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To give or not to give an antibiotic: the threat of antimicrobial resistance.

TONNA, A.

2024

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To give or not to give an antibiotic The threat of antimicrobial resistance

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1st October 2024

**EUROPEAN COMMITTEE ON PHARMACEUTICALS
AND PHARMACEUTICAL CARE**



As early as 1945, Sir Alexander Fleming raised the alarm regarding antibiotic overuse when he warned that the “public will demand [the drug and] ... then will begin an era ... of abuses.”

Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. P T. 2015

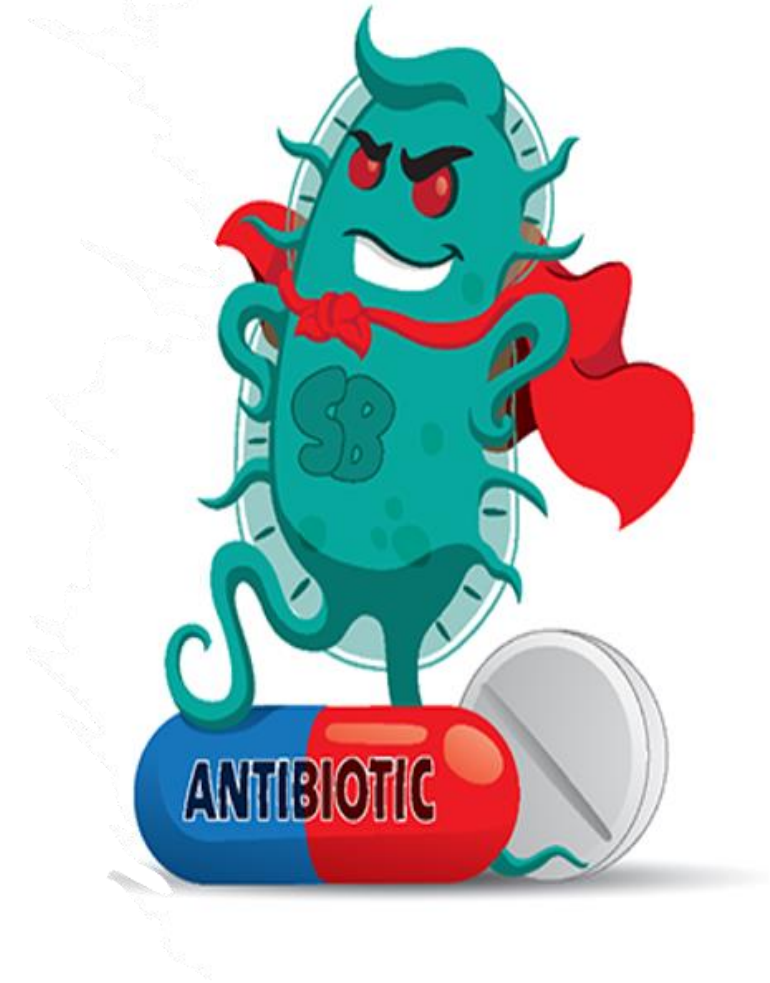
Apr;40(4):277-83. PMID: 25859123; PMCID: PMC4378521

Some glossary to start off with

- An **antimicrobial** is a drug that acts against a virus, fungus or bacteria and either stops its growth (static) or kills the microorganism (cidal).
- Antimicrobials are used in human health, in animal husbandry and to manage crop production – hence the concept of One Health.
- The WHO defines **antimicrobial resistance (AMR)** as occurring
*“when bacteria, viruses, fungi and parasites change over time and no longer respond to medicines making infections harder to treat and increasing the risk of disease spread, severe illness and death.”*¹

¹ <https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance>

- Consequently, resistant organisms can grow, thrive and replicate in the presence of antimicrobials.
- Concern: AMR leads to diseases that are more difficult to treat, sometimes being resistant to more than one antimicrobial [multidrug resistant (MDR); superbugs] or to no antimicrobials [pandrug resistant (PDR)].
- Examples of these include *C difficile* infection, MRSA (Meticillin resistant *Staphylococcus aureus*) and multidrug resistant tuberculosis (MDR TB)
- Inappropriate use of antimicrobials is a key cause of development of AMR



What constitutes inappropriate use of antimicrobials?

Keeping in mind that
around 80% of human
antibiotic consumption is
within the community

Within a **community** inappropriate use of antimicrobials includes:

- Antimicrobials prescribed by a healthcare professional when unnecessary (e.g. for viral infections such as sore throat)
- Use of antimicrobials for self-medication and/or medication of family members without prescription e.g. using leftover antimicrobials prescribed for another purpose
- Obtaining antimicrobials bought without a prescription including availability of purchase online
- In lower income countries, availability of low-quality grade pharmaceuticals including antimicrobials
- The only pharmaceutical class where inappropriate use has individual patient consequences, and community and global consequences





CONSEQUENCES OF INAPPROPRIATE USE OF ANTIBIOTICS

Inappropriate use of antimicrobials is recognized by international organizations such as the WHO, UN and the EU and is likely to disproportionately affect the most clinically and socially vulnerable in the society.

It may lead to among other things:

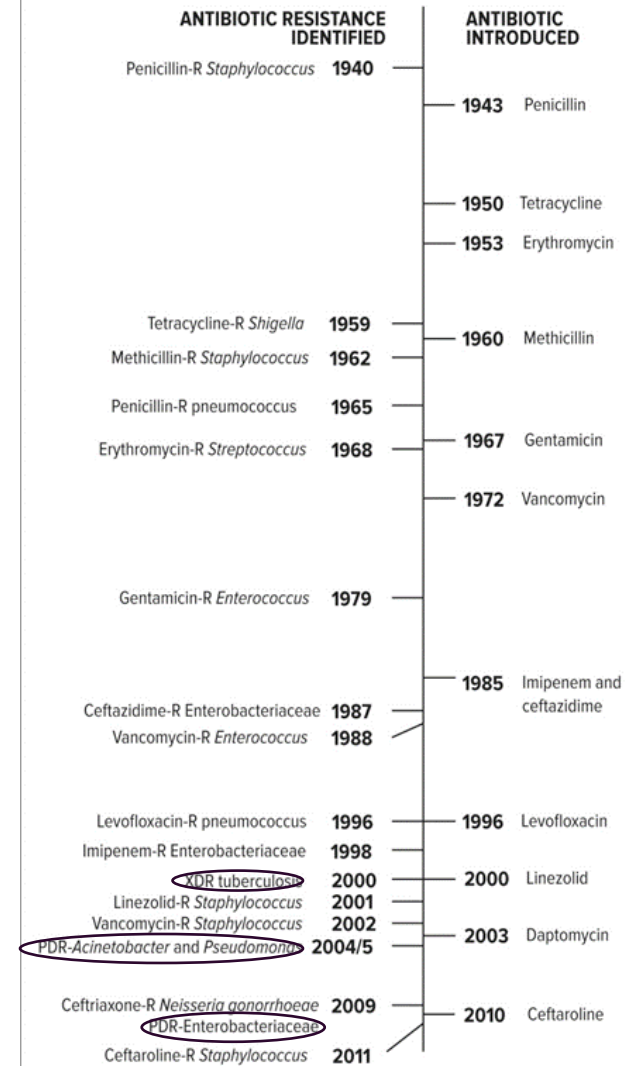
- Antimicrobial resistance (AMR) [potentially the most important in terms of impact]
- Excessive use of plastics when intravenous antimicrobials are administered unnecessarily
- Adverse environmental effects due to the manufacture and transport of antimicrobials or the inappropriate disposal of antimicrobials

Some more glossary:

MDR : multidrug resistant
XDR : extensive drug resistant
PDR : pandrug resistant

Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. P T. 2015 Apr;40(4):277-83. PMID: 25859123; PMCID: PMC4378521.

Figure 1 Developing Antibiotic Resistance: A Timeline of Key Events⁵



PDR = pan-drug-resistant; R = resistant; XDR = extensively drug-resistant

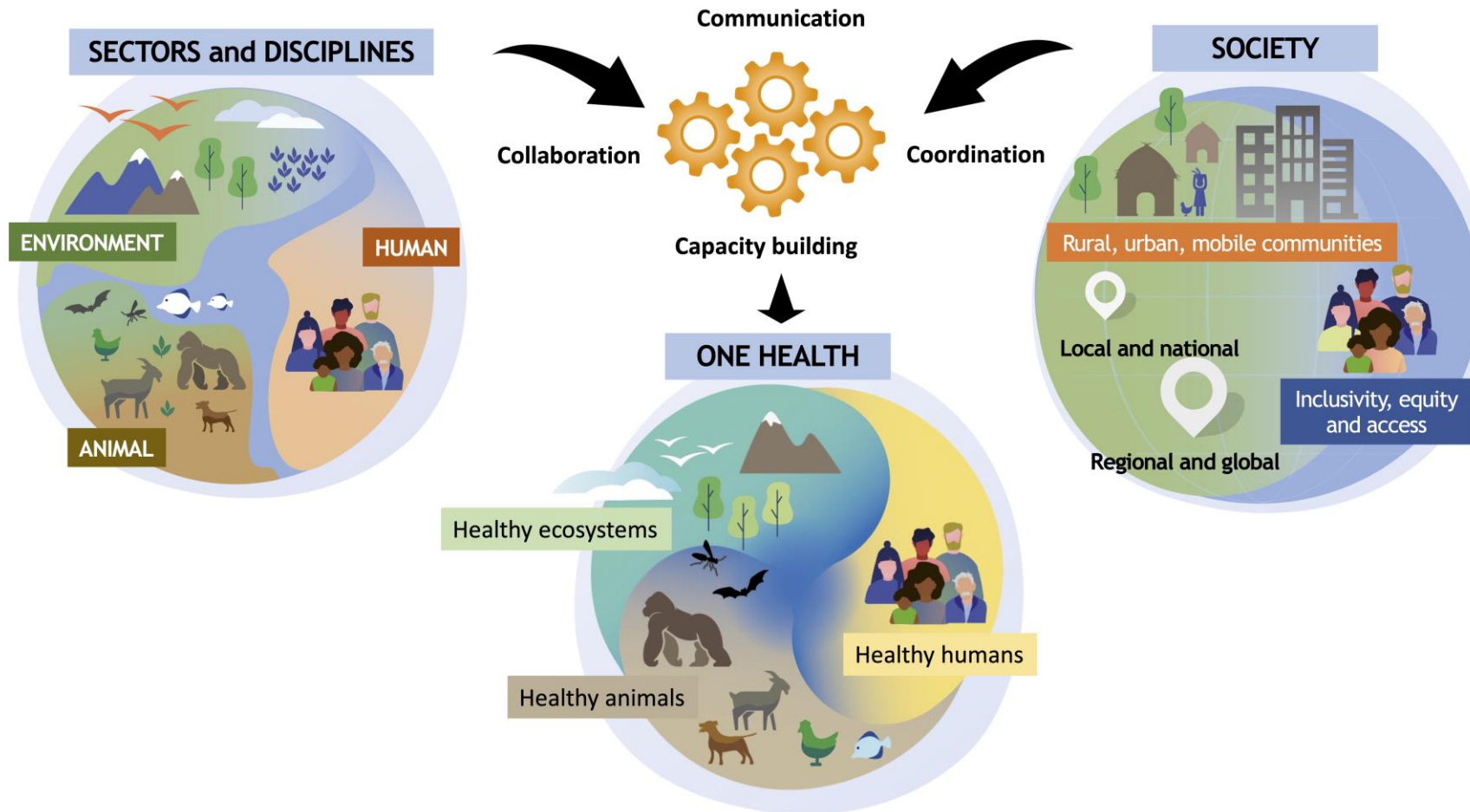
Dates are based upon early reports of resistance in the literature. In the case of pan-drug-resistant *Acinetobacter* and *Pseudomonas*, the date is based upon reports of health care transmission or outbreaks. Note: penicillin was in limited use prior to widespread population usage in 1943.

Putting the consequences of antimicrobial resistance into context

- Approximately 5 million deaths worldwide are associated with AMR, that is more than TB, HIV and malaria combined
- AMR disproportionately affects those most vulnerable in society – e.g. immunosuppressed, children under 5 years of age
- If not tackled, the world may be on the precipice of a “pre-antibiotic” era and no antibiotic or vaccine will be left to cure infection
- The World Bank estimates that by 2050, *“going unchecked AMR could wipe away 3.8 % of global gross domestic product each year and push 28 million people into poverty.”*
- On a patient individual level, there are numerous economical and social consequences e.g. the patient is longer in hospital, cannot attend work etc...
- In response to this ... various global and national initiatives with One Health at the heart of their strategy

One Health

The WHO defines One Health as *“an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals and ecosystems.”²*



² https://www.who.int/health-topics/one-health#tab=tab_1

One Health implies that AMR may spread very rapidly

- It is driven by interconnected factors involving people, animals, plants and ecosystems such as food production and water and sanitation.
- This implies that the pathways to AMR are complex and likely to be multifaceted.
- Misuse and overuse may occur in different sectors including health.
- Since it is so complex it is unlikely for a single intervention to cover all sectors.
- Single-sector interventions are potentially more feasible and are shown to still have an impact – for example European Antimicrobial Resistance Surveillance Network (EARS-Net); initiatives at a local level

UN Sustainability Development Goals (SDGs)

- ❖ SDGs adopted by world leaders in September 2015
- ❖ Made up of 17 goals and 169 domains with an aim to achieve these goals by 2030
- ❖ An implementation progress is published annually
- ❖ Unfortunately, progress has not been as rapidly as projected and in some cases, progress has stalled or gone backwards following the COVID-19 pandemic

SUSTAINABLE DEVELOPMENT GOALS



9 December 2021

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Antimicrobial Resistance Threatens Development, SDGs: Tripartite Report



UN Photo/JC McIlwaine

STORY HIGHLIGHTS

- > Antimicrobial resistance could have significant effects on a range of SDGs, according to guidance published by the World Health Organization and other members of the AMR Tripartite.
- > For example, as AMR increases, treatment costs, universal health coverage will be unattainable for many countries.
- > The publication makes recommendations for UN country teams to address this interlinked threat through the UN Sustainable Development Cooperation Framework.

Tracking antimicrobial resistance in the Sustainable Development Goals

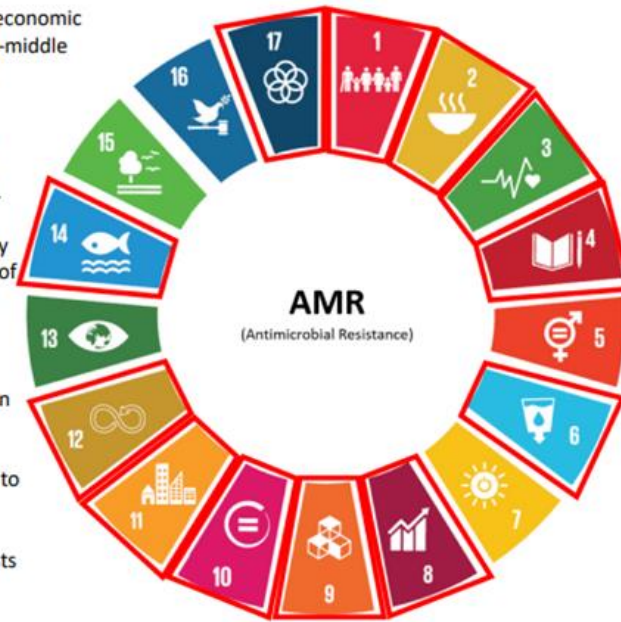
5 Ways Antibiotic Resistance Disrupts the Sustainable Development Goals



stopAMR | Choose Life Over Antibiotic Abuse



- 1 NO POVERTY**
If no action is taken in addressing AMR, the global economic cost by 2050 will be US\$ 100 trillion, impacting low-middle countries the most, widening the inequity gap. (1)
- 2 ZERO HUNGER**
Misuse of veterinarian medicine in animals leads to additional use of other medicines, accumulating in ground water, land, humans, and back into animals. However, as agricultural pathogens become more resistant, we will not be able to ensure food security for our exponentially growing population. Taxation of antibiotics can push farmers to seek alternatives to their current practices. (1, 2, 3)
- 3 GOOD HEALTH AND WELL-BEING**
By 2050, 300 million individuals will die of AMR. Today, it is estimated that more than 30,000 women giving birth and 200,000 newborns die each year because of severe infections that are resistant to available drugs. Moreover, AMR is a huge threat to cancer treatment as antibiotics may no longer be effective. In the EU alone annually, it is estimated that AMR costs €1.5 billion a year in health care costs and productivity losses. (1)
- 4 QUALITY EDUCATION**
Unless AMR is introduced in all school curricula, particularly for health care professionals to promote sustainable development, the rapidly growing number of people dying of AMR will not be reduced. (4)
- 6 CLEAN WATER AND SANITATION**
Pharmaceutical and microbial hazard waste can reach and contaminate groundwater, drinking-water, soils, food crops and sediments. These potentially have serious environmental effects, including toxicity to wildlife and the generation of antibiotic-resistant bacteria. (1, 5)
- 8 DECENT WORK AND ECONOMIC GROWTH**
The cost of drug-resistant infections is estimated to cause a decrease in economic output of US\$ 1-3 trillion. (1)



- 9 INDUSTRY, INNOVATION AND INFRASTRUCTURE**
Current authorization guidelines, such as those in the EU, tend to favour existing products, such as antibiotics or chemical pesticides. They at the same time create significant barriers for the development of alternatives in human health, meat production and agriculture. This obstructs SMEs to innovate and compete on a global market dominated by the antibiotic producing and distributing pharmaceutical industry. (6, 7, 8)
- 10 REDUCED INEQUALITIES**
AMR affects all countries, but the burden is disproportionately higher in LMICs. Inadequate access to safe water and sanitation adds to the emergence and spread of drug resistance and is a key challenge for LMICs. Therefore, most of the direct and indirect impact of AMR will fall on LMICs if clinicians and veterinarians do not prescribe antibiotics when they are not needed. (9)
- 11 SUSTAINABLE CITIES AND COMMUNITIES**
The cheap production of APIs (active pharmaceutical ingredients) particularly in China and India, contaminates local communities' natural resources. Importation of such APIs, in for instance the EU, robs the EU of drug independence and puts populations in emerging economies at serious risk. (10)
- 12 RESPONSIBLE CONSUMPTION AND PRODUCTION**
Global consumption of antimicrobials in food and animal production is estimated to rise by 70% by 2030. Instead of reduction, the use of antibiotics in agriculture is expected to rise by 67% according to the World Bank, due to the increasing demand for meat. (1, 11)
- 14 LIFE BELOW WATER**
The overuse of antibiotics in fish farming results in the presence of many infectious drug-resistant pathogens. For instance, experiments on aquaculture found that farmed fish pathogens are resistant to up to 15 drugs. (12)
- 17 PARTNERSHIPS FOR THE GOALS**
The EU Commission's Scientific Steering Committee in 1999 advised the immediate reduction in production and distribution of antibiotics, in order to prevent a future AMR catastrophe. No body heeded that advice, leading to then-WHO DG Margaret Chan to warn in 2012 about the rapidly dawning post-antibiotic era, which would disable curing of infections and disallow surgical operations. New partnerships are required to ensure the development and production of new antibiotics while securing limited use only. (13, 14, 15)



UN General Assembly High-Level Meeting on antimicrobial resistance 2024

26 September 2024 10:00 – 18:00 ET

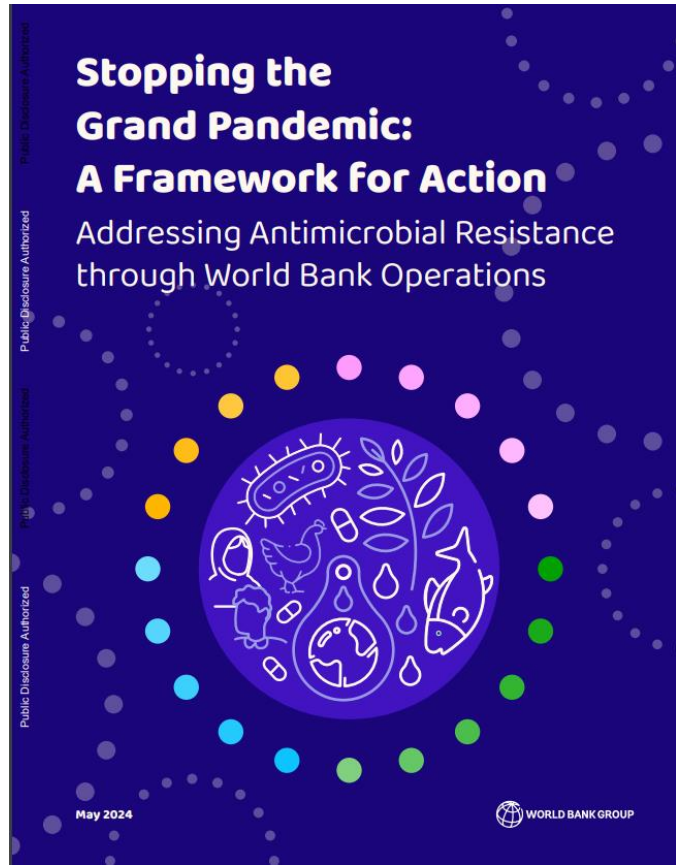
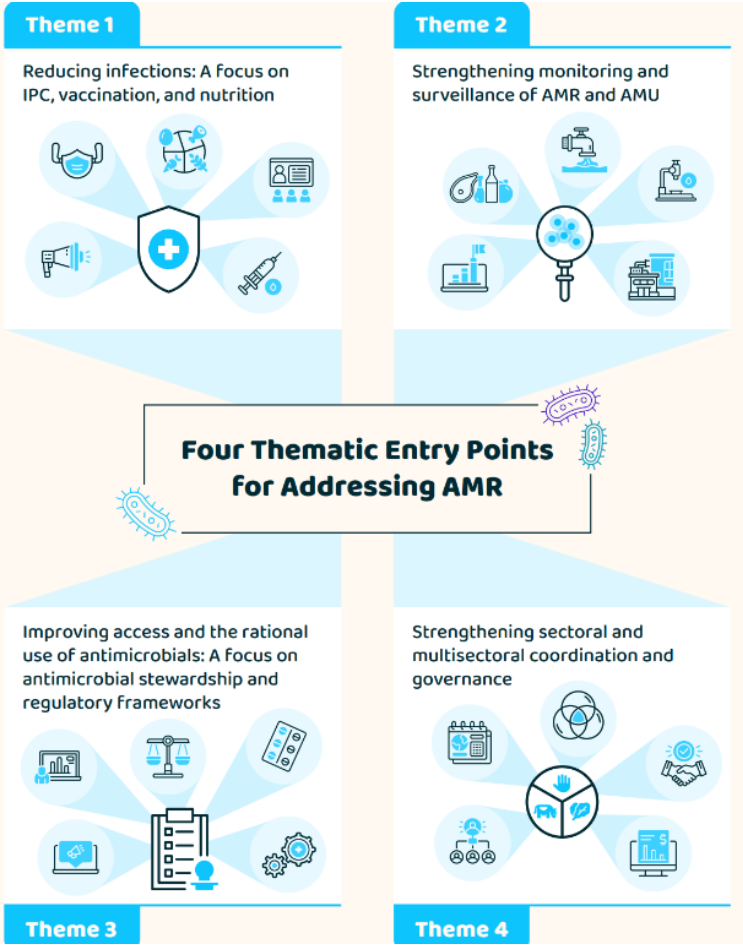
Related

The aim leading up to the meeting will be to draft, and then agree on, a political declaration on AMR, possibly linked to high level targets that can be used globally.

This meeting is an important opportunity for world leaders to collectively address the looming threat AMR poses to global health, food security, and achieving the 2030 Sustainable Development Goals.

In preparation for this meeting, various organisations have been invited to put forward their preferred policy options to tackle AMR

The 20 intervention areas recommended by the World Bank derived following a global literature review and based on AMR “drivers”



- | | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>Health</p> <ol style="list-style-type: none"> 1 Improving infection prevention and control in health care settings 2 Improving prescribing practices through guidelines for health care workers 3 Conducting public awareness campaigns 4 Increasing human health laboratory capacity and access to diagnostics 5 Strengthening surveillance of antimicrobial use (AMU) and AMR in human populations | <p>Water and environment</p> <ol style="list-style-type: none"> 12 Improving infrastructure to provide access to water and sanitation in health care centers 13 Implementing effective treatment and disposal of sewage and wastewater 14 Improving waste management practices in agricultural and aquaculture production/processing 15 Improving safe disposal of unused antimicrobials 16 Monitoring presence of antimicrobial residues and antibiotic-resistant bacteria and genes in water and sanitation systems |
| <p>Agriculture and food</p> <ol style="list-style-type: none"> 6 Increasing oversight of AMU by veterinarians 7 Monitoring AMU, surveillance of AMR, and increasing oversight in plant/crop production 8 Improving animal husbandry practice and biosecurity 9 Monitoring sales and use of antimicrobials and surveillance of AMR in animals 10 Promoting behavior change campaigns in animal production 11 Increasing veterinary laboratory capacity and access to diagnostics | <p>Multisectoral</p> <ol style="list-style-type: none"> 17 Detecting and deterring substandard and falsified antimicrobials (customs/law enforcement/health/agriculture) 18 Improving human and animal nutrition (health/agriculture) 19 Expanding vaccination coverage in humans and animals (health/agriculture) 20 Using closed water systems in aquaculture (agriculture/environment) |



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STATEMENT | 15 MAY 2024

MSF statement and position paper on UNHLM for AMR

ANTIMICROBIAL RESISTANCE

Download v

Statement for the Interactive Multi-Stakeholder Hearing as part of the preparatory process for the 2024 High-Level Meeting on antimicrobial resistance (AMR)

Panel 2: Addressing antimicrobial access, research and development (R&D), and innovation

Thank you, Mr. (President).

I represent Médecins Sans Frontières, a medical humanitarian organisation and a leading actor in the treatment of AMR globally, currently with 47 AMR projects in 38 countries worldwide.

Over the last decade we have treated many thousands of patients with drug-resistant bacterial infections, and have noted with alarm the increasing rates of resistance.

We witness first-hand inequities in health care, resulting in gaps in prevention, diagnosis and treatment that are putting patient lives, and quite frankly, modern medicine, at risk.

We can attest that basic, targeted interventions to strengthen healthcare facilities against AMR in low-resource settings work, and yet, the necessary international financing and mobilisation to implement these measures are still lacking.

We offer 4 recommendations today:

First, focus on prevention. Alongside vaccination and WASH, in order to reduce transmission and the overall burden of infectious disease, we ask States to strengthen capacity for infection prevention and control by investing in infrastructure and healthcare worker training.

Second, focus on diagnostic capacity. We know from experience the importance of microbiology labs for effective diagnosis and treatment of AMR patients, as well as for public health surveillance. We ask States to invest in laboratory infrastructure, training, and innovations for use in low-resource settings.

Third, focus on access to appropriate treatment. Healthcare workers need support in antimicrobial stewardship and existing drugs and diagnostics must be universally accessible and affordable. Developing new drugs is also crucial, but we ask States to ensure that R&D is balanced with other investments that strengthen healthcare provision; targets the most urgent global public health needs; prioritises non-profit initiatives; and comes with upfront conditions that ensure new products will be affordable and accessible to all.

And finally, focus on community engagement. Initiatives to counter AMR must actively engage civil society and place those most affected by drug resistance at the heart of their structure and governance. This will ensure that the most pressing needs are prioritized and that the global response to AMR tackles the healthcare inequities fueling this crisis.

Thank you, (Mr. President).

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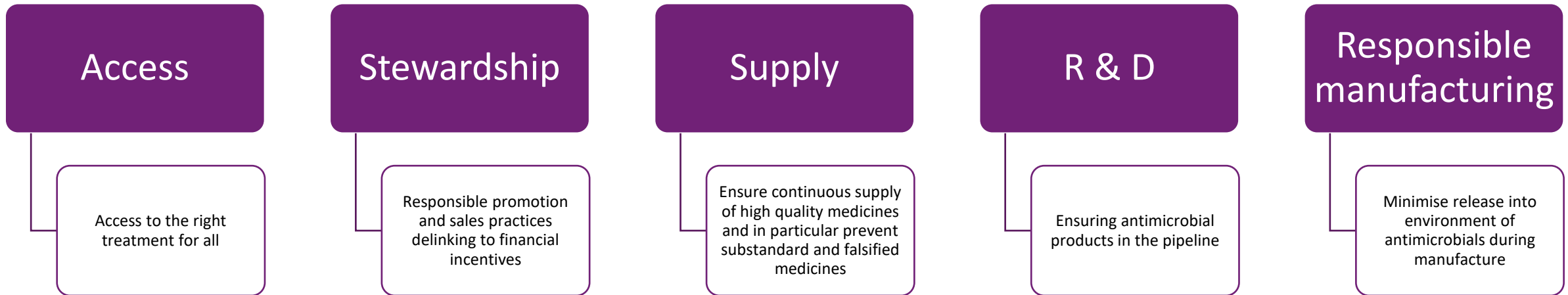
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What the High-level meeting should prioritise when engaging the pharmaceutical industry on combatting antimicrobial resistance



Council recommendation on stepping up EU actions to combat antimicrobial resistance in a *One Health* approach

1st June 2023

Proposes a series of actions including:
Strengthening of national action plans

Improving awareness, education and training

Strengthening antimicrobial stewardship and prudent use of antimicrobials

Strengthening infection control and prevention

Fostering research and development in the area of novel antimicrobial development



Brussels, 1 June 2023
(OR. en)

9581/23

Interinstitutional File:
2023/0125(NLE)

SAN 250
PHARM 90
VETER 61
ENV 509
PHYTOSAN 32
RECH 186

NOTE

From: General Secretariat of the Council
To: Council
Subject: Council Recommendation on stepping up EU actions to combat antimicrobial resistance in a One Health approach
(legal basis proposed by the Commission: Article 168(6)TFEU)
- *Adoption*



Library of AMR national action plans

A library of existing, publicly available national action plans on antimicrobial resistance has been compiled which countries may wish to consult. WHO will update this library regularly as new information becomes available on existing national action plans, and as new plans are published. WHO welcomes any additional information of relevance to existing and newly developed national action plans. Please note that the library contains only those national action plans which have been officially approved.



Physical environment

Antimicrobial resistance

National Action Plans

WHO Regional Office for Africa



10 September 2024

Algeria: National strategic plan



15 November 2022

Benin: National multisectoral



1 January 2018

Burkina Faso: National



26 May 2022

Burundi: Multisectoral national

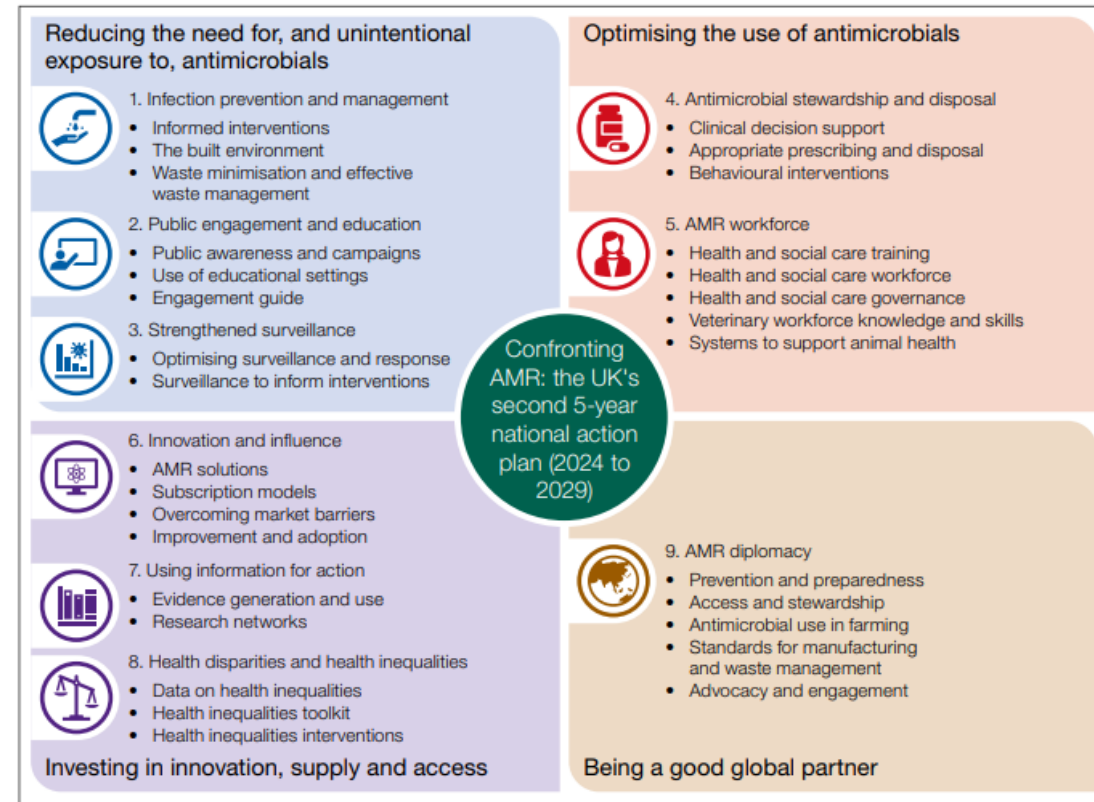
UK national action plan for tackling antimicrobial resistance



Confronting antimicrobial resistance

Executive summary

Figure 1: summary of the 2024 to 2029 NAP



Role of the pharmacist within this plan ...

- Increasing role of the pharmacist in ensuring appropriate AM use – particularly with initiatives such as the Pharmacy First services and keeping in mind that all newly graduating pharmacists in the UK will be independent prescribers as from 2026
- Role in appropriate prescribing and disposal of antimicrobials: right drug, right dose, right time, right route, duration, de-escalation
- Role of the specialist antimicrobial pharmacist – covers both primary and secondary care
- Vaccination programmes

Fighting antimicrobial
resistance

The contribution
of pharmacists

2015



Front line and point of entry into a healthcare systems in most countries
Likely to be the most accessible healthcare profession

Educators on behaviour change relating to infection prevention and control
Lead on immunization programmes

Collect unused medication with less antimicrobials reaching the environment

Lead on stewardship programmes in hospitals

Play a role in triaging patients referring them on to medical profession ONLY if infection suspected
Provide self-care advice if viral infection particularly URTI

Diagnostic tests – point-of-care testing
e.g. influenza, Strep A (GAS) testing

Participation in public health campaigns e.g. WAAR week and EAAD (18th November 2024)



How do we ensure that future workforce is “fit-for-purpose?”

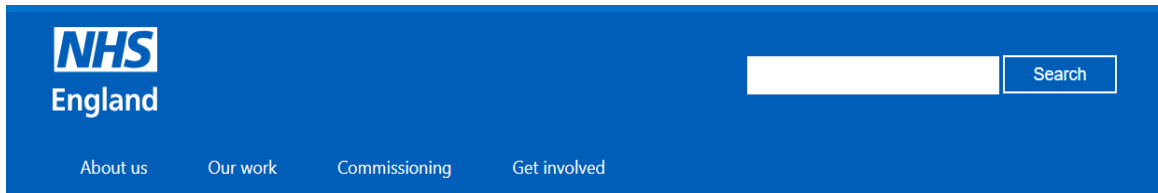
- September 2022: National AMS Pharmacy Education Group (NAPEG) set up
- Membership comprises: academics with interest in AMS, teacher practitioners, antimicrobial specialist pharmacists, pharmacists involved in national policy, students (through the British Pharmaceutical Student Association) and a pharmacy professional body (Royal Pharmaceutical Society)
- Representation from all four nations of the UK



What is the aim of this project?

- To facilitate the development of a UK-wide AMS competency framework tailored for student pharmacists
- To ensure that the principles of AMS are embedded within the undergraduate curriculum to prepare future pharmacists to ensure antimicrobials are prescribed sustainably in future employment
- Having UK-wide competencies ensures a standardized approach to curricula boosting AMS education and future applicability in clinical practice

Overview of curriculum



Antimicrobial resistance and antimicrobial stewardship pharmacy undergraduate competency framework

Document first published: 11 March 2024
Page updated: 15 March 2024
Topic: Pharmacy, Prevention
Publication type: Guidance

[Part of a suite of documents](#) to help guide the teaching content and practical assessment in both the MPharm and the Foundation Training Year. They are not compulsory, but are guides to support educators.

6 Domains

- Infection Prevention and control
- Antimicrobials and antimicrobial resistance
- Antimicrobial prescribing and stewardship
- Vaccine uptake
- Person-centred care
- Interprofessional collaborative practice

... and 74 descriptors

Domain 2

Antimicrobials and antimicrobial resistance

Competency statement

All newly qualified pharmacists need to understand the core knowledge underpinning the action of antibiotics and the concept of antimicrobial resistance; and use this knowledge to help prevent antimicrobial resistance.

Descriptors Examples (2 of 8)

2.01. Demonstrate an understanding of the major classes of antimicrobials, their mechanisms of action and their spectrum of antimicrobial activity in terms of Gram-positive, Gram-negative, anaerobic and atypical bacteria and viruses, fungi and parasites

2.08. Demonstrate an understanding of the concept of One Health where AMR is concerned and the inter-dependencies between human health, animal health, agriculture, food and the environment

Domain 3

Antimicrobial prescribing and stewardship

Competency statement

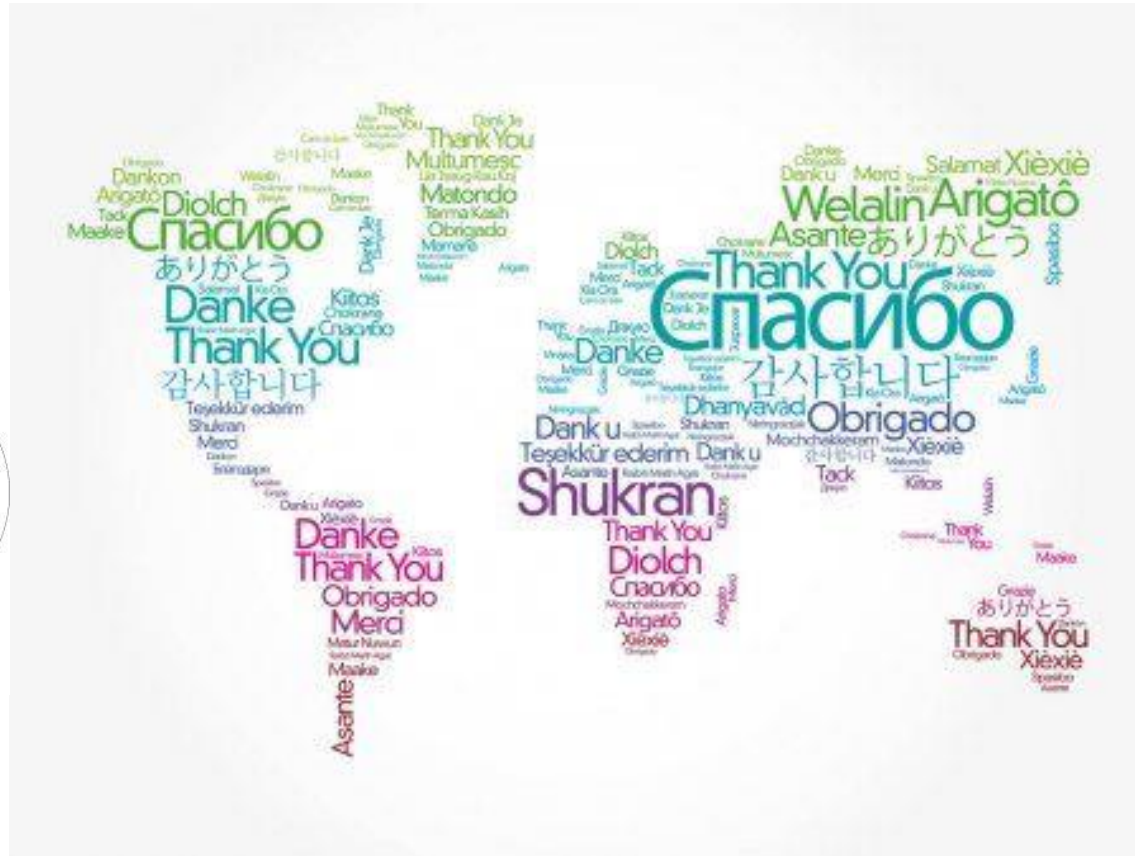
All newly qualified pharmacists need to demonstrate knowledge of how infections are diagnosed and managed and use this knowledge appropriately to manage patients with infections including the appropriate use of antimicrobial agents.

Descriptors Examples (2 of 24)

- 3.09. Understand the concepts of empirical therapy and pathogen-directed therapy, how local microbial/antimicrobial susceptibility patterns impact on the choice of empirical therapy and the significance of using local or national empirical therapy guidelines.
- 3.24. Understand the importance of timely intravenous-to-oral switch and demonstrate the application of appropriate criteria to identify patients eligible for switch.

In summary ...

- There is an urgent need to tackle AMR globally
- Strategies to tackle AMR should closely follow the *One Health* approach
- Strategies may be mapped to the UNSDGs
- There is a potential for expanding the role of the pharmacist within these strategies
- There is a need to ensure our future workforce is competent to tackle this challenge



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