total annual global antibiotic consumption in agriculture vary considerably, due to poor surveillance and data collection in many countries, ranging from 63 000 to over 240 000 tonnes. Only 42 countries in the world collect data on use of antimicrobials in agriculture (FAO, 2016b). Global consumption of antibiotics in agriculture is estimated to increase by 67 percent from 2010 to 2030, and consumption of antibiotics in Brazil, Russia, India, China and South Africa (BRICS) will increase by 99 percent in that same time period. Antimicrobial use in the intensively farmed pig and poultry sector is expected to double. The following figure is taken from Van Boeckel et al., 2015.

Figure 1. Global antimicrobial consumption in livestock in milligrams per 10km² pixels (Top) and average SD of estimates of milligrams per PCU (Bottom)

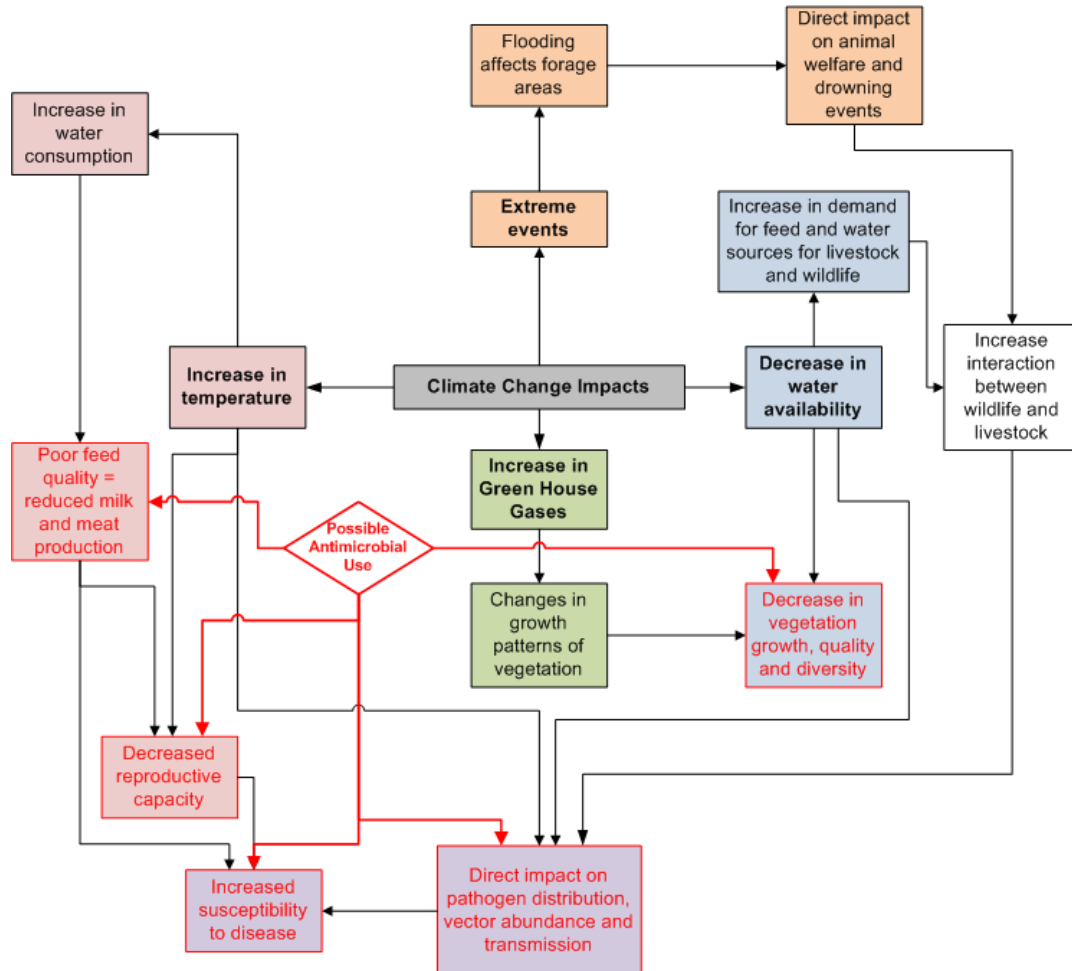


Source: Thomas P. Van Boeckel et al. PNAS 2015; 112:5649-5654

5. The proportion of antibiotics used in livestock compared with humans is unsurprisingly substantially greater. Some publications estimate that more than 70 percent of antibiotics deemed medically important for human health by the US Food and Drug Administration (FDA) sold in the United States (and over 50 percent in most countries of the world) is used for livestock. The most controversial use of these antibiotics is for growth promotion, because they do not serve to maintain the health of the livestock. As with any antibiotic use, it increases the chances that resistant bacteria will develop.
6. Resistance to antiparasitic agents for certain zoonotic parasites has also become a major problem. Antiparasitic agents play an important role in agriculture, and would be difficult to replace.
7. Scientific studies suggest that 75-90 percent of tested antibiotics are excreted un-metabolized by animals and humans and enter sewage systems and water sources. Therefore, animal waste may contain resistant bacteria, but also antibiotics.
8. The World Bank estimates that by 2050, using a high likelihood scenario of antimicrobial resistance (AMR) - whereby antibiotics and other antimicrobial drugs no longer effectively treat infections - could cause low-income countries to lose more than 5 percent of their gross domestic product (GDP) and push as many as 28 million people, mostly in developing countries, into extreme poverty (World Bank, 2016). There would be no prospects for recovery in the medium term because the costly impact of AMR would persist. Since these GDP losses are annual and thus compound over time, they result in a cumulative loss that ranges between USD 2.1 trillion and USD 124.5 trillion.
9. Global warming and the spread of antimicrobial resistance are both important topics in their own right, but the potential impact of changes in climate and the environment on the development and spread of antimicrobial resistance is not well understood. There is a lack of evidence currently to directly link the drivers of increasing temperatures and changing precipitation to AMR. The links will come from increasing infectious disease prevalence thereby increasing the need for antimicrobials, antifungal and antiparasitic drugs.
10. For example, there is a strong link between wetter climates, fungicide use (azole-based therapies) and rise in fungicide resistance (O'Neill, 2015). Indeed, if the drivers for climate change

impacts are examined, there are clear areas where AMR can arise. The following figure is adapted from Rojas-Downing, et al., 2017, which shows the interconnection between temperature and the critical factors for livestock production, such as water availability, animal production, reproduction and health and for crops/feed or forage quantity and quality which may also be affected by variations in availability of carbon dioxide and precipitation. The figure has been adapted to include the areas where antimicrobial use would also come into play.

Figure 2: Impacts of climate change on livestock production factors



Source: Rojas-Downing et al. 2017.

11. As a result of climate change new transboundary zoonotic diseases will reach Europe, and the medicines to defend food systems against diseases are becoming less effective due to growing resistance. Changes in vector, pathogen and host distribution patterns will most likely create a growing demand for medicines and create more risks for AMR.

12. Drug-resistant infections need more emphasis in monitoring programmes, awareness-raising campaigns, good practices to improve biosafety/biosecurity and the search for alternative medicines.

13. There is a need for a One Health approach and close cooperation at national and regional levels between human health and the agricultural sector, and on a Tripartite level between WHO, OIE and FAO. In this regard, WHO/FAO/OIE organized jointly a subregional meeting in Kyrgyzstan, in June 2017, to support Central Asian countries in developing AMR national action plans.

Barriers and evidence gaps

14. However, there are major challenges and barriers to developing effective AMR strategies. For Europe and Central Asia the main issues include the following:

- 1) There is a need to involve stakeholders at every level – farmers, veterinarians, food producers, the pharmaceutical industry and governments, in terms of managing prescribed antimicrobials, ensuring their appropriate use and developing and authorizing new agents.
- 2) There needs to be an understanding and prioritization process on which diseases are priorities and those which may be susceptible to climate change. A One Health approach needs to be then adopted to ensure that TAD control, climate change and AMR are tackled in an integrated way.
- 3) There needs to be improved prevention and diagnosis of all diseases – prevention not cure – to obviate the need for antimicrobial treatments. There is a need for focus on control of other endemic production diseases, for instance managing mastitis, vaccinating against infectious bovine rhinotracheitis (IBR) or controlling parasitic gastroenteritis (Skuce, et al., 2016).
- 4) There are serious gaps in information and data on the usage patterns of antimicrobials and the current patterns of drug-resistant infections in livestock, and the role of the environment in the spread of resistant pathogens or antimicrobials.
- 5) There needs to be consensus on how to monitor antimicrobial use and to create an advisory platform for reducing the use of antimicrobials, while avoiding any consumer confidence problems or trade issues.
- 6) How climate change will effect AMR is still poorly understood and there is still a lack of understanding on the pressure on livestock populations and who is best placed to monitor the use of antimicrobials at country and regional levels.

FAO REU's role

15. The FAO Regional Office for Europe and Central Asia (REU), from the beginning, has been involved in strategizing and drafting the FAO Action Plan on AMR and actively participates in weekly meetings of the AMR Working Group of FAO. An AMR technical programme, funded by the Russian Federation is coordinated by the FAO Regional Office for Europe.

16. FAO assists countries in a multisectoral approach and in developing and implementing their national action plans on AMR.

17. FAO is developing supporting tools such as ATLASS (a tool to assess laboratory work on AMR) and a progressive management pathway on AMR.

Recommendations for members

18. The ECA is invited to recommend that members actively participate in the following actions:

- 1) **Raise awareness** on TADs, climate change and AMR and promote behavioural change through public communication programmes that target different audiences in human health, animal health, the agricultural sector, as well as consumers. Promote the inclusion of AMR as a core component of professional education, training, certification, continuing education and development in the public and veterinary health sectors and agricultural practice.
- 2) **Improve** surveillance and monitoring, including data on incidence, prevalence and trends, to better understand and respond to AMR patterns and their drivers. There are significant gaps in the information available on the development and global economic implications of

antimicrobial resistance. National governments, intergovernmental organizations, agencies, professional organizations, non-governmental organizations, industry and academia should pursue research on the causes and impacts of AMR. Global emphasis on surveillance and evidence-based research will inform policies and actions that REU member countries and intergovernmental agencies can take to address the growing health security challenges of AMR. In addition, more information on AMR can assist research and development of medical and agricultural alternatives to antimicrobials.

- 3) **Strengthen** governance for stronger hygiene and infection prevention measures, including animal vaccination, which limit the spread of resistant micro-organisms and reduce antimicrobial misuse and overuse. Infection prevention measures, such as cleaning and disinfection, farm biosecurity, improved husbandry practices and vaccination, can curtail the spread of micro-organisms resistant to antimicrobial medicines. By preventing infectious diseases, whose treatment would (wrongly) trigger the prescription of antibiotic medicines to treat viral infections, the global community can better steward these essential medicines. Sustainable antimicrobial use extends beyond human well-being to animal production. Antibiotics are frequently used to stimulate livestock growth and prevent infection on farms and in slaughterhouses. Sustainable animal husbandry practices can reduce the risk of resistant bacteria spreading through the food chain to livestock and humans.
- 4) **Promote** good practices to increase the longevity and efficacy of antimicrobials. Veterinary practices must eliminate unnecessary dispensing of antimicrobials. Evidence-based prescribing through effective, rapid, low-cost diagnostic tools are needed to optimize the use of antimicrobials for humans and animals. In addition to better prescribing practices, the global community must adjust patients' and the agricultural industry's inappropriate and unregulated use of antimicrobial agents. Stronger compliance with antibiotic treatment regimes and restrictions on non-therapeutic use of antibiotics within agriculture will provide a foundation for antimicrobial stewardship. Regulations for antibiotic distribution, quality, and use could preserve the effectiveness of antibiotics as a public good. Sharing best practices in the prudent use of antibiotics in both intensive and extensive livestock production systems by EU countries. Exploring approaches for reducing antimicrobial use in livestock which often feature in intensive livestock systems (FAO, 2016a).
- 5) To better understand the level of use of antimicrobials in the region, **improve** data collection and sharing on levels of imports and exports and use across the various sectors.
- 6) **Invest** in research and development (R&D) on new antimicrobial medicines, diagnostic tools, vaccines and alternative interventions. The majority of pharmaceutical companies is located in the region; however they no longer carry out research on new antibiotics; this is of concern globally for human and animal health. R&D is therefore needed to produce new treatments that can be deployed against multidrug-resistant infections and governments should promote the development and production of affordable and accessible new drugs, diagnostic tools, vaccines, and alternatives.

Recommendations for FAO REU

19. The ECA is invited to recommend that FAO and other organizations actively participate in the following actions:

- 1) **Reinforce** AMR regional interventions through new dedicated results under the new 2018-2019 work plans for REU's Strategic Programme of Work, including its regional initiatives.
- 2) **Support** member countries in developing a multisectoral approach and in implementing national action plans on AMR.

- 3) In Europe and Central Asia, **create** mechanisms and models of cooperation between animal production, pharmaceutical companies, the animal feed sector and farmer organizations to address AMR.
- 4) Continue to support the development and use of tools such as ATLASS and the progressive management pathway on AMR.
- 5) Coordinate a study, possibly in cooperation with WHO and OIE, on the potential impacts of changes in climate and the environment, in particular in Europe and Central Asia, on the development and spread of antimicrobial resistance to improve the understanding of these interactions.
- 6) Continue support in the engagement of the private sector and find models to cooperate with different stakeholders, including veterinary and public health authorities, livestock producers, pharmaceutical companies, the animal feed sector and consumer and farmer organizations.
- 7) Develop a strong mobilization exercise to enhance responses to slow down the development of AMR.

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