TOMUN 2024 Research Paper

United Nations General Assembly Topic:

The question of promoting global cooperation to combat antibiotic and antimicrobial resistance.

Introduction of Topic

Antimicrobial resistance (AMR) is a pressing global issue that threatens the effectiveness of medicines, making infections harder to treat and increasing the risk of disease spread, severe illness, and death. The United Nations General Assembly (UNGA) has recognized the urgency of this issue and is actively promoting global cooperation to combat AMR.

In 2021, a record number of countries (163) responded to the annual global survey of implementation of the Global Action Plan on addressing AMR, administered jointly by WHO, FAO, and OIE. However, more than 90% of these countries noted that COVID-19 had negatively impacted the development and implementation of national plans to tackle AMR. Challenges included reduced funding, lack of support for coordination meetings, as well as deferred activities in data collection, capacity building, and campaigns. The UNGA has called for action at global, regional, and national levels to strengthen One Health and multisectoral actions to tackle AMR. This includes keeping AMR high on the political agenda, building awareness, and strengthening coordination, political leadership, and collaboration on AMR actions.

In 2023, the WHO published its first global research agenda to address the most urgent human health priorities to combat AMR. It outlines 40 research topics on drug-resistant bacteria, fungi, and *Mycobacterium tuberculosis* that must be answered by 2030, in line with the Sustainable Development Goals. The UNGA's efforts to promote global cooperation to combat AMR are crucial in the face of this growing global threat. By fostering international collaboration and prioritizing research and action, the UNGA is working towards a future where antimicrobial medicines remain effective, and infections are manageable. Call to action on AMR in 2021 aimed at strengthening One Health and multisectoral actions to tackle AMR, learning from the COVID-19 pandemic to address the growing threat of AMR, which has been referred to as a silent tsunami. The UNGA committed to several actions at global, regional, and national levels, including AMR coordination, accountability, and governance.

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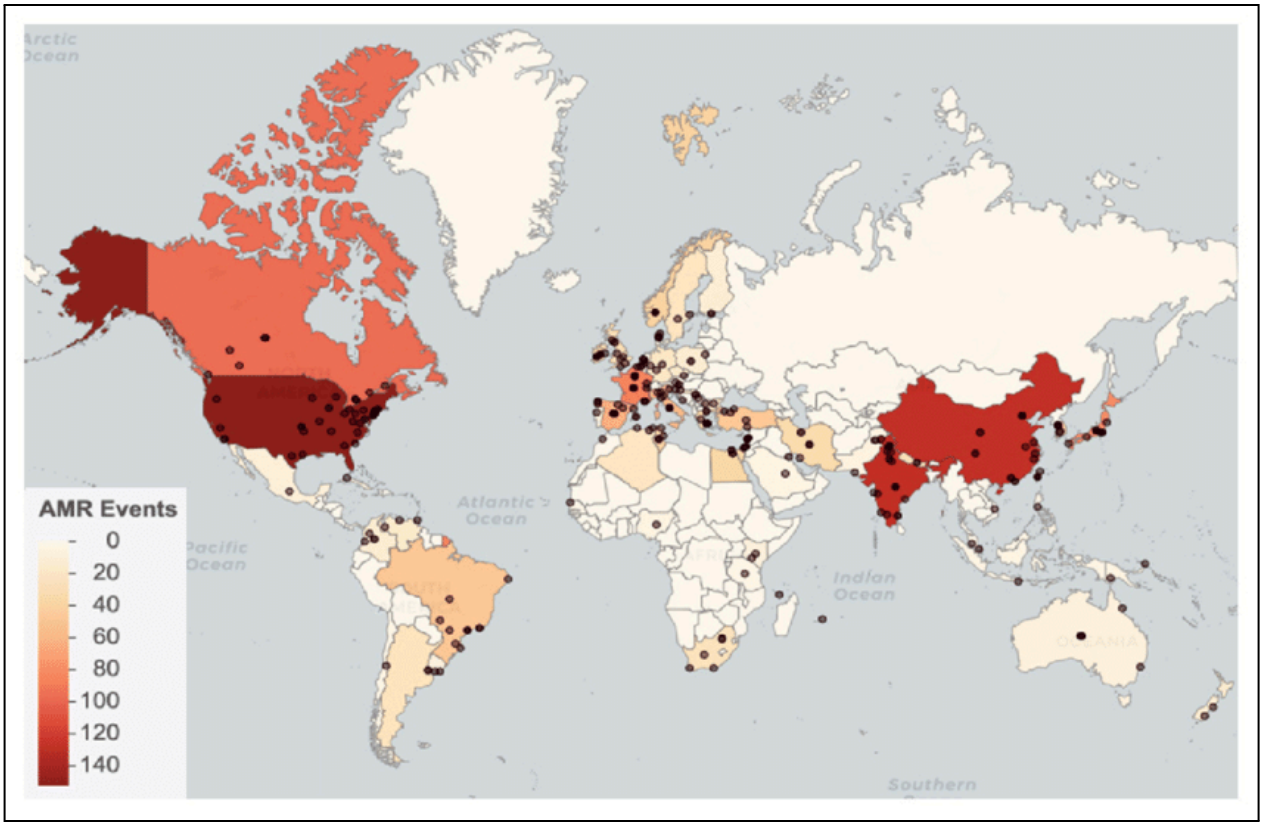
governance.

The UNGA also encouraged all Member States to have a multisectoral AMR national action plan, in line with One Health, that is fully funded, implemented, and evaluated through multisectoral coordination contributed to by appropriate focal points from human health, animal health, the environment, and food production. Efforts to promote global cooperation to combat AMR are crucial in the face of this growing global threat. By fostering international collaboration and prioritizing research and action, the UNGA is working towards a future where antimicrobial medicines remain effective, and infections are manageable.



Global distribution of antimicrobial resistance (AMR) emergence events. Points represent locations. Countries are shaded by event count.

Definition of Key Terms

Antimicrobial resistance (AMR) - Natural process that happens over time through genetic changes in pathogens. Occurs when bacteria, viruses, fungi, and parasites no longer respond to antimicrobial medicines.

Antimicrobials - are medicines (including antibiotics, antivirals, antifungals, and antiparasitics)

used to prevent and treat infectious diseases in humans, animals, and plants.

Drug Resistance - Drug resistance is the reduction in effectiveness of a medication such as an antimicrobial or an antineoplastic in treating a disease or condition.

Pathogens - a bacterium, virus, or other microorganism that can cause disease.

Drug-Resistant Infections - Drug-resistant infections is a term we use to describe illnesses that have been caused by resistant microbes, resulting in an infection that is much harder – or potentially impossible – to treat.

Neglected Tropical Diseases (NTDs) - refers to a diverse group of parasitic and bacterial diseases that cause significant morbidity and mortality in more than 1 billion people worldwide, which disproportionately affect poor and marginalized populations.

Background Information

Key Facts:

- Antimicrobial resistance (AMR) is one of the top global public health and development threats. It is estimated that bacterial AMR was directly responsible for 1.27 million global deaths in 2019 and contributed to 4.95 million deaths.
- The misuse and overuse of antimicrobials in humans, animals and plants are the main drivers in the development of drug-resistant pathogens.
- AMR affects countries in all regions and at all income levels. Its drivers and consequences are exacerbated by poverty and inequality, and low- and middle-income countries are most affected.
- AMR puts many of the gains of modern medicine at risk. It makes infections harder to treat and makes other medical procedures and treatments – such as surgery, caesarean sections and cancer chemotherapy – much riskier.
- The world faces an antibiotics pipeline and access crisis. There is an inadequate research and development pipeline in the face of rising levels of resistance, and urgent need for additional measures to ensure equitable access to new and existing vaccines, diagnostics and medicines.
- In addition to death and disability, AMR has significant economic costs. The World Bank estimates that AMR could result in US$ 1 trillion additional healthcare costs by 2050, and US$ 1 trillion to US$ 3.4 trillion gross domestic product (GDP) losses per year by 2030.
- Priorities to address AMR in human health include preventing all infections, which may result in inappropriate use of antimicrobials; ensuring universal access to quality diagnosis and appropriate treatment of infections; and strategic information and innovation, for example surveillance of AMR and antimicrobial consumption/use, and research and development for novel vaccines, diagnostics and medicines.

A Global Concern:

Antimicrobial medicines are the cornerstone of modern medicine. The emergence and spread of drug-resistant pathogens threatens our ability to treat common infections and to perform life-saving procedures including cancer chemotherapy and caesarean section, hip replacements, organ transplantation and other surgeries. In addition, drug-resistant infections impact the health of animals and plants, reduce productivity in farms, and threaten food security.

AMR has significant costs for both health systems and national economies overall. For example, it creates need for more expensive and intensive care, affects productivity of patients or their caregivers through prolonged hospital stays, and harms agricultural productivity.

AMR is a problem for all countries at all income levels. Its spread does not recognize country borders. Contributing factors include lack of access to clean water, sanitation and hygiene (WASH) for both humans and animals; poor infection and disease prevention and control in homes, healthcare facilities and farms; poor access to quality and affordable vaccines, diagnostics and medicines; lack of awareness and knowledge; and lack of enforcement of relevant legislation. People living in low-resource settings and vulnerable populations are especially impacted by both the drivers and consequences of AMR.

Drug-resistance in bacteria

The global rise in antibiotic resistance poses a significant threat, diminishing the efficacy of common antibiotics against widespread bacterial infections. The 2022 Global Antimicrobial Resistance and Use Surveillance System (GLASS) report highlights alarming resistance rates among prevalent bacterial pathogens. Median reported rates in 76 countries of 42% for third-generation cephalosporin-resistant *E. coli* and 35% for methicillin-resistant Staphylococcus aureus are a major concern. For urinary tract infections caused by *E. coli*, 1 in 5 cases exhibited reduced susceptibility to standard antibiotics like ampicillin, co-trimoxazole, and fluoroquinolones in 2020. This is making it harder to effectively treat common infections.

Klebsiella pneumoniae, a common intestinal bacterium, also showed elevated resistance levels against critical antibiotics. Increased levels of resistance potentially lead to heightened utilization of last-resort drugs like carbapenems, for which resistance is in turn being observed across multiple regions. As the effectiveness of these last-resort drugs is compromised, the risks increase of infections that cannot be treated. Projections by the Organization for Economic Cooperation and Development (OECD) indicate an anticipated twofold surge in resistance to last-resort antibiotics by 2035, compared to 2005 levels, underscoring the urgent need for robust antimicrobial stewardship practices and enhanced surveillance coverage worldwide.

Drug resistance in HIV, tuberculosis and malaria

HIV drug resistance (HIVDR) is caused by changes in the HIV genome that affect the ability of antiretroviral (ARV) drugs to block the replication of the virus. HIVDR can either be transmitted at the time of infection or acquired because of inadequate adherence to treatment or drug-drug

interactions. HIVDR can lead to increased HIV infections and HIV-associated morbidity and mortality. WHO recommends that countries routinely implement HIVDR surveys to inform the selection of optimal ARV drug regimens for HIV prevention and treatment.

Tuberculosis (TB) is a major contributor to antimicrobial resistance. Multidrug-resistant tuberculosis (MDR-TB) is a form of TB caused by bacteria that do not respond to isoniazid and rifampicin, the two most effective first-line TB drugs. MDR-TB is treatable and curable by using second-line drugs, but these medicines are expensive and toxic, and in some cases more extensive drug resistance can develop. TB caused by bacteria that do not respond to the most effective second-line TB drugs can leave patients with very limited treatment options. MDR-TB is therefore a public health crisis and threat to health security. Only about 2 in 5 people with drug resistant TB accessed treatment in 2022.

Drug resistance in neglected tropical diseases (NTDs)

The emergence of drug resistance against medicines for neglected tropical diseases (NTDs) is a significant threat to programmes to control, eliminate and eradicate NTDs, which especially affect vulnerable and marginalized populations. Resistance has been reported in leprosy medicines (dapsone, rifampicine and clofazimine) in several countries, in several anti-helminthics (while resistance has so far only been observed in use in animals, which is a serious concern for the veterinary sector, some of these medicines are also used in humans), in medicines used to treat human African trypanosomiasis (melarsoprol) and leishmaniasis (pentavalent antimonials, miltefosine), and others. It is important to monitor resistance and drug efficacy, put in place strategies to delay or curb resistance, and strengthen the pipeline of second-line medicines for NTDs. For example, WHO provides guidance for surveillance of resistance for the global leprosy elimination programme, and support to control distribution and monitor the standardized use, safety and efficacy of medicines, including donated medicines, in NTD programmes.

Major Countries and Organizations Involved

Major Countries Involved:

Australia: Australia has been proactive in addressing the issue of antimicrobial resistance. The country has implemented a National Antimicrobial Resistance Strategy, which sets a 20-year vision to protect the health of humans, animals, and the environment through minimizing the development and spread of AMR. The Fourth Australian report on antimicrobial use and resistance in human health (AURA 2021) highlights the ongoing public health and safety threat posed by antimicrobial resistance. The report suggests that while antimicrobial use in the community is decreasing, overprescribing and inappropriate prescribing continue to be a problem.

China: China is one of the top consumers of antimicrobials in the world, making it more challenging for the country to face antimicrobial resistance. China has issued a 2016-2020 One Health National Action Plan to Contain Antimicrobial Resistance with 14 ministries to ensure a clear multi-sectoral approach to tackling this growing issue. In 2022, the Chinese government published its new plan to fight antimicrobial resistance, the National Action Plan for Combating Antimicrobial Resistance (2022-2025), which focuses on controlling major pathogens of human and animal origin and gives new annual targets and more detailed indicators for combating AMR.

United States: The United States has taken ambitious steps to fight antimicrobial resistance. The U.S. National Action Plan for Combating Antibiotic-Resistant Bacteria presents coordinated, strategic goals to accelerate the U.S. government's response to antimicrobial resistance and improve the health of all Americans. The Plan has pushed transformative improvements that strengthen and expand the response to resistance threats. The five key objectives of the plan include slowing the emergence of resistant organisms and preventing the spread of resistant infections; strengthening the national health surveillance network that monitors AMR; accelerating basic and applied research and development for new antibiotics, vaccines, and diagnostics; establishing national reference laboratory performance standards for antimicrobial susceptibility; and improving international collaboration and capacities for AMR prevention, surveillance, and control.

AMR National Action Plans

As of November 2023, 178 countries had developed AMR national action plans aligned with the GAP. To ensure sustained progress, countries need to establish a functioning multisectoral AMR governance mechanism, prioritize activities, develop a costed operational plan, mobilize resources (both domestic and external), and effectively implement their plan. Monitoring mechanisms are needed to track progress, identify challenges and report periodically. To globally track the progress in AMR national action plan implementation, countries have committed to completing the multisectoral annual Tracking AMR Country Self-Assessment Survey (TrACSS) that was launched in 2016 with results published at https://www.amrcountryprogress.org/.

Major Organizations Involved:

World Health Organization (WHO): The WHO has identified antimicrobial resistance (AMR) as one of the top global public health threats. It has published its first global research agenda to address the most urgent human health priorities to combat AMR. The WHO Global Research Agenda for AMR in human health aims to catalyze innovation and implementation research, spanning the epidemiology, burden, and drivers of AMR. The WHO also lists AMR among the top 10 threats for global health.

Food and Agriculture Organization (FAO): The FAO has a significant role in combating AMR. It has implemented the FAO Action Plan on Antimicrobial Resistance 2021–2025. The FAO is uniquely placed to contribute to international efforts to combat AMR and to provide support to governments, producers, traders, and other stakeholders in adopting measures to minimize the use of antimicrobials and to contain AMR. The FAO also promotes multi-sectorial actions to prevent antimicrobial resistance.

World Organisation for Animal Health (WOAH): The WOAH is at the forefront of the fight against antimicrobial resistance. Misuse and overuse of antimicrobials in terrestrial and aquatic animals can lead to the development of resistant pathogens and undermine global health. The WOAH has released a landmark report showing encouraging progress in combatting antimicrobial resistance. It has also developed a strategy on antimicrobial resistance and the prudent use of antimicrobials.

Quadripartite Joint Secretariat on Antimicrobial Resistance

To coordinate the One Health global response to AMR, WHO works closely with the Food and Agriculture Organization of the United Nations (FAO), the UN Environment Programme (UNEP) and the World Organisation for Animal Health (WOAH). The 4 organizations (FAO, UNEP, WHO and WOAH) are known as the Quadripartite. A quadripartite joint secretariat is hosted by WHO to drive multi-stakeholder engagement in AMR. This has supported establishment of the Global Leaders Group on AMR, which began its work in November 2020, and the Multi-Stakeholder Partnership Platform, which was launched in November 2022, and several technical working groups.

Timeline of events

1877 – Antibiosis described

Antibiosis, a biological process where one organism inhibits the growth of another, is observed by Louis Pasteur and Robert Koch. They observe that microbes can secrete material to kill certain bacteria.

1910 – First synthetic antimicrobial used in humans

Paul Ehrlich developed the first antimicrobial treatment used to treat humans – Salvarsan. It has severe side effects, partly because it contains arsenic, a poison.

1928 – Resistance identified

Some bacteria become resistant to the antimicrobial Salvarsen.

1928 – Penicillin discovered

Alexander Fleming discovers the first modern antibiotic. He observes that the growth of the

Staphylococcus aureus bacteria living in Petri dishes is inhibited by substances produced by the fungus *Penicillium chrysogenum*. This leads to the creation of the first antibiotic, penicillin.

1930 – Sulphonamides discovered
Sulphonamides are a group of synthetic antibacterial medicines. They are the first truly effective, broad-spectrum antimicrobials used for treating infection in humans and animals. They are still in use today but were largely superseded by the discovery of penicillin.

1933 – More resistance appears
Certain bacteria become resistant to sulphonamides.

1943 – Streptomycin discovered
Streptomycin is the first antibiotic to be successful against tuberculosis.

1944 – Golden age of antibiotics
The discovery of natural product antibiotics peaks in the mid-1950s – including streptomycin, cephalosporins, tetracyclines, vancomycin, and methicillin. Most of the antibiotics discovered in this 'golden age' – 1944 to 1966 – are still in use, but their effectiveness has been eroded by antimicrobial resistance. The rapid and relatively easy discovery of natural product antibiotics during a relatively short period leads to the excessive use of these drugs.

1944 – Penicillin resistance identified
Shortly after the introduction of penicillin, resistance is identified in the bacteria Staphylococcus aureus, a common cause of serious infection in people and animals.

1961 – Methicillin resistance identified in the bacteria Staphylococcus aureus
The resistant bacteria are described as MRSA (methicillin-resistant Staphylococcus aureus). These bacteria are resistant to all antibiotics in the penicillin class of antibiotics so infection is difficult to treat.

1986 – Vancomycin resistance identified in the bacteria Enterococcus
Vancomycin-resistant gram-positive bacteria can become resistant to all antibiotics.

1987 – Lipopeptides discovered
The last class of clinically used antibiotics is discovered.

1990 – Resistance to different antibiotics continues to emerge
Resistance to common antimicrobial drugs increases, and readily treatable infections are becoming increasingly challenging to manage.
1997 – Some countries restrict the use of growth-promoting antibiotics
The European Union bans the use of certain antibiotics used as growth promoters in animals.

2002 – New Zealand bans use of antibiotics as growth promoters
Concerns about the development of antibiotic-resistant bacteria and the potential impact on human health led to a ban on the use of antibiotics as growth promoters in animal feed in New Zealand. The ban applies to all antibiotics that pose an antimicrobial resistance risk to animals or humans.

2015 – Global AMR emergency declared
Antimicrobial resistance has been declared a global emergency by the World Health Organization. The World Health Assembly adopts a global action plan on AMR.

2023 – 2024 onwards
In just over 100 years, antibiotics have drastically changed modern medicine and extended the average human lifespan by 23 years. The dangers of a post-antibiotic era have prompted policymakers to acknowledge this threat to human health. Appropriate use of antibiotics and preventing infection by vaccination and good hygiene are critical.

Relevant UN Treaties and Events

Resolution A/RES/76/257

In March 2022, United Nations General Assembly resolution A/RES/76/257 established a second High-level Meeting on AMR to be held in 2024, in collaboration with the Quadripartite Organizations and with the support of the Global Leaders Group. In October 2023, The President of the General Assembly appointed the Permanent Representatives of Barbados and Malta to co-facilitate the high-level meeting. The high-level meeting is an important opportunity for countries to make ambitious commitments and agree targets, and the Quadripartite Joint Secretariat is working closely with the co-facilitators and Global Leaders Group to ensure optimal participation and inputs from the human, animal, agri-food and the environment sectors.

In addition, three Global High-level Ministerial Conferences on AMR, in the Netherlands in 2014 and 2019, and in Oman in 2022, led to the Global Action Plan, the AMR Multi-Partner Trust Fund, and groundbreaking multisectoral AMR targets. A fourth high-level ministerial conference will be hosted by the Kingdom of Saudi Arabia in 2024.

United Nations General Assembly High-Level Meeting on Antimicrobial Resistance

In 2016, the United Nations General Assembly held a high-level meeting on antimicrobial resistance in New York City. This was only the fourth time a health issue was discussed by the UN General Assembly, demonstrating the urgency of this threat. The meeting aimed to increase awareness of antimicrobial resistance and secure strong commitments from the national, regional, and international community. World leaders agreed to address the causes of

antimicrobial resistance in both humans and animals, and they emphasized taking a One Health approach. Countries reaffirmed their commitment to develop national action plans to combat drug resistance, and pledged to strengthen regulations on the use of antimicrobial drugs, improve knowledge and awareness, promote best practices, and foster innovative non-drug approaches and new technologies for diagnosis and vaccines.

The Global Leaders Group Side Event at UN General Assembly on Antimicrobial Resistance

The Global Leaders Group hosted a side event at the UN General Assembly on Antimicrobial Resistance in 2022. The group has been calling for specific actions from G7 and G20 countries that include fully funding their own national action plans on AMR, contributing to fund multi-sectoral national action plans of resource-limited countries through support to existing financial structures, financially supporting the AMR Multi-Partner Trust Fund, supporting financial incentives and mechanisms for the development of new antimicrobials (particularly antibiotics), vaccines, diagnostics, waste management tools, and safe and effective alternatives to antimicrobials, with a defined timeline and following through on their existing AMR commitments and finally, monitoring their progress annually.

Main Issue

Antimicrobial resistance (AMR) is a significant global challenge that requires international cooperation to address effectively. The main issue is the growing threat posed by resistant genes and drug-resistant infections, which could lead to 10 million deaths each year by 2050 if no action is taken. This could also cause damage to the economy as catastrophic as the 2008-2009 global financial crisis. The Centers for Disease Control and Prevention (CDC) has outlined a comprehensive plan to combat AMR globally. This includes setting goals across multiple sectors such as healthcare, food, communities (local and global), and the environment (soil and water). The plan also involves implementing infection prevention and control practices, improving antibiotic use, implementing data and tracking systems to track resistance, and improving lab capacity to identify resistant bacteria.

However, the multifaceted, multi-sector, and multi-stakeholder nature of the AMR challenge means that any approach used to address AMR on the global stage must be carefully considered. The One Health approach, which includes coordination of human, animal, plant, and environmental policies, is recommended. This approach recognizes that the health of people is connected to the health of animals and the environment. The CDC is leading the public health fight against AMR and supports activities in nearly 30 high-burden countries throughout the world to improve antibiotic and antifungal use, track resistance, and implement infection

prevention and control activities. In addition, the CDC collaborates in global activities, including participating in the Transatlantic Taskforce on Antimicrobial Resistance (TATFAR), a collaborative effort between Canada, the European Union, Norway, and the U.S. to address antimicrobial resistance together.

In conclusion, promoting global cooperation to combat antibiotic and antimicrobial resistance is crucial in our world today. It requires a comprehensive, multi-sectoral approach that includes improved antibiotic use, enhanced surveillance and laboratory capacity, and the development of new drugs and diagnostics. The challenge is complex, but with international cooperation and a commitment to the One Health approach, it is possible to combat AMR effectively.

Previous Attempts to Solve the Issue

One Health Approach

AMR is a complex problem that requires both sector-specific actions in the human health, food production, animal and environmental sectors, and a coordinated approach across these sectors. One Health refers to an integrated, unifying approach that aims to achieve optimal and sustainable health outcomes for people, animals and ecosystems. It recognizes that the health of humans, domestic and wild animals, plants and the wider environment are closely linked and inter-dependent. The One Health approach to preventing and controlling AMR brings together stakeholders from relevant sectors to communicate and work together in the design, implementation and monitoring of programmes, policies, legislation and research to mitigate AMR and attain better health and economic outcomes.

Global Action Plan (GAP) on Antimicrobial Resistance

To address AMR globally, countries adopted the Global Action Plan (GAP) on AMR during the 2015 World Health Assembly and committed to the development and implementation of multisectoral national action plans with a One Health approach to tackle AMR. The GAP was subsequently endorsed by the Governing Bodies of the Food and Agriculture Organization of the United Nations (FAO) and the World Organisation for Animal Health (WOAH, formerly known as OIE) and the United Nations Environment Program.

World AMR Awareness Week (WAAW)

World AMR Awareness Week (WAAW) is a global campaign to raise awareness, understanding and best practices with the public, One Health stakeholders, and other policymakers. One of WHO's official health campaigns since 2015, WAAW is celebrated from 18 to 24 November every year.

Antimicrobial Stewardship and AWaRe

Antimicrobial stewardship is a systematic approach to educate and support health care professionals to follow evidence-based guidelines for prescribing and administering

antimicrobials. The education of the health workforce is of crucial importance, as they form the front line in safeguarding the effectiveness of antimicrobial medicines. WHO guides countries to develop and implement Antimicrobial Stewardship Programmes as one of the most cost-effective interventions to optimize the use of antimicrobial medicines, improve patient outcomes and reduce AMR and health care-associated infections. To improve access to appropriate treatment and reduce inappropriate use of antibiotics, WHO developed the AWaRe (Access, Watch, Reserve) classification of antibiotics. The WHO AWaRe antibiotic book provides concise, evidence-based guidance on the choice of antibiotic, dose, route of administration, and duration of treatment for more than 30 of the most common clinical infections in children and adults in both primary health care and hospital settings.

Global Antimicrobial Resistance and Use Surveillance System (GLASS)

WHO launched the Global Antimicrobial Resistance and Use Surveillance System (GLASS) in 2015 to fill knowledge gaps and inform strategies at all levels. GLASS progressively incorporates data from surveillance of AMR in humans, surveillance of the use and consumption of antimicrobials, and integrated AMR data in the One Health sectors including the food chain and in the environment. GLASS provides a standardized approach to the collection, analysis, interpretation and sharing of data by countries, territories and areas. It also monitors the status of existing and new national surveillance systems, with emphasis on representativeness and quality of data collection. Some WHO regions have established surveillance networks that provide technical support to countries and facilitate enrollment into GLASS. WHO is committed especially to supporting low- and middle-income countries to improve data collection and usage for policymaking, both through GLASS and by supporting nationally representative AMR prevalence surveys.

Priority-setting for AMR research and product development

The clinical pipeline of new antimicrobials is almost dry and there is a pipeline and access crisis for antibiotics. WHO's latest annual review of the pre-clinical and clinical antibacterial pipelines identified 27 antibiotics in clinical development that address WHO bacterial priority pathogens, of which only 6 were classified as innovative. To guide research and development into new antimicrobials, diagnostics and vaccines, and inform public health action, WHO developed the first WHO bacterial priority pathogens list in 2017 and updated this in 2023 (publication forthcoming), and published the WHO fungal priority pathogen list in 2022. To help fill the major gaps in R&D for antimicrobials, vaccines and diagnostic tools, WHO works closely with organizations such as the Global Antibiotic Research & Development Partnership (GARDP), the AMR Action Fund, and the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X). Various governments are also piloting different models to incentivize research and development of newer antimicrobials to ultimately ensure access to treatment.

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