WHO

AGENDA ITEM: FORMULATING AND ENHANCING GLOBAL COLLABORATIVE EFFORTS TO ADDRESS THE ESCALATING CHALLENGE OF ANTIMICROBIAL RESISTANCE (AMR)

UNDER SECRETARY GENERAL:
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"It's all begins in the Sky"

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1.Letter from the Secretaries-General.

Honourable participants of ÇAĞDAŞMUN’25,

As the secretary generals of ÇAĞDAŞMUN’25, taking place from November 14th to November 16th, we would like to extend our warm welcome to all participants of this prestigious conference.

Model United Nations conferences are more than just a simple event, it is a torch that shines its light upon a variety of great opportunities, guiding the youth to the future through the brightness it eradiates. It grants the opportunity to be in the minds of diplomats and decision makers allowing the participants to learn the ways of decision making and debating, at the same time giving the chance to apply the learnings in real time debates. When organised with utmost care and responsibility, one conference can shape hundreds of individuals into leaders of the future.

In the first official edition of ÇAĞDAŞMUN, our mission is to achieve what most struggle to do: committees with a wide grasp of the past, present and the future, a marvelous organisation team to be in our most perfect form and most importantly, a mission to create space for bright minds to shine the most powerful, hidden gems to come to light for the greatest jewelries and disregarded souls to prove themselves as unignorable leaders.

It all begins in the sky.

With our warmest regards,

Secretary Generals of ÇAĞDAŞMUN’25,
Mustafa Aslan and Kuzey Karlık.

2.Letter from the Under-Secretary General.

My dear delegates,

It is our pleasure to welcome you all to ÇAĞDAŞMUN'25 and the United Nations Human Rights Council. My name is Gülşah, and it is my honor to serve you as your Under-Secretary-General, accompanied by my esteemed Academic Assistant, Ali Emre Üzülmez.

Our agenda, "Formulating and Enhancing Global Collaborative Efforts to Address the Escalating Challenge of Antimicrobial Resistance" represents one of the most pressing challenges of our time. As antimicrobial resistance continues to undermine the effectiveness of modern medicine, its impact on public health, socioeconomic stability, and fundamental human rights becomes increasingly severe. Understanding this issue is not only scientifically and politically significant, but also essential to safeguarding the future of global health.

I kindly urge you to read this study guide thoroughly and attentively. While it will provide you some significant information about the topic, it should not be your only source. Independent and comprehensive research will be crucial in strengthening your understanding and enriching the debates ahead.

I would also like to express my sincere gratitude to my Academic Assistant, whose dedication and hard work were vital in preparing this study guide. Due to my academic workload, they undertook the main drafting, and I contributed during the review process. Their effort and excellence truly made this study guide possible, and I am deeply thankful.

It is my sincere wish that you not only engage in productive, insightful discussions but also create lasting memories and friendships throughout this conference. May your experience be both intellectually rewarding and personally unforgettable.

Warm regards,

Gülşah Dirlik

Under-Secretary-General

3.Letter from the Academic Assistant.

Honored Delegates

I'm Ali Emre Üzülmez, and I have the privilege to submit this study guide to you. I wish you have also selected this committee and our conference meetings will have good results.

At the outset, I share your enthusiasm in our representation on the World Health Organization (WHO) committee, and I foresee that this gathering will provide a new angle on the Model United Nations. In a similar vein to this committee, the topics have been carefully considered to maximize participation and enjoyment. Assuming that you have gone through the guide, I wish to introduce the topic of Antimicrobial Resistance (AMR). Antimicrobial Resistance, known in short as AMR, poses a global threat to public health in everyday life and lets bacteria evolve into ever-more deadly strains. As a delegate of the United Nations, I assume you will consider possible solutions to reduce this menace. After careful review of this guide, you will observe that we have tried to give complete details so that you have all the necessary information to participate in the committee. This committee has been carefully crafted in consultation with my dear Under-Secretary General Gülşah Dirlik. I again assure you that this committee shall come up with innovative solutions and produce tangible results. I extend my sincere gratitude to the Executive team of ÇağdaşMUN for putting me in front of this opportunity.

Best regards
Ali Emre Üzülmez
Academic Assistant, World Health Organization (WHO)

4.Overview of the World Health Organization(WHO).

The World Health Organization (WHO) began back in 1948, soon after the end of the Second World War, and it represented the idealism and ambition that the creation of the United Nations system represented more generally. The idealism could be seen in its objective 'the attainment by all peoples of the highest possible level of health' and the ambition took the shape of the 22 broad functions listed within its constitution, and the first among them was 'to act as the directing and co-ordinating authority on international health work.'

WHO, as the directing and coordinating authority on international health within the United Nations system, aligns with the UN values of integrity, professionalism and respect for diversity.The WHO workforce's values also reflect the principles of human rights, universality and the spirit of equity embedded in WHO's Constitution and the ethical obligations of the Organization.These values are rooted in WHO's vision of a world where all peoples can enjoy the highest possible level of health and our mission to promote health, make the world safer and better serve the disadvantaged, with measurable impact on the people at country level.

Regarding country needs for support from the WHO, another fundamental change has been the development of indigenous capacity in the field of health, which profoundly alters the nature of the support and advice that countries may need and expect from the WHO. Militating against this development of national capacity has been the massive rise in the international migration of health workers as a result of increased ability to train health workers and the economic opportunities that globalization has opened up for them. The WHO has to date responded more to the latter trend by drawing up its Global Code of Practice on the International Recruitment of Health Personnel.

The WHO’s professional staff are predominantly either health professionals or administrators. Addressing the social, economic and environmental determinants of health and non-communicable disease, and advising countries on the attainment of universal health coverage and financial protection would seem to demand a very different distribution of skills from that which exists currently. Because the WHO has a rapid turnover of staff, significant changes could be made in a relatively short period of time

5.Introduction of the Agenda Item.

This committee's agenda item highlights one of the biggest health challenges of the century. Widespread resistance among bacteria and other microorganisms to deployed therapies is an imminent threat to global health security, and formerly treatable infections now can be life-threatening. Antimicrobial Resistance (AMR) also undermines the efficacy of modern medicine, threatening routine surgery, tumor management, and control of communicable diseases.

Antimicrobial Resistance (AMR) is the condition where various microorganisms, i.e., bacteria, fungi, parasites, and viruses, gain an evolutionary adaptation to be resistant to antimicrobial agents, i.e., antibiotics, employed to treat these infections. AMR has now become the defining problem of the world in the 21st century due to the increasing rates of AMR infection at an exponentially fast pace and the absence of adequate research and development and introduction of new antimicrobial therapeutics to match this critical requirement. One of the main causes of the current issue could be the consequences of overuse or irresponsible use of antibiotics in various situations, primarily in clinical treatment along with agricultural usage, animal healthcare and the food system. AMR is widely referred to as the "Silent Pandemic" and is a problem where urgent action is needed immediately and should be managed more effectively and not be considered as a future situation .

Previous research has shown that one of the main causes of AMR is the inappropriate and excessive use of antibiotics, both in humans, as well as in animals. Since the 1950s, when the "golden era" of antibiotics began, Alexander Fleming had expressed concerns about the potential emergence of resistance if treatment is used for an inadequate amount of time . "Since then, there has been an increasing demand for new and novel antibiotics, in order to combat highly resistant strains that have been emerging."The use of antibiotics in treating infectious diseases and other conditions has become widespread in modern medicine. Nevertheless, the misuse and even over-prescription of these antimicrobials has fast outpaced their efficacy as AMR has grown markedly.Series of recent studies have indicated antimicrobial involvement in agriculture and food systems may have a significant impact on driving AMR . According to estimates, in the US, 70% of antibiotics used to treat humans are available for use in veterinary medicine .In addition, zoonosis also poses a serious transmission factor of AMR, where antibiotic-resistant bacteria are spread between animals and humans, through either direct or indirect interaction, as well as through foodborne or waterborne events.

Studies conducted in China have reported that mediated colistin resistance (MCR-1) poses a high risk to AMR due to zoonosis transmission from animal to human . According to this study, MCR-1 was detected in E. coli isolates from animal and commercial meat sources and MCR-1 is believed to have been widely transmitted in food-producing animals in south China. In contrast, relatively low MCR-1 was detected from human origin, this difference in the prevalence of MCR-1 between animals and humans is likely to be a form of zoonotic transmission from animals to humans.

Colistin is regarded as a “last resort” antibiotic that is increasingly being utilised to treat patients with multiresistant bacteria, although it is still effective it was not typically used to treat common infections due to its potentially adverse side effects. However, if colistin resistance evolves rapidly, these bacterial infections may be more difficult-to-treat.

The creation of antimicrobials is one of the most effective drug treatments in medical history. The introduction of antimicrobials has helped to manage and greatly reduce death rates caused by infectious diseases, previously the leading cause of death in humans . Human life expectancy has increased on average by 23 years, since the first antibiotic was introduced in 1910 . With regard to that, the discovery of the antibiotic penicillin, by Sir Alexander Fleming was one of the greatest medical advancements of the 20th century which initiated the “golden era” of antibiotics. However, shortly after, the production of penicillinase by antibiotic-resistant strains was reported, which led to inactivation of the antibiotic molecule, thereby rendering it clinically ineffective . This is important to note, as penicillin and its derivatives (cephalosporins, carbepenems) are the major class of antibiotics still employed today, in treating human and animal infections.

Microbes are under selective pressure to become resistant and acquire adaptive mutations or genes when antimicrobial agents are misused or overused in healthcare, veterinary, and agricultural settings. This then enables their survival and persistence in environments saturated with antibiotics and antiseptics that would previously have readily destroyed them. Bacteria and other microbes have a remarkable ability to rapidly adapt, mutate, and share adaptive genetic elements via horizontal gene transfer mechanisms allowing them to develop diverse resistance mechanisms. Microorganisms that develop AMR may make human and animal diseases challenging to cure. Resistance prolongs sickness, increases spread risk, lengthens hospital stays, requires more costly therapies, and raises fatality rates. This escalating cycle of resistance development is not only a contemporary concern but has roots deeply embedded in the history of antimicrobial use.

5.1.Improper/unregulated usage of Antibiotics, Antivirals, Antifungals, and Antiparasitics

Although the process of development of antibiotic resistance occurs as a natural phenomenon, it has been accelerated by the misuse of antibiotics in both humans and animals over the years. There is a causal relationship between overuse and development of microbial resistance to antibiotics as revealed by epidemiological studies . Despite being warned repeatedly by health organizations, unfortunately, misuse and overuse of antibiotics continue at a disproportionate level worldwide, and the current scenario seems to be at the point of no return.

Tackling the emergence of AMR presents complex challenges with no facile resolutions. Efforts to reduce humanity's vast utilization of antimicrobials are obstructed by their widespread integration into medical care and food animal production economics. Lacking rapid point-of-care diagnostics, physicians often depend on empiric antibiotic prescribing to safeguard against bacterial infections, while modern farming systems predicate the regular administration of antimicrobials to livestock for infection prevention and growth promotion. Implementation of antimicrobial stewardship programs in healthcare and updated animal husbandry policies lag considerably despite awareness of resistance risks associated with antibiotic overuse.

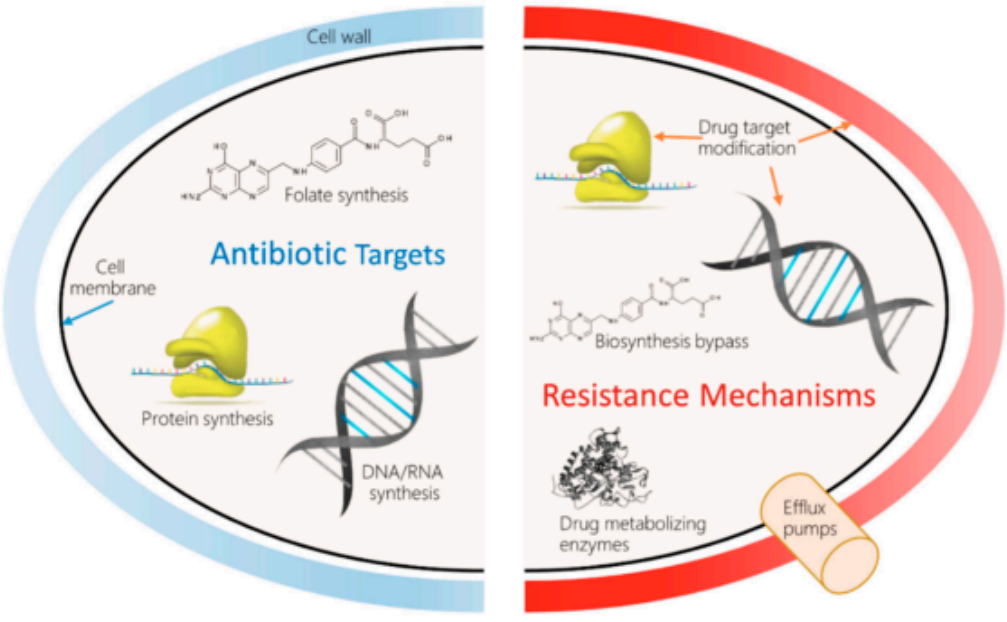


Figure 1. Molecular mechanisms of antimicrobial resistance (AMR) and drug resistance.

Natural selection, overutilization and misutilization of antibiotics, insufficient safe drinking water and proper sanitation facilities, and substandard and counterfeit medicines are among the causes of AMR. Over- and inappropriate uses of antibiotics include but not limited to incomplete treatment, inappropriate prescription, and self-medication. Bacteria surviving on incompletely used antibiotic courses can acquire resistance. Also, prescription of medicines to viral diseases, self-administration, or the administration of leftover antibiotics without medical advice can contribute to AMR. Inadequate sanitation and inappropriate hygiene measures cause the transference and proliferation of infectious diseases and enhance dependence on the antibiotic and resultant resistance. Finally, substandard medicines can contain an insufficient quantity of active ingredients or the wrong quantity and yield an inefficient treatment causing the production of resistance.

Exacerbating these challenges is the inability of the antibiotic discovery pipeline to keep up with the everlasting adaptation of MDR pathogens. Pharmaceutical firms increasingly scrap expensive antimicrobial research projects with minimal profit potential. And while policy expansions financing antibiotic development mark progress, near-term solutions seem unlikely considering phase trial durations. Further frustrating containment efforts, international coordination on AMR surveillance and stewardship guidelines remains piecemeal despite organizations like the WHO, CDC, and UN recognizing its borderless risks.

Variable access to quality diagnostics and antibiotic oversight across countries enables local emergence and global spread of novel resistance factors. Patches of weak stewardship may continually undermine and negate localized progress. Ultimately, the unique ‘tragedy of the commons’ nature of antibiotic resistance demands equitable, cooperative global action and shared responsibility. However, geopolitical complexities continue obstructing consensus on binding international policies and funding channels needed to strengthen antimicrobial stewardship and innovation worldwide.

AMR transcends geographical boundaries and has a global impact on populations. During the past decades, hitherto controlled infections have emerged as significant health problems. The absence of effective antimicrobial agents increases the risk of common medical procedures, e.g., surgery, chemotherapy, and organ transplants. In addition to the harmful impact on human health, AMR also represents enormous economic challenges for healthcare systems, governments, and society. The financial burden of managing resistant infections is significantly boosted as a result of extended hospitalization, more

healthcare consultations, and the need for costly drugs as a last option. The capacity of bacteria and other microbes to rapidly evolve resistance threatens a pillar of modern medicine effective antimicrobial therapies. Humanity's rampant overuse of antibiotics in healthcare and agriculture has applied immense selective evolutionary pressure, enabling pathogenic bacteria to develop diverse mechanisms undermining previously potent antimicrobials. With antibiotic discovery failing to keep pace as multidrug resistance proliferates globally, we have entered a dangerous post-antibiotic era. Further delays risk forecasted reversals to the pre-antibiotic susceptibility patterns underpinning infectious disease mortality's historical dominance, an outcome threatening modern medical capabilities and global health security.

5.2.Impact of antimicrobial resistance on public health

With AMR emerging at a rapid rate, the infection and death rates of AMR are closely monitored at all times. In the United Kingdom, the estimated AMR infection rate was 65,162 people diagnosed in 2019, which increased from 61,946 patients recorded in 2018. In comparison, the European Centre for Disease Prevention and Control (ECDC) has reported in the EU alone, the infection rate of AMR has reached over 670,000 cases annually.According to data analysis from a prior study, there were 4.95 million deaths worldwide in 2019 that were linked to bacterial AMR, and 1.27 million of those deaths were directly caused by bacterial AMR. In a well-known review, it was previously reported that the annual death rate directly caused by AMR is predicted to rise to 10 million by 2050. With the highest estimated deaths of this being in Asia followed by Africa, mainly due large populations and lack of regulation associated with AMR prevention. According to previous research, Sub-Saharan Africa has the highest all-age mortality rate in the Global Burden of Diseases (GBD) region that is directly linked to or related to AMR, in contrast to Australasia which had the lowest rate of AMR-related mortality in 2019.

Without preventative measures, it is estimated that by 2050, AMR could potentially become the world's primary cause of death. According to estimates provided globally, the number of deaths directly linked to AMR has risen to more than 1.2 million in 2019 and this is forecast to increase to approximately 10 million deaths per year by 2050, if insufficient action is taken to control AMR. Uncomplicated infections and minor injuries could once again become life-threatening, while major procedures like organ transplants, chemotherapy, or hip replacements may become overwhelmingly risky. The economic losses associated with AMR will reach $100 trillion USD by 2050.

Surveys have revealed that people across the globe, especially noneducated sections, do have misconceptions and beliefs about antibiotics, for example, that they help to recover from most common viral diseases, such as the common cold or flu. Moreover, it has been observed that antibiotics are a frequently prescribed medicine for patient management, particularly observed in many developing countries where there is a lack of adequate diagnostic facilities. Administering antibiotics without a clear indication is a good example of common misuse. The emergence and spread of drug-resistant pathogens are facilitated further when antibiotics can be bought for human as well as animal use as over-the-counter (OTC) drugs.

Unethical though it is, sometimes to gain financial incentives from pharma companies and to satisfy patients' expectations, many physicians especially in the developing countries prescribe antibiotics without indication. Antibiotic abuse is also contributed to by lack of antibiotic policy and standard treatment guidelines, frequently seen in developing countries. Antibiotics are often overprescribed by health workers, pharmacy dealers, and veterinarians in many underdeveloped and developing countries. Substandard or poor quality antibiotics in the supply chain has made the situation of AMR worse in many developing countries

6.International Actions and Agreements.

AMR is an emerging issue where a unified global approach is required. “One Health” embraces the concept that there is a clear connection between the health of both humans and animals and the shared surrounding environment as shown. It was evidenced that humans and animals can share the same bacteria, diseases and more importantly, the sharing of the same antibiotics to treat infectious diseases in animals, as well as in humans . With all aspects considered, AMR has emerged as one of the most prominent “One Health” issues, since AMR has the ability to spread rapidly across the population as well as in the food chain, healthcare settings and the environment, thereby making it more challenging to manage many infectious diseases in both humans and animals.

WHO’s Global Health Strategy (GHS) and General Programme of Work (GPW) is a strategic document that sets a high-level roadmap and agenda for WHO's work on global health. Each edition describes the Organization's priorities and strategic direction for a specified period. The Strategy also provides a framework for resource allocation and decision-making for WHO.

There is no commonly accepted global definition of One Health, although a number of definitions have been proposed. “One Health is defined as a collaborative, multisectoral, and transdisciplinary activity working at local, regional, national, and global levels to achieve optimal health outcomes in recognition of the relationship between people, animals, plants, and their common environment,” as proposed jointly by the US Centers for Disease Control and Prevention and the One Health Commission.

Another possible definition is that of One Health Global Network, as follows: “One Health recognizes that human, animal, and environmental health are inextricably linked. Another proposed definition is that of One Health Global Network, as follows: "One Health understands that human, animal, and environmental health are inextricably linked."

The One Health concept clearly focuses on consequences, responses, and actions at the animal human ecosystems interfaces, and especially emerging and endemic zoonoses, the latter being responsible for a much greater burden of disease in the developing world, with a major societal impact in resource-poor settings; antimicrobial resistance (AMR), as resistance can arise in humans, animals, or the environment, and may spread from one to the other, and from one country to another; and food safety . However, the scope of

One Health as envisaged by the international organizations (WHO, FAO, OIE, UNICEF), the World Bank, and many national organisations also clearly embraces other disciplines and domains, including environmental and ecosystem health, social sciences, ecology, wildlife, land use, and biodiversity. Interdisciplinary collaboration is at the heart of the One Health concept, but while the veterinarian community has Trop. Med. Infect. Dis. 2019, 4, 88 3 of 4 embraced the One Health concept, the medical community has been much slower to fully engage, despite support for One Health from bodies such as the American Medical Association, Public Health England, and WHO. Today's health problems are frequently complex, transboundary, multifactorial, and across species, and if approached from a purely medical, veterinary, or ecological standpoint, it is unlikely that sustainable mitigation strategies will be produced.

6.1.WHO Global Health Strategy

The Fourteenth General Programme of Work (GPW 14), which Member States adopted at the Seventy-seventh World Health Assembly, is a bold new global plan for 2025–2028. It builds on GPW 13's legacy, COVID-19 pandemic lessons, and progress to date in the WHO Transformation, and charts a path for health and well-being in a world gone mad. Underpinning it is a vision to save 40 million lives over the next four years through a three-pronged mission: to speak up for health by addressing drivers of disease, such as climate change; to get health to everyone by establishing effective health systems centered around primary health care and expanding access to health services and financial protection; and to protect health by preventing, preparing for, reducing the risk of, detecting and responding early to health emergencies.This mission is supported by six strategic objectives formulated through one of the most consultative processes ever undertaken by WHO; 15 joint outcomes that define specific actions needed to implement GPW 14 by countries, The Strategy is developed in consultation with Member States, experts and stakeholders across the global health ecosystem and beyond for multi-year periods. It is approved by the World Health Assembly.

The term global health has replaced tropical medicine and international health, disciplines linked to the history of colonialism, the post-independence era of the former European colonies, and the experience of development assistance.
Global health is multidisciplinary, encompasses many elements besides development, and requires coordination of multiple parties, rather than direction by one organization or

discipline. The increased technical and The New Global political complexity of global health, with many actors, including philanthropic and faith-based organizations, is reflected in its breadth, which covers diverse diseases but deals also with health systems issues and financing. Global health reflects the realities of globalization, especially the increased movement of persons and goods, and the global dissemination of infectious and noninfectious public health risks. Global health is concerned with protecting the entire global community, not just its poorest segments, against threats to health and with delivering essential and cost-effective public health and clinical services to the world's population. A fundamental tenet is that no country can ensure the health of its population in isolation from the rest of the world, as articulated in the Global Health Strategy of the United States Department of Health and Human Services. This vision reflects today's health realities but was arrived at through milestones such as the 1993 World Development Report (Investing in Health), the 2000 report of the Commission on Macroeconomics and Health , and the tremendous investment in HIV/AIDS begun earlier this century.

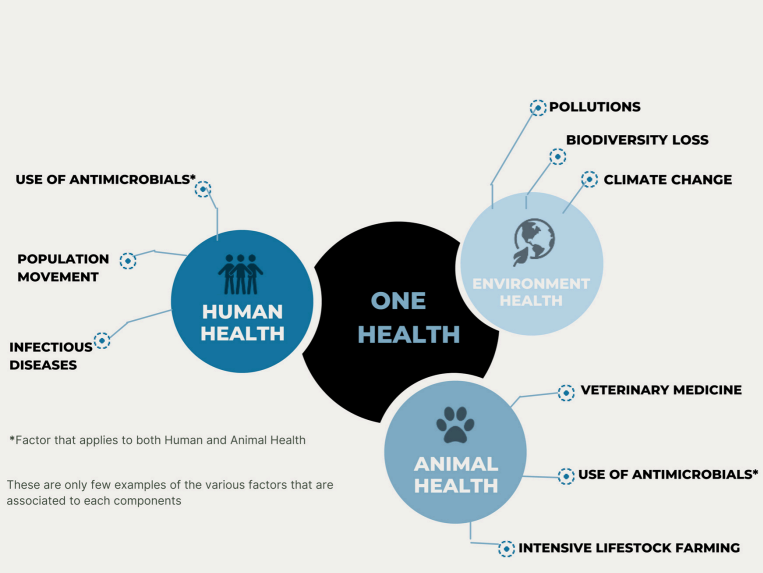
Drawing on earlier United Nations perspectives that characterized poor health as one of several threats to human security and well-being, health security captures the need for collective action and preparedness to reduce vulnerabilities to public health threats that transcend borders. Earlier optimism predicting the end of infectious diseases was replaced by recognition of the threat to global health from emerging infectious diseases and widespread antimicrobial drug resistance.

The global framework for health security is embodied in the International Health Regulations that were revised in 2005 and adopted by the World Health Assembly, but whose implementation is lagging behind the 2012 target date. The diversity of health threats results in involvement of other sectors, such as defense and diplomacy, and linkage with other international agreements, such as those relating to control of chemical, biological, and nuclear weapons. Surveillance and laboratory capacity through strong National public health institutes are essential components of functioning health systems that provide the basis for health security. Ensuring the ability to detect, investigate, diagnose, and rapidly contain public health events of concern wherever they occur requires commitment to global health capacity development in all countries and widespread and supportive public health networks.

Population growth, increased life expectancy of the world's citizens, and decreased age-specific mortality rates in children and young adults, especially those for infectious diseases, have contributed to the altered global health landscape. The New Global Health concerns health in all countries and encompasses poverty alleviation, universal health security, and delivery of appropriate public health and clinical services, including for the increasing prevalence of noncommunicable diseases. Equity, universal health coverage and access, and fairness in health financing are global aspirations likely to feature prominently in discussions about what comes after the 2015 MDG target date.

6.2.Collaborative efforts of FAO, OIE and UNEP (One Health approach).

AMR is a complex problem that requires both sector-unique interventions in the human health, food producing, animal and environment sectors, and an intersectoral, coordinated approach through these sectors. One Health is an integrated, transdisciplinary approach directed towards achieving maximal and sustainable health outcomes for people, animals and ecosystems. It recognizes that the well-being of human beings, domestic and wild Animals, plants and the wider environment are inter-dependent and inter-linked. The One Health approach to preventing and controlling AMR brings together stakeholders across interested disciplines to exchange and work together on the development, execution and evaluation of programs, policies, regulations and research to prevent AMR and obtain better health and economic outcomes.



WHO is integrating One Health across its units and offices, providing strategic advice relating to policy, and conducting training at the local, national and regional levels. The goal is stronger programmes that are led and owned by countries.

7.The Current Global Status of AMR and International Implications.

AMR is exacerbated by the easy availability of medicines without a prescription. An estimated one in ten medicines globally is substandard or falsified, and the African region is one of the most affected in the world. In markets and on street corners, people are buying antimicrobials of unknown quality. Without proper medical supervision, people often stop their drug course too soon or they double-dose rather than keep to a prescribed strict time interval for appropriate drug-taking. The same happens in treatment of animal diseases coupled with underdosing, disrespect to drug withdrawal periods, and use of antimicrobials as growth promoters.

The improper use of antimicrobial medicines enables bacteria, viruses, fungi and microscopic parasites to mutate into superbugs that are resistant to the drugs designed to kill them. These superbugs can travel across countries, resulting in thousands, or potentially millions, of deaths. Their treatment is resulting in prolonged hospital stays and the need for more expensive medicines, leading to huge additional costs in health expenditure by governments and individuals. The World Bank projects that the additional health care cost by 2050 could be between US$ 0.33 trillion and US$ 1.2 trillion.

In a well-known review, it was previously reported that the annual death rate directly caused by AMR is predicted to rise to 10 million by 2050. The highest estimated deaths from this are in Asia, followed by Africa, mainly due to large populations and a lack of regulation related to AMR prevention. According to previous research, Sub-Saharan Africa has the highest all-age mortality rate in the Global Burden of Diseases (GBD) region that is directly linked to or related to AMR, whereas Australasia had the lowest rate of AMR-related mortality in 2019.

Previous literature focusing on the different national responses to antibiotic resistance highlighted the key risk factors contributing to AMR between developing and developed countries and how each leads to AMR in a different manner. Several AMR contributing factors were found in developing countries, including poor regulation and control of antimicrobial drugs, insufficient monitoring of the emergence of AMR, inappropriate use of antibiotics in clinical settings, and inadequate quality checks for antibiotics supplied. Recent studies on the accessibility of antibiotics in low- and middle-income countries found that Vietnam and Bangladesh had the highest proportion of unlicensed locations where antibiotics are administered, with relevant antibiotics frequently found in typical drug stores for mild illnesses, where they are widely available to the general public.

Since those communities have easy access to antibiotics, maintaining this attitude would lead to a number of issues, such as improper use of antibiotics due to a general lack of knowledge about antibiotics and AMR, and a lack of consideration for the quality of the antibiotics distributed. All such factors may contribute to the emergence of AMR.
The occurrence of the COVID-19 pandemic in 2020 created an unprecedented scenario for the treatment of suspected or proven bacterial infections with antibiotics. The changing dynamic in the movement of patients within healthcare (community and hospital), largely driven by the patients' SARS CoV-2 status, combined with reduced diagnostic ability due to redeployment of laboratory staff to SARS CoV-2 testing, resulted in a temporary redefining of "Best Practice" antimicrobial stewardship programmes, due to pandemic-related constraints. A recent study investigating global antibiotic use during the pandemic, through examination of pharmaceutical sales data from 71 countries during the years, 2020–2022.sales of cephalosporins, penicillins, macrolides, and tetracyclines decreased dramatically during April–May 2020, after which there was a gradual rise to nearly pre-pandemic rates through May 2022.

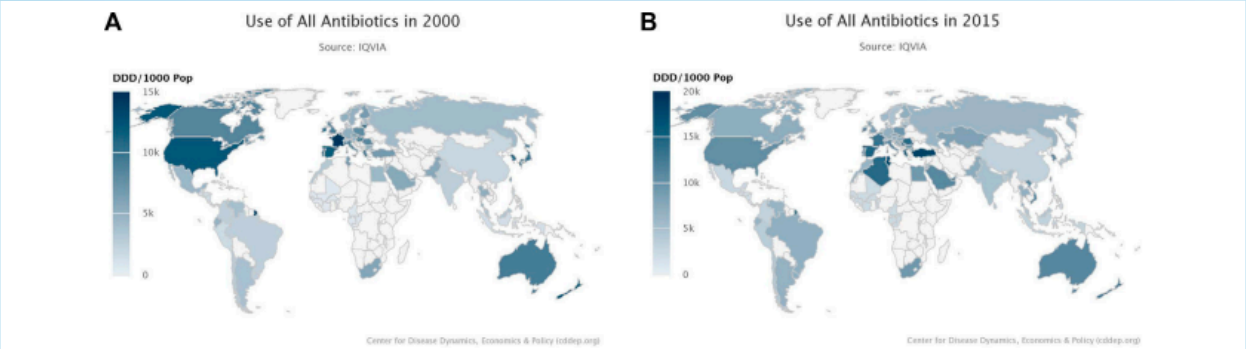


FIGURE 2 | (A) Resistance Map showing the Global usage of antibiotics in 2000 [36]. **(B)** Resistance Map showing the Global usage of antibiotics in 2015 [36].

AMR to be highest in the WHO Africa region at 0.17 (0.15–0.18)million deaths and 12 (11–13) million DALYs, followed by the WHO South-East Asia region at 0.16 (0.15–0.18)million deaths and 7.5 (6.8–8.5)million DALYs in 2019. The vaccine avertable AMR burden for the WHO Africa and South-East Asia regions accounts for around two-thirds of the vaccine avertable AMR burden globally in 2019. In the high potential scenario, we estimated that vaccines would avert an additional 0.19 (0.18–0.20)million deaths and 9.6 (8.8–11)million DALYs associated with AMR in the WHO Africa region, and 0.32 (0.30–0.33)million deaths and 11 (10–11) million DALYs associated with AMR in the WHO South-East Asia region.

7.1.Disparities in the developed and developing countries and the post-pandemic increase in the consumption of antibiotics.

There is now a growing body of research that investigates global antibiotic consumption. The Global Research on Antimicrobial Resistance (GRAM) Project, conducted the first known long-term study to estimate the global consumption of antibiotics, which covered 204 nations from the years 2000–2018. According to this estimation of the average daily dose, a significant increase of 46% in the global antibiotic consumption rate was observed throughout this period of time. This historic analysis, utilizing the spatial disparities/geostatistical model identified the large national and sub-national disparities in the use of antibiotics in Low- and Middle-income countries (LMICs), the lowest rates residing in sub-Saharan Africa and the highest rates in Eastern Europe and Central Asia.

In addition to the previous findings mentioned above, the authors also found the global antibiotic consumption rate to be 14.3 (95% uncertainty interval 13.2-15.6) defined daily doses (DDD) per 1,000 population per day in 2018 (40.2 [37.2-43.7] billion DDD), representing a 46% increase from 9.8 (9.2-10.5) DDD per 1,000 per day in 2000. Third generation cephalosporins and fluoroquinolones consumption rose substantially in North Africa and the Middle East and South Asia.

The country and region seeing the highest consumption of carbapenems was the high income country, rising from 0.05 to 0.09 DDD per 1,000 per day between 2000 and 2018. The surge in the misuse of antibiotics has remained the main factor in causing this trend and the emergence of AMR. The characteristic of inappropriate use of antibiotics includes using antibiotics for an insufficient amount of time than specified, treating conditions other than bacterial infection using antibiotics, as well incorrect administration methods and dosage taken.

On the contrary, in developed countries, the risk factors that exist in developing countries may not necessarily apply. These include the excessive use of antimicrobials in agricultural use and over-prescription in clinical settings. Research on this issue presents conflicting findings as a more recent study reported that China, as a developing country, became the top consumer of veterinary antimicrobials in 2017, accounting for up to 45% of global consumption, and is estimated to remain the biggest user in 2030.In addition, with evidence that developed countries have reduced their total antimicrobial sales, for example, the UK had a 39.2% decrease from 2015 to 2017.

8.Unconscious use of prescriptions on AMR

Antimicrobial resistance (AMR) is a universal issue hindering the efficacious management of infectious diseases. It is directly linked to the irrational use of antibiotics either by the prescribing physicians or by the end users. This has multifaceted repercussions with the emergence of resistant strains of microorganisms that threaten the recovery from several infectious agents. Irrational and inappropriate antibiotic use in primary healthcare settings has led to the emergence of widespread drug resistance. Antibiotics are prescribed widely and are inappropriately utilized without adhering to standard guidelines.

This has led to apprehension regarding antibiotic usage and appropriate prescription of antibiotics. The knowledge of appropriate antimicrobial prescription, and its surveillance among the general population and also the health practitioners, particularly the primary care physicians along with associated policymakers, is the leading approach to combat antimicrobial resistance and limit the extent of further exposure and growth of resistance. The World Health Organization (WHO) is creating awareness among medical healthcare faculties on AMR and mentioned it as one of its highest strategies in decreasing the emergence and spread of AMR.

Antibiotics are advised regularly and there is always an increased chance of overuse. Improper use of antimicrobials in medical practice is one of the prime drivers for antimicrobial resistance. Therefore, to seek a solution to this problem of global magnitude, there is a necessity to assess the prescribing patterns among primary care physicians and other health professionals to assess the gaps in the sensible and prudent use of antimicrobials.

Due to the rampant emergence of antimicrobial resistance, infections can no longer be treated by first-line antibiotics, multi-drug regimens are prescribed that have been shown to increase the economic burden on patients. Antibiotic resistance is overshadowing the achievements of modern medicine demanding solutions to this problem facing mankind.

Chemotherapy, surgeries, and organ transplantation have become much more hazardous without effective antibiotics for the prevention and treatment of infections. Methicillin-resistant Staphylococcus aureus, rifampicin-resistant Mycobacterium, multi-drug resistant (MDR) Klebsiella, etc. are the major examples of antibiotic resistance, which have created havoc in human healthcare through the widespread dissemination of drug-resistant strains of these organisms.

Assigning antibiotics is a composite process controlled by many factors involving medical staff, paramedical staff, the health care system, supplementary healthcare sources, patients,and the general population.

A deficient attitude, perception, misunderstanding, and lack of knowledge about the sensible work of antimicrobials and the increasing growth of antibiotic resistance conclude supreme barriers to the use of antimicrobial resistance.Because modifications in antimicrobial prescribing strategies will require modification in prescriber's action, it is important to know the basic root parameters impacting their advising patterns and what alterations may effect change.

When the right, first-line antibiotics and antifungals are not locally accessible, a doctor may resolve to prescribing a less effective alternative. Not only is this less likely to cure the patient's infection, but it can also contribute to AMR. Pathogens can adapt to the pressure of antibiotics by selecting genes that are resistant to the antibiotic.

The wrong antibiotic kills only some susceptible pathogens and allows for the pathogens with resistant genes to survive and spread unchecked. When firstline treatments are unavailable, doctors may also resort more quickly to antibiotics that should be second- or third-line treatments, which should be held in reserve in order to protect their effectiveness for as long as possible. Lack of access to diagnostics exacerbates this problem, making it even harder for doctors to prescribe the correct antibiotic.

The implications for AMR are even wider when no antibiotics or antifungals are available and the patient does not receive any treatment. Appropriate access to the right treatment not only prevents suffering and death, but it also helps to control the spread of infection and limit the rise of AMR. When infections are allowed to spread unchecked among a population, pathogens may develop resistance due to natural selection, despite the absence of antibiotics.

The need for older, generic antibiotics Some older, generic antibiotics may no longer be produced or supplied by companies because of a lack of expected profit and a lack of awareness of or misunderstood demand, even though these medicines are still clinically useful. Most older antibiotics are produced by multiple companies, yet those living in low-and middle-income countries (LMICs) have very little access to these products since they are filed for registration in only 5 out of 102 LMICs on average.One example of how older antibiotics can be made available is colistin, which is an off-patent antibiotic discovered in the 1940s.

Since colistin can have side effects related to toxicity in the kidneys, it was largely abandoned in the 1970s due to safer alternatives. As resistance to other commonly used antibiotics increased in the 1990s, colistin was then seen as an alternative for the treatment of multidrug-resistant bacteria.

It is now listed on the 2021 WHO Model List of Essential Medicines in the Reserve group for the treatment of multidrug-resistant pneumonia and urinary tract infections. The AMR Benchmark recommends that this antibiotic is made available by companies in LMICs, provided there are good stewardship practices in place to prevent toxicity and excessive use and reduce the risk of driving resistance.

In 2007 in India, an infectious disease expert from a large private hospital made a direct approach to the generic medicine manufacturer Cipla to request access to colistin at their hospital after hearing the company's global medical officer speak at a private hospital event. At the time, the 50-year-old antibiotic was little used in India except in private hospitals, which imported the medicine from the UK to treat individual patients.

High unmet medical need obviated the need for clinical trials, so Cipla conducted a Phase IV pharmacokinetic study and one effectiveness and safety study. After successful trials, Cipla introduced colistin to the Indian market. Fifteen years later,

8.2.Disorganization in health systems and slowdown in the production of new antibiotics.

The latest AMR Benchmark report, published by the Foundation in 2021, found that just one third of the products analysed were covered by an access strategy in the 102 resource-limited countries in scope. A wide range of access strategies were considered in the report, including technology transfers, equitable pricing strategies and voluntary licensing agreements. Pharma can break the pattern of inaction. While there are many ways to improve access to vital antibiotics and antifungals in poorer countries, these are not being widely used.

While pharmaceutical companies expect governments to prioritise stewardship measures and prevent an influx of low-quality medicines, governments expect companies to communicate which antibiotics or antifungals they are planning to introduce into their health systems. This leads to a stalemate that affects people in poorer countries the most. Low-income countries (LICs), home to nearly 700 million people, are particularly overlooked by companies' access strategies even though the pharmaceutical industry can save lives by reaching more people with more products, both old and new.

Biotechs and small- and medium-sized enterprises (SMEs) are developing the bulk of the pipeline of novel, late-stage antibiotics and antifungals.16 In general, these companies do not yet have products available on the market and depend on research funding to survive. Yet, due to the lack of a healthy market for new products and the lack of acquisition of SMEs by large pharmaceutical companies, these SMEs must navigate the so-called financial "valley of death," where research funding runs out before financial returns of products kick in. When SMEs struggle to secure resources to complete the development of their product and support its launch, often leading to bankruptcy, this results in the loss of their pipelines of promising products. However, some SMEs are turning to partnerships with local companies in emerging economies, such as China, India and South Africa, to reach worldwide markets.

To allow technology transfer for on-patent products, research-based companies can use (non-exclusive) voluntarily licensing, which allows local generic medicine manufacturers to produce and sell on-patent products. However, these licenses are seldomly used for antibiotics and antifungals. License agreements are more commercially attractive for generic medicine manufacturers when they are exclusive or only a few manufacturers can participate.

When this is the case, research-based companies may have more bargaining power regarding the requirements to be included in the license, for example on access, quality of the product, stewardship and proper waste management for production. However, such exclusivity does not drive competition between generic medicine manufacturers, which means pricing of products might also not be competitive.
Affordability of products is further worsened when manufacturers need to warrant appropriate use, compensate for low sales volumes with higher prices.

The product is difficult and costly to manufacture, as previously seen in the case of delamanid, an antibiotic used to treat MDR-TB.18,19 In fact, to date, no voluntary licence has been issued yet for a novel antibiotic, other than for delamanid. In sum, while the market for antibiotics and antifungals is fundamentally unstable with fragile supply chains and tough market conditions, there are factors that can contribute to better access to essential off-patent/generic medicines in LMICs. Insight into local demand, diversifying supply chains and long-term procurement strategies via tenders can mend the go-to-market model for older medicines.

On-patent medicines are not introduced at scale because poorer countries often do not have suitable healthcare infrastructure or stewardship measures in place. Yet effective partnerships such as the Global Fund to fight AIDS, Tuberculosis and Malaria, increasing local manufacturing via technology transfer and the use of voluntary licensing can expand access to patented products. The following six case studies include practical examples of how pharmaceutical companies have used access strategies to make both off-patent/generic and on-patent medicines more widely available.

9.Questions To Be Addressed

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1. How can the inappropriate or unregulated use of antibiotics, antiviral drugs, antifungal drugs, and antiparasitic drugs could potentially be prevented?

2. How do the effects of antimicrobial resistance (AMR) and its impact on public health be minimized in Low-income countries and Developed Countries.

3. How to do afford the integration and raising awareness of international actions among all member states be ensured in response to the effects of AMR? “the One Health concept”

4. Given the current global situation of AMR, how do international economic impacts be minimized in developed or developing countries?

5. How do we prevent medicine shortages caused by the lack of old, generic antibiotics that are no longer produced or supplied by companies, even though they are still clinically useful in developing countries?(Colistin)

6. How should member states take measures to ensure that biotechnology companies and small and medium-sized enterprises (SMEs) are able to maintain their position in the current market and to ensure the continuity of new antibiotic products?

7. How can member states enhance global data-sharing frameworks to ensure that research findings, resistance patterns, and treatment guidelines are accessible, standardized, and effectively utilized across borders?

8. What mechanisms can be established to enhance coordination between UN bodies, regional organizations, and non-state actors to ensure coherent, long-term, and sustainable global governance against the rise of AMR?

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