

**THE URGENT THREAT OF
DRUG-RESISTANT INFECTIONS**
PROTECTING CHILDREN WORLDWIDE
A UNICEF Guidance Note on Antimicrobial Resistance

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The emergence and spread of antimicrobial resistance threaten children everywhere. Children must have access to effective infection prevention measures such as immunization, clean and regularly available water and sanitation, nutrition and education about these important health issues to mitigate the impact of AMR. And we must also promote the rational use of medicines to protect children from the growing threat of drug-resistant infections; otherwise, we may not be able to treat common infections in a very near future. AMR is an urgent problem that requires strong coordination and collaboration among different sectors. As a multisectoral organization, UNICEF already works in several areas that can protect children from AMR, but much more is needed to protect them from one of the greatest threats to child survival and global health of our time.

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ACRONYMS AND ABBREVIATIONS

AMR	antimicrobial resistance
ART	antiretroviral treatment
ARV	antiretroviral drug
AWaRe	Access, Watch and Reserve categorization of antibiotics
CHW	community health worker
HAI	hospital-acquired infection
HIC	high-income country
iCCM	integrated community case management
IHR	International Health Regulations
IPC	infection prevention and control
IMNCI	integrated management of newborn and childhood illness
LMICs	low- and middle-income countries
MDR-TB	multidrug-resistant tuberculosis
PHC	primary health care
PMTCT	prevention of mother-to-child transmission
SBC	social and behaviour change
SDG	Sustainable Development Goal
TB	tuberculosis
UHC	universal health coverage
UNICEF	United Nations Children's Fund
WASH	water, sanitation and hygiene
WHO	World Health Organization
XDR-TB	extensively drug-resistant tuberculosis



EXECUTIVE SUMMARY

This guidance note discusses the impacts of antimicrobial resistance (AMR) on UNICEF’s ability to achieve its mission and goals for children, including how the COVID-19 pandemic has made it more difficult to confront the serious and growing global threat of AMR to child survival, growth and development. The document maps UNICEF’s existing programmes, many of which have direct (AMR-specific) and indirect (AMR-sensitive) impacts on the response to AMR, and identifies potential strategic areas for future engagement where UNICEF has comparative advantages in the global AMR response.

The problem: overall AMR threats and particular risks and impacts among children

Antimicrobial resistance (AMR) is steadily growing around the world and has particularly devastating effects on the health and well-being of children, with the poorest and most vulnerable bearing the brunt. AMR occurs when pathogens develop resistance to the antimicrobial drugs commonly used to treat a wide variety of infections, and which as a class of drugs has saved countless millions of lives the past several decades. This makes many infectious diseases more difficult to treat and increases the costs of hospitalizations and treatment, the risk of spreading such diseases and the risk of death. AMR is further aggravated by the fact that the emergence and spread of drug resistance is far outpacing the rate at which new drugs capable of thwarting such infections are being developed.

Global estimates for 2019 indicate that children disproportionately carry the burden of deaths, with 254,000 of the 1.27 million deaths directly attributable to AMR – about 20 per cent of the total – occurring among those under the age of 5. This is equal to one child dying nearly every two minutes.¹ Of those 254,000 children, more than 99 per cent are from low- and middle-income countries (LMICs) and over half die in their first month of life.²

AMR has the potential to undo many of the gains in child health and well-being achieved by UNICEF and the global development community in recent years. For instance, there are major physical and financial costs to children and their families related to AMR affecting children, including impaired child development,³ a loss in earnings due to hospitalizations, limited or inconsistent school attendance, and the consequences of higher toxicity and side effects of second-line antimicrobials that can lead to lifelong disability.⁴ Costs related to failure to halt increasing AMR in general across society could include more precarious food security and the lack of effective antimicrobials to be used for surgery prophylaxis and organ transplants, or to ward off infections from cancer chemotherapy.⁵

Children living in poverty and those with limited access to basic services face heightened risk. A lack of access to vaccinations and safe water, sanitation and hygiene (WASH) in communities, hospitals and schools makes children in low-resource settings more vulnerable to AMR infections. For these and numerous other reasons, AMR negatively affects progress in achieving the overall 2030 Agenda for Sustainable Development, with its impact being especially direct on eight of the Sustainable Development Goals (SDGs), ranging from SDG 3 (good health and well-being) to SDG 8 (decent work and economic growth) to SDG 5 (gender equality).

The factors that drive and sustain AMR

A main reason for the growing threat of AMR is that antimicrobial drugs are not used properly, often due to weak knowledge of how they work and poor-quality products. Ongoing risk factors include unrestricted sales and suboptimal use of antimicrobials and 'irrational' prescribing and availability of these potent drugs. Excessive use of antimicrobials, one prominent example of irrational

prescribing, can occur when prescribers are not trained appropriately; when prescribers are unsure of the cause of a patient's symptoms (due, for example, to the lack of diagnostics, which can lead to the prescribing and use of antibiotics against viral infections); or the correct antimicrobial and/or dosage is not available and another antimicrobial is prescribed instead. Excessive use of these drugs often results as well from unrestricted and insufficiently regulated sales.

Substandard or falsified medicines reported as antibiotics are another factor contributing to AMR and more broadly to ill health and death by people experiencing infectious diseases – by preventing those in need from receiving the correct and strongest doses to treat such diseases. According to the World Health Organization (WHO), 17 per cent of substandard or falsified medicines reported are antibiotics and more than 169,000 childhood pneumonia deaths annually are caused by falsified antibiotics.⁶ Counterfeit and poor-quality antimicrobials not only fail to treat the cause of an infection, but may also foster the emergence of drug resistance.

The COVID-19 pandemic has also contributed to worsening global and local conditions regarding AMR. Recent reports evaluating the effects of COVID-19 on AMR indicate that levels of drug resistance have risen worldwide since the start of the pandemic. For example, a global review showed an increase in reported cases of some multidrug-resistant organisms in hospital settings after the pandemic began, a development attributed in part to the absence or weakening of infection prevention and control (IPC) protocols.⁷ Moreover, throughout the first two years of the pandemic there have been reports of widespread improper use of antibiotics in many countries, including many LMICs that have used them to treat non-serious cases of COVID-19 – even though WHO guidelines on the clinical management of COVID-19 do not recommend antibiotic therapy or prophylaxis in patients with mild/moderate COVID-19.⁸

Additional drivers of AMR include the incorrect use (including overuse) of antimicrobials outside the human sectors, including in animals, plants and crops, as well as the release of pharmaceutical manufacturing by-products and human and animal waste into the environment. If antimicrobials continue to be used indiscriminately in food production (including animal husbandry practices), the levels of resistant pathogens will continue to

rise, infections will become harder to treat, and outbreaks among food animals that can wipe out entire herds or flocks will become more likely. This could have a direct impact on food security due to higher food prices and food scarcity, with those living in poverty (including many children) facing dire health and well-being consequences.⁹

An important environment-related contributing factor in AMR is climate change, which can increase threats and risks both directly and indirectly. For example, unusual and lengthy droughts, more severe storms and other erratic weather patterns that can result in water shortages, food insecurity, poor sanitation and displacement are linked to climate change. Warmer temperatures on their own, a climate change impact in much of the world, are directly linked to increasing threats of drug resistance.

UNICEF's current and future roles: promoting safe and proper use of antimicrobials

Antimicrobial drugs are instrumental for global health and well-being and will continue to play that vital role around the world. It is therefore important that the AMR response does not focus on restricting access to antimicrobials but instead emphasizes the optimal use of these drugs. Effectively addressing AMR requires a global coordinated, intersectoral and interdisciplinary response that should be developed and implemented with a sense of urgency.

For UNICEF, this entails doing much of what it already does in regard to AMR in a more scaled-up and targeted fashion while also expanding support and programming as needed. UNICEF currently works to improve access to good-quality health services, potent antimicrobials and diagnostics through engagement with industry, as well as supply chain, procurement and financing initiatives. UNICEF supports AMR stewardship or coordinated programmes that promote the appropriate and rational use of antimicrobials through supporting countries in adopting and implementing WHO guidelines and initiatives regarding primary health care (PHC); universal health coverage (UHC); maternal, newborn, child and adolescent health; HIV; malaria; integrated management of newborn and childhood illness (IMNCI); and integrated community case management (iCCM).

To further harness UNICEF's strengths for the global response to AMR in a sustainable way, it will be necessary to strengthen institutional capacities relevant for AMR such as developing skills and competencies of teams around AMR, ensuring minimum levels of human resource capacity in key country offices, and investing appropriately on the implementation of programmes at scale that can lead to improved policy and programming around AMR.

As suggested above, much of the organization's ongoing work that is highly relevant for AMR is in three broad areas: disease prevention, AMR stewardship, and raising awareness and implementing social and behaviour change. These closely link with the three priority areas that this guidance document suggests will shape UNICEF's future AMR work:

- **Objective 1: Reduce the incidence of infection**
 - Entry points in this area: improve access to health and infection prevention services; strengthen health, community and supply systems; generate evidence to improve interventions
- **Objective 2: Ensure access to and optimal use of antimicrobial agents**
 - Entry points in these areas: promote antimicrobial stewardship; engage with industry to strengthen the global AMR response; support advocacy initiatives and access to medicines and diagnostics
- **Objective 3: Ensure awareness and understanding of AMR to improve political commitment and resource mobilization; catalyse social engagement and behavioural change to combat AMR**
 - Entry points in these areas: raise awareness of AMR and its impact on children; deploy social and behavioural change (SBC) interventions to address AMR; promote AMR educational initiatives among children and young people; empower community organizations to educate communities and prevent the emergence and spread of AMR at the community level



PURPOSE OF THIS GUIDANCE NOTE

This guidance note discusses the impacts of antimicrobial resistance (AMR) on the ability of the United Nations Children’s Fund (UNICEF) to achieve its mission and goals for children and how the COVID-19 pandemic has made it more difficult to confront the serious and growing global threat of AMR to child survival, growth and development. The document maps UNICEF’s existing programmes, many of which have direct (AMR-specific) and indirect (AMR-sensitive) impacts on the response to AMR, and identifies potential strategic areas for future engagement where UNICEF has comparative advantages in the global AMR response. Implementing activities to advance such strategic areas will further position UNICEF as a global leader in the prevention and treatment of drug-resistant infections among children.

The document is intended for use at multiple levels within UNICEF, including country, regional and global levels, and across divisions and sections. It serves to inform UNICEF’s internal initiatives, programming and activities, as well as external engagement with governments, partners and organizations concerned by the rapid spread and devastating implications of AMR among children.

This revised version of the AMR guidance note has been updated to consider lessons learned from and developments related to the COVID-19 pandemic. It reflects UNICEF's concerns that the threat has been made worse by the pandemic and identifies AMR-specific and AMR-sensitive actions in three priority areas: (1) reducing the incidence of infection; (2) ensuring access to and optimal use of antimicrobial agents; and (3) ensuring awareness and understanding of AMR to improve political commitment and resource mobilization and to catalyse social engagement and behavioural change to combat the threat.

UNICEF's expertise across various sectors and disciplines relevant for AMR allows the organization to pursue a multisectoral response to AMR on a global scale. It is important to recognize that UNICEF's existing and proposed work in response to AMR directly contributes to global efforts to achieve the Sustainable Development Goals (SDGs), and in particular SDG 3,¹⁰ as well as UNICEF priorities in its Strategic Plan 2022–2025. Of the Strategic Plan's five interconnected goal

areas, addressing AMR is especially relevant for the following three: Goal Area 1 – Every child, including adolescents, survives and thrives, with access to nutritious diets, quality primary health care, nurturing practices and essential supplies; Goal Area 4 – Every child, including adolescents, has access to safe and equitable water, sanitation and hygiene services, and lives in a safe and sustainable climate and environment; and Goal Area 5 – Every child has an equitable chance in life.

To ensure sustainable work on AMR across UNICEF, it will be necessary to strengthen institutional capacities relevant for AMR such as developing skills and competencies of teams around AMR, ensuring minimum levels of human resource capacity in key country offices, and investing appropriately on the implementation of programmes at scale that can lead to improved policy and programming around AMR. The coordination and collaboration necessary to work across sectors to address AMR are also in alignment with UNICEF's commitments to the Global Action Plan for Healthy Lives and Well-being for All.¹¹





1. INTRODUCTION

The World Health Organization (WHO) has declared antimicrobial resistance (AMR) one of the top health threats facing humanity.¹² It is steadily growing around the world and has particularly devastating effects on the health and well-being of children, with the poorest and most vulnerable bearing the brunt. According to a report on the global burden of AMR published in *The Lancet* in 2022, about 1 in 5 of the estimated 1.27 million people who died from antibiotic-resistant infections in 2019 were younger than age 5.¹³ That corresponds to a young child dying from AMR nearly every two minutes.¹⁴ All but less than 1 per cent were from low- and middle-income countries (LMICs).

AMR occurs when pathogens develop resistance to the antimicrobial drugs commonly used to treat a wide variety of infections. This makes many infectious diseases more difficult to treat and increases the costs of hospitalizations and treatment, the risk of spreading such diseases and the risk of death. AMR is further aggravated by the fact that the emergence and spread of drug resistance is far outpacing the rate at which new drugs capable of thwarting such infections are being developed.

The impacts span a huge range of health and well-being areas. Relatively common conditions such as urinary tract infections, respiratory tract infections and sexually transmitted diseases are becoming untreatable. Lifesaving medical procedures are becoming more dangerous due to the risk of infections with drug-resistant pathogens, and food security is threatened by drug resistance in agriculture. The World Bank has warned that AMR could cause damage to the global economy of up to US\$1 trillion and force over 28 million people into extreme poverty by 2050.¹⁵

AMR's effects have already been seen in many programmes operated or supported by UNICEF, and its impacts if unaddressed could be catastrophic. Similar to what has been observed

with other disease outbreaks and health crises such as the COVID-19 pandemic, the progress UNICEF has made towards improving children's development, health, survival and education could be halted or even reversed.¹⁶

Given the extent of these current and potential future impacts, more effective and targeted responses are needed from stakeholders across sectors, including governments, international organizations, donor agencies, the private sector, academia, professional organizations, civil society and communities. All should recognize their responsibility and work together to mitigate the impact of AMR on humans, animals and environmental health through a coordinated, multisectoral and interdisciplinary One Health approach.¹⁷

How AMR limits progress toward the SDGs

AMR negatively affects progress in achieving the overall 2030 Agenda for Sustainable Development, with its impact being especially direct on eight of the SDGs:¹⁸

- SDG 3 (good health and well-being): Losing effective antimicrobial drugs compromises the achievement of several targets for both communicable diseases (e.g., pneumonia, sepsis); conditions associated with non-communicable diseases (e.g., complications of diabetes); and lifesaving medical procedures (e.g., surgery, cancer treatment, organ transplantation, complicated deliveries, treatment of preterm babies).
- SDG 2 (zero hunger): The misuse of antibiotics in agriculture, particularly in regard to food-producing animals, threatens food security and the livelihood of farmers.
- SDG 8 (decent work and economic growth): Economic growth, which is closely linked to the achievement of many of the SDGs, can be undermined by AMR due to increased treatment costs to treat drug-resistant pathogens and lower economic productivity resulting from greater morbidity and mortality.
- SDG 5 (gender equality) and SDG 10 (reduced inequality): Like most infectious diseases, AMR's impact varies among different groups. Given what is known about who is most at risk – in particular socially and economically vulnerable individuals and groups such as women, children, migrants and refugees – drug-resistant infections exacerbate existing inequalities within societies.
- SDG 6 (clean water and sanitation), SDG 14 (life below water) and SDG 15 (life on land): Drug-resistant bacteria can contaminate soil and water sources used by humans and animals and spread into the environment through untreated waste or sewage, or through wastewater treatment facilities that are incapable of removing them from the wastewater.

In a welcoming signal that AMR is being taken more seriously as a threat over the course of the 2030 Agenda for Sustainable Development, two indicators on AMR were added in 2020 as part of SDG 3 (good health and well-being). They included indicator 3.d.2 – percentage of bloodstream infections due to selected antimicrobial-resistant organisms – and indicator 3.d.3: proportion of health facilities that have a core set of relevant essential medicines available and affordable on a sustainable basis (where antibiotics will be disaggregated from the core set of data used in the metadata).¹⁹

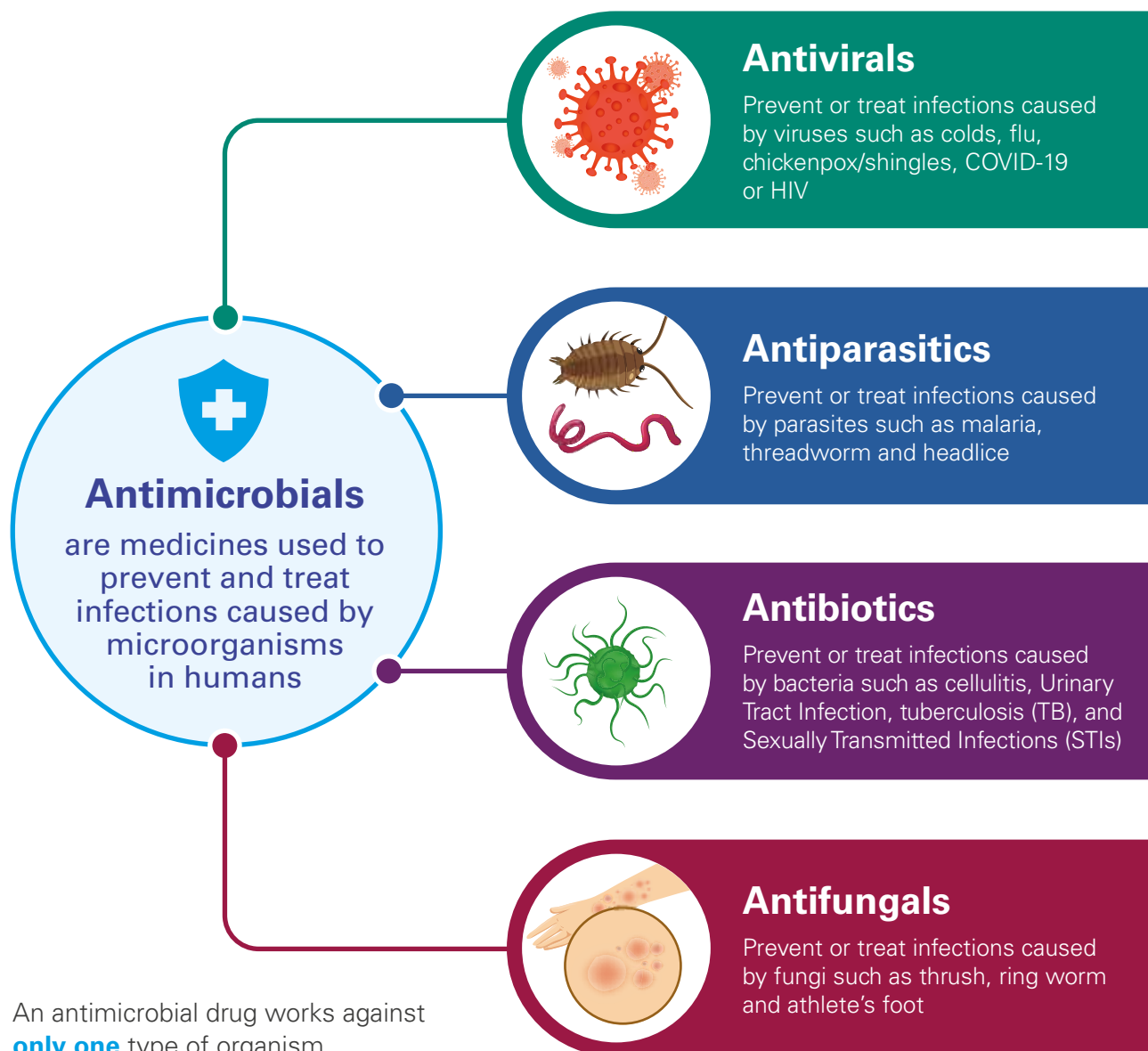


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2. AMR IN CHILD HEALTH AND SURVIVAL

What is AMR? AMR is a natural process whereby microbes change over time and develop ways to evade the antimicrobials that are meant to inhibit or kill them. This process is accelerated by the incorrect use of antimicrobial drugs, which include antibiotics (e.g., drugs used against bacterial diseases such as pneumonia, tuberculosis [TB], and typhoid fever); antivirals (e.g., antiretroviral drugs used to treat HIV infection); antiparasitic drugs (e.g., drugs used to treat malaria); and antifungals (also known as fungicides, including for example drugs used to treat yeast infections).

Resistance to antibiotics, antiretroviral drugs (ARVs), antimalarials and fungicides represents a significant danger to global health, with multidrug resistance in particular threatening to reverse gains made in the fight against major infections that are prevalent among children. Failure to stop the increase in drug-resistant pathogens coupled with limited and lagging development of effective new antimicrobials has the potential to result in a return to conditions before modern medicine when there were no antimicrobials to treat infectious diseases. Child survival rates and life expectancies in the antimicrobial era are far above what they were then due to the lifesaving impact of these medicines.

FIGURE 1 An overview of antimicrobials

Source: Adapted from UK Health Security Agency, Antimicrobials: a simple overview.

Impacts of AMR on children. AMR has been increasing at an alarming rate over the past 20 years.²⁰ According to comprehensive estimates for 2019, at least 1.27 million deaths worldwide were directly caused by drug-resistant infections that could not be successfully treated.²¹ An estimated additional 3.68 million people that year died with a resistant infection that might have contributed to their deaths.

Insufficient research has been undertaken and limited data made available to provide extensive insights into the impacts of AMR on children. What is known is of huge concern, however. Global estimates for 2019 indicate that children disproportionately carry the burden of deaths, with 254,000 of the 1.27 million deaths directly attributable to AMR – about 20 per cent of the total – occurring among those under the age of 5. This is equal to one child dying nearly every two minutes.²² Of those 254,000 children, more than 99 per cent are from LMICs and over half die in their first month of life.¹¹ In other words, only about 900 children in high-income countries (HICs) died as a direct cause from AMR compared with nearly 253,000 in LMICs.¹¹ To further put this in context,

in just one country, India, more than 56,000 children died in their first month of life in 2019 from infections resistant to antibiotics, and children in sub-Saharan Africa were 58 times more likely to die of AMR than those in HICs.¹¹

It is essential that children are not left behind in the global AMR response, which must explicitly address their specific needs and vulnerabilities. AMR has the potential to undo many of the gains in child health and well-being achieved by UNICEF and the global development community in recent years. For instance, there are major physical and financial costs to children and their families related to AMR affecting children, including impaired child development,²³ a loss in earnings due to hospitalizations, limited or inconsistent school attendance, and the consequences of higher toxicity and side effects of second-line antimicrobials that can lead to lifelong disability.²⁴ Costs related to failure to halt increasing AMR in general across society could include more precarious food security and the lack of effective antimicrobials to be used for surgery prophylaxis and organ transplants, or to ward off infections from cancer chemotherapy.²⁵



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Common causes of mortality among children due to infectious diseases: trends and impact of AMR

- Nearly one-third of newborn deaths are caused by systemic infections, also referred to as neonatal sepsis.²⁶ Up to 30 per cent of deaths from neonatal sepsis have been attributed to AMR. Recent reports indicate increasing rates of resistance to first-line and alternative therapies in some sub-Saharan African countries.^{27, 28}
- Across Africa, about 80 per cent of all malaria deaths occur in children under age 5.²⁹ Artemisinin-based combination therapies are recommended by WHO as the first- and second-line treatment for uncomplicated *Plasmodium falciparum* malaria as well as for chloroquine-resistant *Plasmodium vivax* malaria. However, artemisinin resistance has been spreading in parts of East Africa, including in Uganda and Rwanda, as well as in parts of Southeast Asia. This poses a real threat to other malaria-endemic regions³⁰ as there are currently no alternative antimalarial drugs with the same level of efficacy and tolerability.³¹
- An estimated 450,000 people worldwide in 2021 developed TB that was resistant to rifampicin, the most effective first-line drug. Also that year, nearly 142,000 people were diagnosed with multidrug-resistant TB (MDR-TB) and about 25,000 diagnosed with the even more severe extensively drug-resistant TB (XDR-TB).³² An estimated 5 million children are exposed to rifampicin-resistant TB (RR-TB) annually, and 30,000 children under 15 die every year due to RR-TB. Estimates also indicate that about 2 million children are exposed to MDR-TB and 100,000 to XDR-TB ever year.³³
- One out of every two infants newly diagnosed with HIV is infected with a virus already harbouring resistance to efavirenz or nevirapine, two of the most commonly used first-line ARVs.³⁴ Based on findings from 10 sub-Saharan African countries reported in 2021, resistance to first-line ARVs was as high as 45 per cent in infants newly diagnosed with HIV.³⁵ HIV drug resistance among people starting or restarting antiretroviral treatment (ART) has been increasing annually since the roll out of ART.¹⁹
- The deadliest bacterial infectious disease globally is pneumonia, which kills more than 700,000 children under the age of 5 every year.³⁶ This equates to 14 per cent of all under-five deaths and 22 per cent of all deaths in children aged 1 to 5 years. In Bangladesh, a study in one hospital found that nearly 90 per cent of children whose blood tested positive for bacteria were infected with antibiotic-resistant bacteria. Close to 20 per cent of these children had infections that were resistant to all routinely used antibiotics (e.g., ampicillin, gentamicin, ciprofloxacin and ceftriaxone). According to that study, children with antibiotic-resistant bacterial pneumonia were 17 times more likely to die than those without a bacterial infection.³⁷

CHILDREN'S RISK FACTORS FOR DRUG-RESISTANT PATHOGENS

People can be infected with drug-resistant pathogens even if they have never taken or been exposed to antimicrobials. Children are particularly vulnerable to diseases caused by drug-resistant microbes for reasons that include their immune systems not being fully developed and the process by which they learn and develop. Babies crawl on the ground and put their hands and objects in their mouths, unaware of risks and unable to make choices to prevent infection and protect their health.³⁸

Children living in poverty and those with limited access to basic services face heightened risk. Inadequate and inconsistent access to vaccinations and safe water, sanitation and hygiene (WASH) in communities, hospitals and schools make children in low-resource settings more vulnerable to AMR infections. The scope of the problem is massive; for example, approximately one in three primary schools worldwide do not have basic sanitation and water.³⁹ The lack of WASH infrastructure and supplies can also increase environmental levels of AMR, and thereby increase a child's risk of acquiring a drug-resistant infection, when people who have taken antibiotics release their waste in unsanitary ways. Improper waste management at health facilities is an important contributor to AMR in general, and health care facilities serving an estimated 680 million people in sub-Saharan African alone do not have basic waste management services.⁴⁰

Prolonged stays in health care facilities increase risks of hospital-acquired infections (HAIs). A recent study showed that up to 84 per cent of HAIs in LMICs displayed resistance to at least one antibiotic.⁴¹ Strong infection prevention and control (IPC) programmes in health facilities can help reduce such risks. IPC programmes aim to prevent patients, health workers and visitors to health care facilities from contracting and spreading avoidable infections, including those caused by drug-resistant pathogens.⁴² To date, however, fewer than half of LMICs have evidence-based and standardized national IPC guidelines.⁴³

Furthermore, preterm births, prolonged rupture of membranes and maternal infections are all risk factors for severe infections that often affect children, such as neonatal sepsis. These threats underscore the importance of access to high-quality antenatal, intrapartum and postnatal care.^{44, 45}

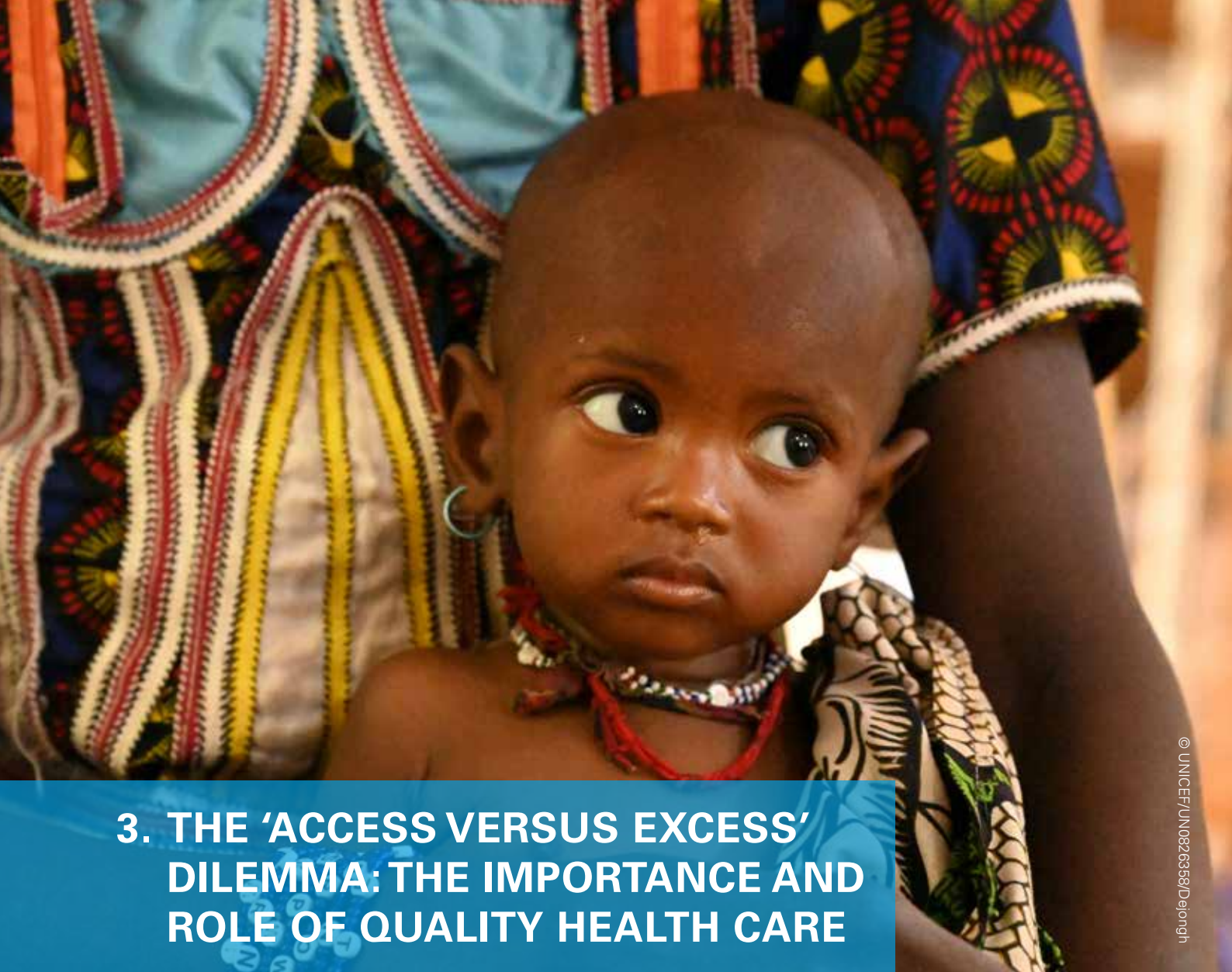
UNICEF has several longstanding initiatives to reduce infections in children, such as leading WASH, IPC and vaccine programmes and supporting countries in the development and implementation of WHO guidelines on intrapartum care and maternal and newborn health. (See the section of this document titled 'Harnessing UNICEF's strengths for the global response to AMR' for more details on what UNICEF is currently doing in these areas.)

The role of sex and gender in AMR

The interplay between sex and gender and their relation to AMR can best be exemplified by urinary tract infections (UTIs). UTIs are the third most common infections in people, but women and girls of all ages are more likely to contract a UTI than men or boys. Thus, UTIs are a risk factor for many but not all children. The susceptibility of women and girls to UTIs is due in part to anatomical differences, namely the length of the urethra and the sex-based variation in the levels of testosterone and estrogen. However, gender factors (social constructs or the psychosocial dimension) also play a role. For instance, lack of sanitized menstrual products, clean water and sanitation for personal hygiene during menstrual cycles also contribute to UTIs, with women in lower-income settings affected disproportionately. In some contexts, stigma and cultural beliefs around menstruation and women have led to women self-treating for sexual health and urinary problems such as UTIs.^{46, 47}

Other contextual examples of where gender plays a role in increasing women's and girls' risks for resistant infections include a preference for male children and gender-assigned household cooking roles. In areas where male children are preferred, boys were more likely to be taken to qualified health care professionals when ill than girls. In some lower-income settings women are more likely to cook with solid fuel at home, which exposes them to indoor air pollution and a greater risk of contracting pneumonia and acute lower respiratory diseases.⁴⁸





3. THE 'ACCESS VERSUS EXCESS' DILEMMA: THE IMPORTANCE AND ROLE OF QUALITY HEALTH CARE

Untreated pneumonia and sepsis are the cause of over a million child deaths each year.⁴⁹ If antibiotics were readily available and used properly, they could avert some 445,000 deaths in children under age 5 from community-acquired pneumonia alone.⁵⁰ Yet in addition to being directly responsible for such unnecessary deaths, the lack of access to quality health care (including appropriate use of antibiotics) further increases the levels of resistant pathogens.

Unrestricted sales and suboptimal use of antimicrobials

Even if patients access health services and are prescribed antimicrobials, they may not be able to afford the medicines, leading them to go without or to buy a lesser quantity and take only part of the prescribed therapy.⁵¹ One study in Uganda found that 29 per cent of respondents could not afford all the drugs prescribed to them for a full course of treatment and 48 per cent reported that their available funds determined the amount of drugs they purchased.⁵² Failure to take a full course of antimicrobial drugs or stopping and starting therapy often results in failure to overcome the infection. Moreover, suboptimal use can expedite the emergence of drug resistance due to insufficient exposure to the antimicrobial, which may allow microbes to change in order to replicate in the presence of the drug.

Meanwhile, people who cannot afford health services sometimes choose to self-treat by going to their local pharmacy or other outlets where antimicrobial drugs can be purchased over the counter without a prescription. Half of all antibiotic sales worldwide are due to such unrestricted sales,⁵³ which can cause or contribute to AMR when the medicines purchased are not appropriate for a specific infection or when they are used incorrectly (often due to patients' lack of knowledge). In countries where people are used to self-treating, this behaviour can be difficult to change. A study in the United States comparing self-medication practices among different populations found that those born in countries where antibiotics were available over the counter were significantly more likely to self-medicate themselves and their children with antibiotics than those born in countries where a prescription is required to obtain antibiotics.⁵⁴

Irrational prescribing and availability of potent antimicrobials

AMR is a naturally occurring process, but every time a microbe is exposed to an antimicrobial drug, there is a risk of speeding up the process. Excessive use of antimicrobials is one example of 'irrational' prescribing, a term used to refer to improper prescription practices for antimicrobials by physicians and others who prescribe medicines to patients. Excessive use and other irrational prescribing may occur when prescribers are not trained appropriately; are unsure of the cause of a patient's symptoms (e.g., lack of diagnostics, use of antibiotics against viral infections); or the correct antimicrobial and/or dosage is not available and another antimicrobial is prescribed instead.

The availability and use of reliable diagnostic tests are key to prescribing the correct antimicrobials. One study found that only 1.3 per cent of 50,000 medical laboratories surveyed in 14 countries throughout Africa conduct bacteriology testing.⁵⁵ Without appropriate diagnostics, prescribers cannot be certain if they should prescribe antimicrobials or which ones to prescribe. Yet, children under age 5 in LMICs receive an average of 25 prescriptions for antibiotics throughout their first five years of life.⁵⁶ In recent years there has been an increased focus on strengthening inpatient care of small and sick newborns, with the Every

Newborn Action Plan (ENAP) for example having a dedicated target of 80 per cent coverage of small and sick newborn care units at district levels.⁵⁷ The experience and data from countries that have scaled up these units show a tendency for irrational use of antibiotics among them, including disproportionately high use.⁵⁸

Yet even when diagnostic tests are reliable and conducted regularly and properly, good-quality antimicrobials may be unavailable. In India, research indicated chronic shortages by showing that only 50 per cent of required antibiotics were available in some states.⁵⁹ If the antimicrobial is available, it might not be in a dosage form suitable for children, of poor quality (e.g., suboptimal therapeutic strength), or it could be counterfeit (e.g., a fake drug not containing the stated active or therapeutic ingredients). WHO reports that 17 per cent of substandard or falsified medicines reported are antibiotics, and that more than 169,000 childhood pneumonia deaths annually are caused by falsified antibiotics.⁶⁰ Counterfeit and poor-quality antimicrobials not only fail to treat the cause of an infection, but may also foster the emergence of drug resistance. This can occur because they contain lower amounts of the active ingredient, which allows microbes to grow in the presence of sub-therapeutic doses of the antimicrobial.

It is therefore important that the AMR response does not focus on restricting access to antimicrobials but instead emphasizes the optimal use of these drugs. UNICEF currently works to improve access to good-quality health services, potent antimicrobials and diagnostics through engagement with industry, as well as supply chain, procurement and financing initiatives. UNICEF supports antimicrobial stewardship or coordinated programmes that promote the appropriate and rational use of antimicrobials through supporting countries in adopting and implementing WHO guidelines and initiatives regarding primary health care (PHC); universal health coverage (UHC); maternal, newborn, child and adolescent health; HIV; malaria; integrated management of newborn and childhood illness (IMNCI); and integrated community case management (iCCM). (See the section of this document titled 'Harnessing UNICEF's strengths for the global response to AMR' for more details on what UNICEF is currently doing in these areas.)

Linking community AMR efforts with primary health care (PHC) and universal health coverage (UHC)

It is difficult to address AMR in the absence of a good-quality PHC system. Such a system promotes health and disease prevention; has effective IPC and WASH services; includes an essential public health package with trained staff necessary to prevent and fight infections, including those caused by resistant pathogens; and ensures that a patient's first contact with the health system involves comprehensive, continuous, coordinated and patient-centred care. This comprehensive care includes vaccinations, the availability of effective antimicrobials and the rational use of those antimicrobials through antimicrobial stewardship programs that integrate monitoring of antimicrobial use and emerging resistant infections at the community level. In this way, prescribing can be based on accurate diagnosis and local resistance patterns.⁶¹

Expanding access to quality PHC is the main approach to attain UHC, which aims to ensure that all people and communities can receive the health services they need without experiencing financial hardship. Integrated care through PHC is key to providing good-quality and affordable care to communities. One such strategy is integrated community case management (iCCM), which provides community health workers (CHWs) with a simple treatment algorithm to treat children with fever, diarrhoea, coughing or breathing difficulties. CHWs in Pakistan trained in iCCM who treated children with severe pneumonia demonstrated lower treatment failure than those who referred patients to a health facility, largely due to treatment being initiated sooner.

Similarly, providers at the health care facility level are trained on integrated management of newborn and childhood illness (IMNCI) protocols that include clinical guidelines and standardised medical practices on criteria for prescribing antimicrobials. IMNCI-trained health providers are more likely to administer the first dose of an antimicrobial in the facility, to give patients information on the proper use of antimicrobials, and to prescribe antimicrobials appropriately even in facilities where diagnostics were not available.⁶²

Addressing AMR through a community-based approach also helps expand PHC and make greater progress towards UHC. For example, in the Lao People's Democratic Republic a campaign was launched to decrease infections in communities by distributing hygiene educational materials through families considered to be leaders in the community. In India, in an effort to increase public awareness of AMR and to decrease the inappropriate use of antimicrobials, the 'redline campaign' was initiated. It entailed labelling legitimate antimicrobial packaging with a red line.⁶³



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4. IMPROPER USE OF ANTIMICROBIALS BEYOND THE HUMAN SECTOR

Additional drivers of AMR include the incorrect use (including overuse) of antimicrobials in animals, plants and crops, as well as the release of pharmaceutical manufacturing by-products and human and animal waste into the environment.

Antimicrobials are often used as growth promoters in animals raised for food and other purposes (e.g., agriculture and aquaculture). Lack of adequate animal husbandry practices, transport, storage and processing exacerbates the problem, as do other factors in farming such as overcrowding that often prompt the use of antibiotics prophylactically to prevent the spread of infectious diseases among animals. Antimicrobials are also used in veterinary medicine for disease prevention and treatment in pets. Outside of some HICs, antimicrobials are widely used by farmers without veterinary supervision because of their relatively low cost and availability due to unrestricted sales. Antimicrobials are often used to boost crop productivity, including for vegetables, fruits and cut flowers. Furthermore, waste from animals that have been given antimicrobials may be used as fertilizer for crops.^{64, 65}

Vast amounts of evidence show that AMR in bacteria can colonize and infect humans by spreading through the food chain to consumers, through direct contact by anyone involved in meat and crop production, poor hygiene measures and unregulated slaughter practices.⁶⁶ The biggest and most direct public health threat caused by the overuse of antimicrobials in food production is foodborne illnesses, to which infants, young children, pregnant women, the elderly and people with weak immune systems are especially vulnerable. Foodborne illnesses range from mild and self-limiting to severe cases that are much more debilitating and sometimes even fatal. Undernourished infants and children are most at risk to develop severe infections.

If animal husbandry and production practices do not improve, and if antimicrobials continue to be used indiscriminately in food production, the levels of resistant pathogens will continue to rise, infections will become harder to treat, and outbreaks among food animals that can wipe out entire herds or flocks will become more likely. This could have a direct impact on food security due to higher food prices and food scarcity, with those living in poverty (including many children) facing dire health and well-being consequences.⁶⁷ These examples of AMR risk beyond the human sector underscore the extent to which AMR is driven by a large variety of factors (see Figure 2).

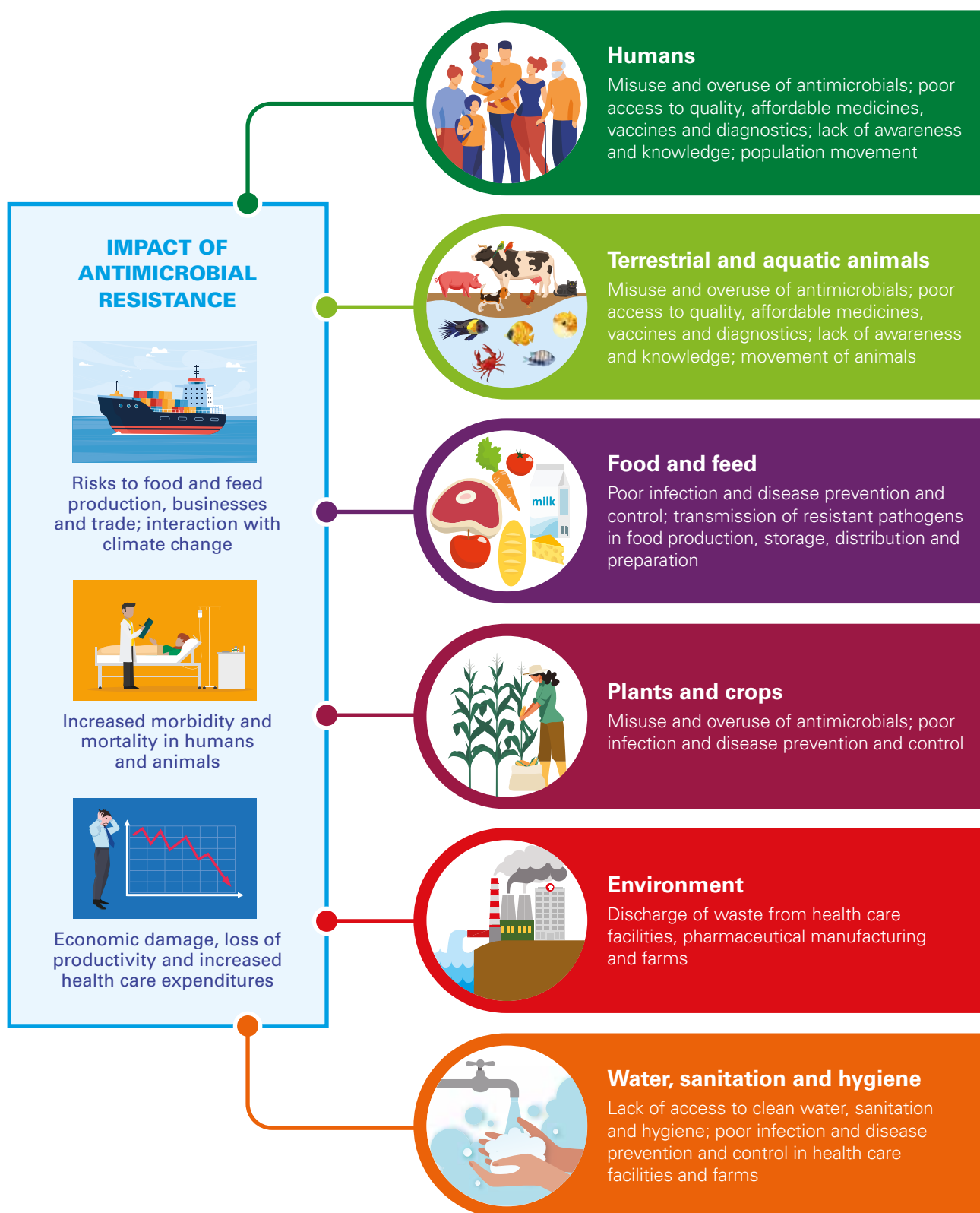
AMR AND CLIMATE CHANGE

An important environment-related contributing factor in AMR is climate change, which can increase threats and risks both directly and indirectly. For example, unusual and lengthy droughts, more severe storms and other erratic weather patterns that can result in water shortages, food insecurity, poor sanitation and displacement are linked to climate change. All of these consequences increase the likelihood of malnutrition and weak immune systems, which in turn make people more vulnerable to contracting infections.⁶⁸ Changes in weather patterns associated with climate change also contribute to the spread of resistant microbes. Flooding can spread resistant pathogens to areas where

there previously were none and can lead to sewer overflows, which increase risks of contamination of treated and clean water supplies.⁵⁴

More direct impacts of climate change include warming temperatures that expand the geographic area where many pathogens such as parasites that cause malaria can survive, thereby increasing levels of resistant microbes in circulation.⁶⁹ The higher temperatures coupled with increased concentrations of oxygen and carbon dioxide in the environment, which result from climate change, can increase the survival and proliferation of microbes.⁷⁰ Higher temperatures also increase the rate at which microbes become resistant to treatments.⁵⁴

FIGURE 2 Drivers of AMR⁷¹



Source: Adapted from Figure 1 in World Health Organization, No Time to Wait: Securing the future from drug-resistant infections. Report to the Secretary General of the United Nations, April 2019.



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5. COVID-19 AND AMR

Recent reports evaluating the effects of COVID-19 on AMR indicate that levels of drug resistance have risen worldwide since the start of the pandemic. For example, a global review showed an increase in reported cases of some multidrug-resistant organisms in hospital settings after the pandemic began, a development attributed in part to the absence or weakening of IPC protocols.⁷²

In the United States alone, both drug-resistant HAIs and deaths from HAIs increased by 15 per cent in the pandemic's first year.⁷³ The number of cases associated with an emerging multidrug-resistant fungus, *Candida auris*, in US hospitals increased by 60 per cent from 2019 to 2020.⁷⁴ *Candida* species are a common cause of life-threatening bloodstream infections typically acquired in hospitals and only three classes of antifungals are available to treat severe cases. Another complication is that many clinical laboratories cannot test *Candida* for drug resistance.⁷⁵ In another example of the surging health threat over the same period, HAIs caused by carbapenem-resistant *Acinetobacter* increased by 78 per cent. Carbapenem is a last line of defence antibiotic, which makes this resistant pathogen nearly untreatable.⁷⁶

The increase in these and other AMR cases in the first year of the pandemic was likely due to overcrowding of sicker patients, staff shortages and poorer adherence to IPC protocols and practices such as hand hygiene, cleaning equipment, separating patients and using personal protective equipment (PPE).⁷⁷ Globally, analysis showed that predictors of getting an infection due to resistant pathogens during the pandemic included being in an intensive care unit (ICU), having diabetes, being on antibiotics and being in an LMIC.⁷⁸

The WHO guidelines on the clinical management of COVID-19 do not recommend antibiotic therapy or prophylaxis in patients with mild/moderate COVID-19.⁷⁹ For COVID-19 patients with severe or critical disease, the WHO recommends the collection of blood cultures prior to initiation of antimicrobial therapy and that antibiotics be chosen based on the Access, Watch and Reserve (AWaRe) classification, in which antibiotics are organized in three different groups used for antibiotic stewardship with the aim of optimizing antibiotic use and reducing antibiotic resistance. In the AWARe system, antibiotics in the Access group should be used as first-line treatment for bacterial infections and should be widely available; Watch group antibiotics have a higher potential for resistance and could be used as first- or second-line treatment; and antibiotics in the Reserve group should be reserved for treatment of confirmed or suspected infections due to multidrug-resistant organisms.⁸⁰ Yet despite these WHO recommendations discouraging use of antibiotics to treat most cases of COVID-19 infection, a review of national treatment guidelines for COVID-19 in 10 African countries revealed that three countries recommended antibiotics in mild/moderate COVID-19 cases, including drugs from the Watch category.⁸¹

Although misguided and potentially harmful to public and individual health, these countries' guidelines are perhaps not surprising given the history of antibiotic use in response to the new virus. During the first two years or so of the pandemic, antibiotics were commonly prescribed globally regardless of guidelines and whether a patient had mild, moderate or severe COVID-19. According to WHO's Clinical Platform for COVID-19, nearly 4 of 5 patients (79 per cent) admitted to hospitals around the world for COVID-19 in 2020–2021 received at least one antibiotic, and there was often no difference in Watch and Reserve antibiotic therapy between severe/critical patients and mild/moderate ones. In many cases, mild/moderate

patients were treated with two or more antibiotics.⁸² In addition, a global systematic review showed that although only 6 per cent of 76,176 COVID-19 cases reviewed had bacterial or fungal co-infections, 62 per cent received antibiotics.⁸³

In general, antibiotic use increased during the pandemic, including in outpatient settings involving people who had not been diagnosed with COVID-19. A study in the United Republic of Tanzania and Uganda showed that close to 80 per cent of pharmacies and drug outlets in Uganda and more than 40 per cent in Tanzania sold antibiotics without a prescription during the pandemic.⁸⁴ Of those sellers, more than 70 per cent in Uganda and 30 per cent in Tanzania, respectively, sold antibiotics to patients they suspected had COVID-19 without confirming whether a co-infection was present.⁸⁵ Several reports indicate that overall antimicrobial use increased in children as well after the start of the pandemic. A study in Spain, for example, showed that both antibiotic and antifungal use rose in children under 18 years during the first wave of COVID-19.⁸⁶

The detection and reporting of antimicrobial resistance data slowed significantly during the pandemic due to changes in patient care, laboratory supply challenges and the decreased capacity of health care facilities in much of the world to focus on routine detection and data-gathering processes. For instance, drug-sensitive TB diagnosis and screening fell by over 40 per cent across 24 countries in Africa and 7 countries in Asia from 2019 to 2020.⁸⁷ This development is likely partially responsible for a 19 per cent decrease in the number of people treated for drug-resistant TB between 2019 and 2020 globally.⁸⁸

Access to and uptake of longstanding effective high-coverage interventions for preventive health have also been negatively affected by the pandemic. It was estimated that 23 million children missed out on basic childhood vaccines in 2020, the highest number since 2009. As many as 17 million did not receive any vaccinations at all in 2020.⁸⁹ The global decline in vaccine coverage, combined with and exacerbated by a vocal and influential anti-vaccine movement and increased vaccine hesitancy, may lead to the re-emergence of vaccine-preventable diseases and the subsequent inappropriate use of antimicrobials to treat them. This development would further fuel the drug-resistance crisis.⁹⁰



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6. GLOBAL AMR COOPERATION AND COORDINATION

Effectively addressing AMR requires a global coordinated, intersectoral and interdisciplinary response that should be developed and implemented with a sense of urgency. Currently, AMR is under the global leadership of four UN organizations: WHO, the Food and Agriculture Organization (FAO), the World Organisation for Animal Health (WOAH) and the United Nations Environment Programme (UNEP), also known as the Quadripartite.⁹¹ These organizations separately but collectively are assigned to tackle the human, animal, plant and environmental drivers fuelling AMR. An AMR Quadripartite Joint Secretariat (QJS) was established with a mandate to ensure collaboration with other UN agencies and stakeholders, including UNICEF. Within the Quadripartite, WHO's main role is to lead the human sector global public health efforts including to promote research and development (R&D) and monitor the AMR burden and response.^{92, 93}

UN Member States in September 2016 during the 71st General Debate of the UN General Assembly adopted a political declaration on AMR. Presiding UN Secretary-General Ban Ki-moon urged strong action, noting that AMR poses a fundamental, long-term threat not only to human health, but also to sustainable food production and development in all parts of the world.⁹⁴



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7. HARNESSING UNICEF'S STRENGTHS FOR THE GLOBAL RESPONSE TO AMR

UNICEF has the capacity to pursue a global, multisectoral response to drug-resistant infections. Fighting AMR therefore should be understood as being central to UNICEF's core values and commitments. The organization can add significant value to the global AMR response by building on core competencies and priorities, including by strengthening existing programmes that mitigate the impact of AMR on child survival, growth and development.

UNICEF is present in 192 countries and territories as a leading voice and advocate for children at both national and sub-national levels, supporting governments to reach the most vulnerable and marginalized populations, especially in challenging environments and hard-to-reach communities. UNICEF is a trusted partner with a solid reputation for expertise across sectors and disciplines, and the organization has strong networks and strategic partnerships with UN partners and academic and research institutions that enable it to efficiently and effectively develop, gather and analyse evidence that can inform policy on paediatric AMR. These comparative advantages allow UNICEF to pursue a multisectoral response to AMR.

Much of the organization's ongoing work that is highly relevant for AMR is in three broad areas: disease prevention, antimicrobial stewardship, and raising awareness and implementing social and behaviour change.

Disease prevention

UNICEF improves access to disease prevention initiatives by scaling existing services, such as expanding WASH services to households, schools and health facilities⁹⁵ and promoting and supporting immunization. As the world's largest buyer of childhood vaccines, the organization supports governments by financing procurement and delivery of vaccines in addition to WASH commodities and services. UNICEF's immunization-related activities include support and advocacy for the introduction of new vaccines, investment in supply chains, and support for responses to adverse events following immunization. These activities are key parts of ongoing efforts to mitigate negative perceptions towards vaccination and ensure vaccine acceptance and immunization coverage.

UNICEF's work in other key areas related to disease prevention among children include in nutrition, such as promotion of exclusive breastfeeding and food supplementation and fortification, and counselling on optimal food preparation and storage to prevent contamination – all activities that can help to prevent infections. The organization's HIV and AIDS programme is dedicated to preventing and treating HIV among women, children and adolescents, especially the most marginalized. Through this programme, UNICEF is supporting the delivery of lifelong antiretroviral treatment to pregnant and lactating women living with HIV to prevent mother-to-child transmission of the virus and expanding access to adolescent-friendly services such as pre-exposure prophylaxis (PrEP) to reduce HIV infection risk. Through its promotion and support of treatment adherence among adolescents and women living with HIV, it helps to reduce the emergence of HIV drug resistance.

To help address the persistent challenges of TB, UNICEF is seeking to close the gaps in case detection, prevention and treatment for childhood

and drug-resistant TB through decentralized service delivery models and integrated child- and family-centred approaches. Such efforts are characteristic of UNICEF's overall disease prevention initiatives that include developing, implementing and advocating for policies that promote effective enabling environments for child health (such as allowing treatment at the community level and seeking to achieve universal health coverage). As part of this work, UNICEF is expanding IMNCI and iCCM in health facilities to reduce major causes of child mortality, including pneumonia, diarrhoea, malaria, severe acute malnutrition, newborn infections, TB and HIV.

To make services accessible to all and thus uphold the principle of equity, UNICEF and partners established the Every Newborn Action Plan (ENAP),⁹⁶ a global road map to reduce newborn mortality launched in 2014. UNICEF supports countries in achieving mortality reduction by promoting adoption of ENAP to improve the quality of newborn care services and practices and increase the percentage of women who deliver in a health facility. As part of this commitment, UNICEF supports countries to provide essential packages of high-quality maternal and newborn services such as home visits, emergency obstetric care, small and sick newborn care, and 'kangaroo care' (skin-to-skin contact between caregivers and preterm babies to increase their chances of survival).

UNICEF's support for strengthening health and community systems – including health infrastructure and capacity – is also an essential component of broader disease prevention among children. A top focus is on making systems more resilient to shocks and better able to manage several health priorities and emergencies simultaneously. For instance, UNICEF, jointly with partners, works to build capacity of health care providers to implement IPC as a first step to minimizing infections that could lead to inappropriate antibiotic use.

Antimicrobial stewardship

UNICEF actively supports programmes and governments to select antimicrobials appropriate to their context and collaborates with industry and partners to promote the adaptation of existing products and development of new ones to ensure more rational use of antimicrobials. A central priority is to respond to the unmet needs of children, including in terms of paediatric formulations of drugs, and to promote appropriate use of antimicrobials among them. These are essentially antimicrobial stewardship programmes, though not always branded as such, and they rely on health care professionals' ability to diagnose and manage infections – and therefore the availability and use of diagnostics are as important as the drugs themselves. Such stewardship policies should be implemented at all health system levels.

UNICEF supports antimicrobial stewardship in HIV/AIDS programmes by facilitating timely transition to different approved treatment regimens upon detection of treatment failure, a step that is crucial for preserving existing antiretroviral drugs and minimizing the development of HIV drug resistance and the spread of drug-resistant strains. Other important initiatives with the same goals in HIV programming include improving access to drug adherence counselling and viral load monitoring in children, adolescents and mothers in order to prevent and detect treatment failure as early as possible.

UNICEF coordinates antimicrobial stewardship efforts to promote the effective management of malaria cases, from appropriate diagnosis of malaria to improved administration of antimalarials and antibiotics within the context of holistic management of the febrile child at the community level. Through this work, UNICEF provides technical and financial support to adopt and scale up evidence-based guidelines for appropriate antibiotic use for the treatment of malaria infection in infants aged less than 2 months at primary level of health care facility. These guidelines also

highlight the importance of prompt referral to hospitals for these infants even after they have initiated proper antibiotic treatment.

More broadly, UNICEF is expanding coverage of institutionalized community health programmes that ensure appropriate use of quality-assured medicines through implementation of IMNCI/iCCM guidelines. An important element of this work is its support for the development and scale-up of diagnostics (e.g., rapid diagnostic tests, acute respiratory infection diagnostic aids) to improve diagnosis and guide clinical management of childhood illness, which encourages more rational use of antimicrobials both in community and facility levels. UNICEF supports product selection, procurement and delivery to the frontline of quality-assured essential diagnostics and antimicrobials for childhood conditions, as well as in evidence generation and dissemination around innovative approaches to improve the diagnosis and care of infectious diseases including pneumonia, HIV (including early infant diagnosis), and malaria in the context of fever management.

Raising awareness and implementing social and behaviour change

UNICEF's ongoing social and behaviour change (SBC) efforts focus on preventive practices such as vaccination, hygiene promotion, timely care-seeking, adequate nutrition and broader efforts around HIV, TB and malaria prevention, as well as curative practices such as rational drug use and adherence to and completion of treatment regimens. Currently, UNICEF's SBC efforts include promoting WASH initiatives like Hand Hygiene for All;⁹⁷ implementing behavioural change strategies that are important for effectively promoting the use and maintenance of WASH infrastructure; promoting community acceptance of new vaccines; promoting adherence to completion of antibiotic treatment for diseases such as acute respiratory infections, TB, etc.; and promoting exclusive breastfeeding supplementation.



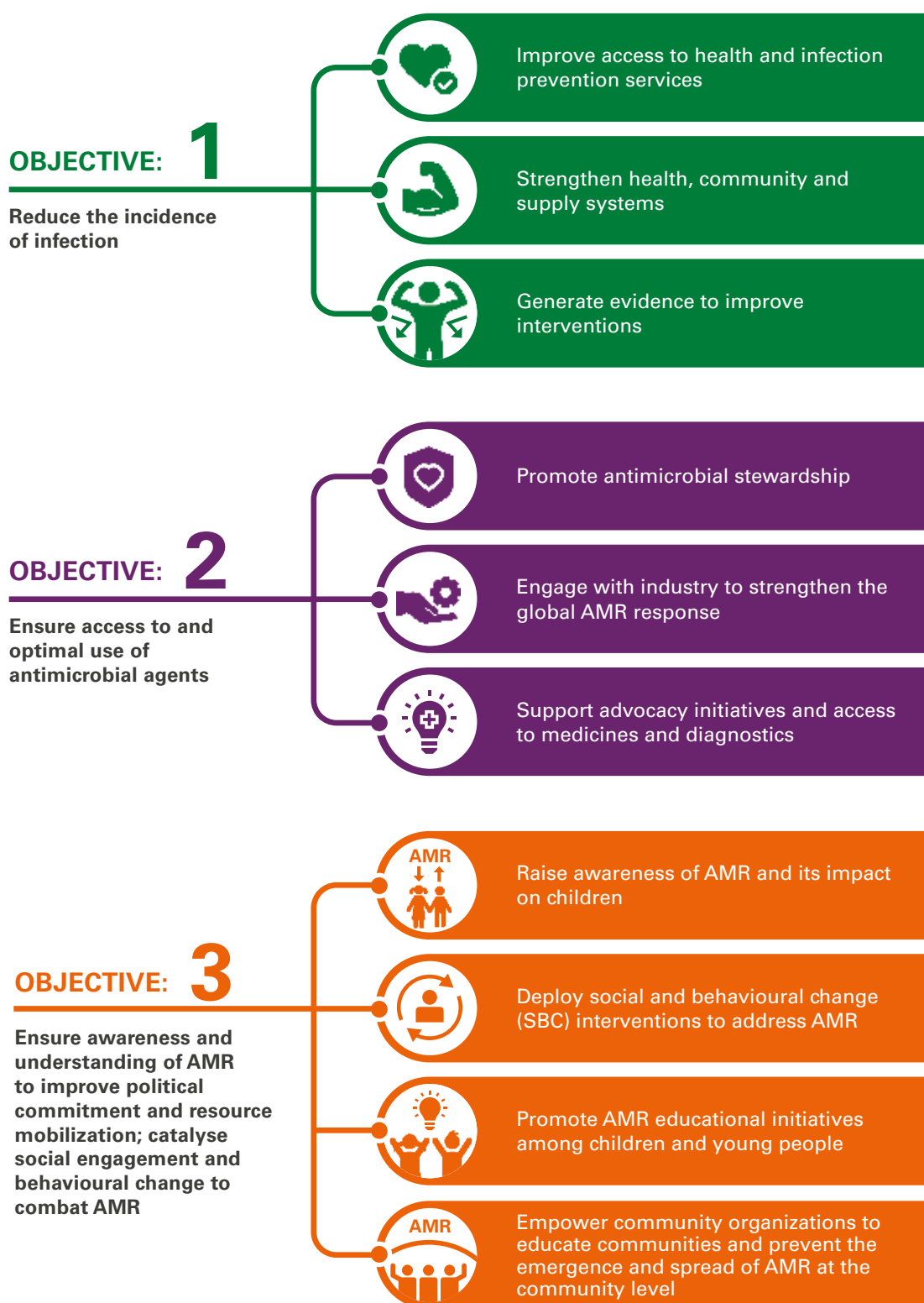
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8. THREE PRIORITY AREAS SHAPE UNICEF'S CURRENT AND PROPOSED AMR WORK

UNICEF's engagement in tackling AMR aligns with global efforts in achieving the SDGs, the Global Action Plan for Healthy Lives and Well-being for All and WHO's Global Action Plan on AMR as well as the organization's contributions toward advancing child-centred primary health care and the UHC agenda. All of these are important components of successful efforts to achieve goal areas 1, 4 and 5 of the UNICEF Strategic Plan 2022–2025.⁹⁸

More extensive UNICEF engagement on AMR would build on UNICEF's current work and comparative advantages in three main priority areas, each of which is framed as an objective in this guidance:

1. Reduce the incidence of infections;
2. Ensure access to and optimal use of antimicrobial agents; and
3. Ensure awareness and understanding of AMR to improve political commitment and resource mobilization, and catalyse social engagement and behavioural change to combat AMR.

FIGURE 3 Three Priority Objectives for AMR

OBJECTIVE 1

REDUCE THE INCIDENCE OF INFECTION

Preventing the spread of disease reduces the incidence of infection and minimizes the need for antimicrobial drugs. Disease prevention can be achieved by reaching zero-dose children/communities through immunization, creation of healthy environments and reduced exposure to pathogens through IPC and hand hygiene for all initiatives, health systems strengthening, education and SBC, assisted births and clean deliveries, early and exclusive breastfeeding, and appropriate complementary feeding practices.

Listed below are proposed entry points for how UNICEF can further help to reduce the incidence of infections among children by improving access to health and IPC services, strengthening systems, and generating research and evidence that can then be used to inform future work.

Improve access to health and infection prevention services

- Support advocacy efforts to improve and expand WASH services in communities, schools and health care facilities.
- Support introduction and scale-up in LMICs of new products (e.g., vaccines, diagnostics) that are appropriate for low-resource settings and paediatric formulations of new antimicrobials, as they become available.
- Build and maintain existing immunization initiatives such as the introduction of new vaccines to fight major killers of children (e.g., pneumococcal disease and rotavirus) and support supplementary immunization campaigns and outbreak response to reduce the burden of disease and consequent antimicrobial use.
- Scale up iCCM, including in emergency and humanitarian settings.
- Support adoption of service delivery models within a 'treat all' strategy for HIV to ensure uninterrupted ARV supply and to maximize retention in care and adherence to treatment, particularly among highly vulnerable groups such as adolescents, pregnant and breastfeeding women and key populations.⁹⁹
- Collaborate closely with WHO and partners to promote the rapid uptake of new, child-friendly treatments for TB and drug-resistant TB.
- Accelerate access to point-of-care diagnostic technologies and strengthen auxiliary health and laboratory systems that support such technologies.

Strengthen health, community and supply systems

- Improve supply chain systems to ensure availability of drugs and commodities to prevent and treat infectious diseases at the frontline.
- Support national governments to strengthen community health systems, including building the capacity of community health workers to deliver an integrated package of preventive, promotive and basic curative services.
- Support resource mobilization efforts to improve WASH services in communities, schools and health care facilities.
- Coordinate with other pooled procurement and/or funding mechanisms – e.g., the Global Drug Facility, the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund), the US Agency for International Development (USAID) and the US President’s Emergency Plan for AIDS Relief (PEPFAR) – to improve access to antimicrobials for those who need them while supporting policies, regulatory frameworks, supply chain and programmatic interventions to prevent their irrational use.
- Leverage Gavi, the Bill & Melinda Gates Foundation and the US Centers for Disease Control and Prevention (CDC) investments, together with other collaborations, to enhance the contribution of immunization to addressing AMR (e.g., advocating for resources in Gavi’s new strategic plan).
- Improve affordability of vaccines through pooled procurement services, market shaping and efforts by UNICEF’s Supply Division to reduce vaccine costs, especially for middle-income countries.
- Build on ongoing efforts to institutionalize integrated PHC supply chain management.
- Support quality improvements to IMNCI implementation.
- Provide technical support for developing and implementing of national AMR action plans; linking them as appropriate to maternal, newborn and child health programmes; and ensuring these plans are prioritized in both surveillance and policy changes.

Generate evidence to improve interventions

- Support evidence-generation efforts to improve WASH services in communities, schools and health care facilities.
- Strengthen implementation research aimed at increasing access to and uptake of vaccinations, reducing inequities, and achieving national and global coverage targets.
- Conduct a review to identify key drivers of inappropriate antimicrobial consumption, the role of supply chains and distribution in addressing AMR, and the potential and use of non-physicians as competent antibiotic prescribers. Such a review should also consider the degree to which promotive and preventive interventions reduce the need for antibiotics and effective methods for implementing stewardship programmes in LMICs that do not restrict antibiotics from children who need them.
- Accelerate access to virologic HIV testing in infants by introducing innovative point-of-care diagnostic technologies and strengthening the enabling environment around decentralized testing.
- Ensure that research and development efforts target the needs of children.

Addressing AMR through iCCM in Zambia

CHWs train in integrated community case management (iCCM) have the skills and knowledge to provide a package of essential health services to treat pneumonia, malaria, diarrhea, malnutrition and other causes of child mortality. They are especially important to efforts to reduce mortality in the hardest-to-reach communities.

A study in Zambia¹⁰⁰ showed that of 537 observations, 92 per cent of children suspected of having pneumonia, or had fast breathing, were treated correctly with antibiotics by CHWs through iCCM. CHWs in the country are trained with simple job aids that include clinical algorithms, diagnostic tools and have antimicrobials in color-coded blister packaging that they can give to their patients.

Through supportive supervision, CHWs in Zambia are essentially practicing antibiotic stewardship. Another example is that they often counsel caregivers to adhere to correct treatment regimens by giving instructions on the number of doses to be given per day and the number of tablets per dose. The study noted that some of the CHWs interviewed specially mentioned that their patients valued guidance in the necessity of finishing a course of antibiotics.

The findings of this study are important not only in Zambia, but nearly everywhere else in the world. Since the main drivers of AMR include antimicrobial use without a prescription, the use of poor-quality and counterfeit antimicrobials, and not taking the antimicrobials as directed, iCCM-trained CHWs have the potential to improve rational use of antimicrobials and reduce the spread of AMR.



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OBJECTIVE 2

ENSURE ACCESS TO AND OPTIMAL USE OF ANTIMICROBIAL AGENTS

Stewardship programmes are essential to address the ‘access versus excess’ dilemma by ensuring access to antimicrobials to those who need them while preventing excessive or irrational use among those who do not need the drugs.

Listed below are proposed entry points for how UNICEF can further ensure access to and optimize the use of antimicrobial agents among children through advocacy efforts, implementing antimicrobial stewardship initiatives and engaging with industry.

Promote antimicrobial stewardship

- Encourage national health authorities, including regulators, to ensure that national guidelines and essential medicines lists are aligned with WHO recommendations, notably the AWaRe (Access, Watch, Reserve) categorization of antibiotics in the Essential Medicines List for Children. This may require supporting local adaptation of the stewardship programmes that ensure access to antibiotics in the Access category but prevent the excessive use of Watch and Reserve antibiotics throughout the health care delivery system.
- Evaluate interventions aimed at improving the rational use of antimicrobial drugs.
- Support capacity building to improve quality of care – e.g., proper use of diagnostics, changes in prescribing practices, and efficient patient flow within health facilities through stewardship committees.
- Strengthen the interpersonal communication skills of health providers and other relevant providers (e.g., pharmacists) to promote rational use of antibiotics.
- Build antimicrobial stewardship capacity of the vast UNICEF-supported networks of community workers for integrated package of service delivery.
- Align AMR work with the multisectoral approach to immunization service delivery within the primary health care platform.
- Integrate antimicrobial stewardship with UNICEF’s renewed emphasis on reaching mothers and adolescents with immunization services to address issues related to proper use of antibiotics.
- Engage community health workers and other community-based agents in supporting rational antimicrobial drug use.
- Support private-sector providers to ensure adherence to management and treatment guidelines, an important activity that recognizes the increased availability and uptake of private services.

Engage with industry to strengthen the global AMR response

- Leverage UNICEF's leadership role to engage with industry to develop and expand immunization-related innovations and new approaches to help reduce the threat of AMR.
- Encourage industry to ensure responsible disposal of antibiotic manufacturing waste, including through UNICEF's procurement mechanisms and upgrades to manufacturing facilities.
- Facilitate collaborations with developers and suppliers of products for prevention, diagnosis and treatment of infectious diseases affected by AMR.
- Incentivize development of innovative point-of-care AMR diagnostic technologies.
- Support procurement, introduction and scale-up of new portable devices and technologies for detection of fake and counterfeit antimicrobials.
- Work with industry and partners to ensure supply security, access to and preservation of existing antimicrobials through development of healthy markets, stewardship promotion, public health-oriented marketing and distribution practices, and adaptations of packaging and instruction materials to facilitate rational use.
- Work with industry regulators and policy makers to ensure that there is a pipeline of new antimicrobials that provide better options for children and adolescents.

Support advocacy initiatives and access to medicines and diagnostics

- Develop a global advocacy strategy and adaptations to national contexts to achieve policy and programmatic changes to reduce the threat of AMR.
- Ensure availability of quality-assured diagnostics and antimicrobials through UNICEF's procurement mechanism.
- Coordinate with other pooled procurement and/or funding mechanisms (e.g., the Global Drug Facility, the Global Fund, USAID, PEPFAR) to improve access to antimicrobials for those who need them while supporting policies, regulatory frameworks and supply chain and programmatic interventions to prevent their irrational use.
- Support country participation in HIV drug-resistance testing programmes.
- Support the expansion of coverage, quality and use of diagnostic tests, including the roll out of point-of-care diagnostic technologies, and strengthen literacy of health care workers on how to interpret results.

An implementation research approach to AMR stewardship in Tanzania

Findings from a 2015 Global Antimicrobial Resistance Partnership (GARDP) surveillance study in the United Republic of Tanzania showed increasing trends of antibiotic resistance. Over a six-year timespan, resistance to an antibiotic commonly used to treat *Streptococcus pneumoniae* increased from 25 to 80 per cent for children under age 5 in the country. The following year, results from Tanzania's 2016 International Health Regulations (IHR) Joint External Evaluation indicated that AMR was a major problem.

These findings led the Government of Tanzania to take action to try to reduce antibiotic misuse in the country. Although antibiotic use requires a prescription in hospital settings, antibiotic misuse remained high for various reasons including prescriptions without diagnostics, and antibiotic shortages in hospitals that led patients to seek community pharmacies and accredited drug dispensing outlets (ADDO) where antibiotic control is limited, and patients could not always afford complete antibiotic regimens. All of these findings pointed to the need for robust antimicrobial stewardship programmes that implement antibiotic use evaluation and monitoring in health facilities, regularly review and update standard treatment guidelines, train health care providers, and create and promote AMR community awareness and One Health initiatives.

When the government launched the National Action Plan on Antimicrobial Resistance (NAPAR) for 2017–2022, key strategies included a coordinated response and strengthening of national antimicrobial stewardship programmes. Activities undertaken have included the development of hospital formularies, the establishment and strengthening of medicine and therapeutic committees, and training of health care providers (e.g., prescribers, pharmacists, nurses and laboratory personnel).

With the support of UNICEF and Wellcome Trust, the government conducted a series of quantitative and qualitative studies to investigate antibiotic use in the paediatric population three years after the launch of the NAPAR and to devise concrete recommendations moving forward. These studies included examining knowledge, attitudes and practices among parents/caregivers, health care providers, and dispensers regarding the rational use of antibiotics among children.

In summary, about 89 per cent of parents/caregivers surveyed had poor knowledge, practices and attitudes on the rational use of antibiotics, with education and family income found to be determinants of good rational antibiotic use. The majority of prescribers (82 per cent) and dispensers (80 per cent) had good knowledge of rational antibiotic use in children but reported poor practices (70 per cent among prescribers and 48 per cent among dispensers). ADDO dispensers were willing to dispense antibiotics without a prescription 90 per cent of the time in simulated patient cases, and 83 per cent were willing to provide incomplete regimens.

Best practices from Tanzania that can be applied towards improving the rational use of antibiotics in children include more engagement of communities in the implementation of antimicrobial stewardship programmes, launching community awareness campaigns, and building capacity through continuing education of antimicrobial stewardship programmes in all health facilities at regional levels as stipulated in the Tanzania NAPAR, as well as in dispensaries.

OBJECTIVE 3

ENSURE AWARENESS AND UNDERSTANDING OF AMR TO IMPROVE POLITICAL COMMITMENT AND RESOURCE MOBILIZATION; CATALYSE SOCIAL ENGAGEMENT AND BEHAVIOURAL CHANGE TO COMBAT AMR

Improving awareness and understanding of AMR through effective communication, education and training are necessary to catalyse social engagement and positive behavioural change. SBC strategies can promote changes in behaviour that result in more rational use of antimicrobials, based on an understanding of the factors that drive their inappropriate use.

Listed below are proposed entry points for how UNICEF can further ensure that stakeholders understand AMR, including how it affects children, and value AMR-reducing services by raising awareness, implementing SBC strategies and education initiatives, and facilitating greater community engagement.

Raise awareness of AMR and its impact on children

- Strengthen awareness of the risks of HIV drug resistance among health care workers and improve the quality of ART service delivery to prevent emergence of resistance.
- Build drug-resistance language into all relevant technical materials, guidance documents and tools.
- Engage health care providers to increase awareness of AMR in paediatric populations and promote optimal drug use.
- Use traditional and social media outlets to reach health care workers and the general public with messages and information about AMR.
- Develop an AMR communications package that is easily accessible and shareable by country and regional offices and includes succinct key messages, talking points, priority actions, scientific knowledge and meaningful data.
- Develop a global communication strategy to increase awareness of AMR.
- Develop an internal AMR communications strategy to catalyse institutional momentum, which could facilitate increased collaboration, awareness campaigns and funding.

Deploy social and behavioural change (SBC) interventions to address AMR

- Seek to better understand the beliefs and values, as well as the psychosocial and cultural triggers, that drive antibiotic consumption and how to broaden access to quality-assured, essential antibiotics in low-resource settings.
- Apply new behaviour change tools such as behavioural insights to addressing AMR.

- Leverage SBC platforms (e.g., faith-based, community, social media/digital) as well as collaboration with relevant public- and private-sector partners (e.g., in the media) to promote rational use of antibiotics and preventive behaviours.
- Build on UNICEF's ongoing efforts aiming to improve the capacity of UNICEF staff, governments and civil society partners to implement data-driven SBC interventions.
- Support demand creation for diagnostics (e.g., HIV viral load testing, antibiotic susceptibility testing) and ensure clinicians and programmes respond to this demand.

Promote AMR educational initiatives among children and young people

- Integrate education and SBC approaches to promote appropriate use and stewardship of antimicrobial drugs at facility level.
- Coordinate public education and SBC around rational use of antibiotics, with particular focus on educating children and young people.
- Support education of communities and families about the consequences of AMR, self-medication and irrational use of antimicrobial drugs.
- Support large-scale national and sub-national public health education on rational use of antimicrobials, especially in countries where antimicrobial drugs are widely prescribed or available over the counter.

Empower community organizations to educate communities and prevent the emergence and spread of AMR at the community level

- Strengthen the capacity of governments, civil society organizations and community-level partners to promote rational use of antibiotics.
- Strengthen community linkages and involvement in vaccination service provision.
- Engage partners, including civil society, to implement country-level communication strategies to improve understanding and awareness of the risks of drug resistance at all levels.
- Support community-level actions to generate demand for quality services by community health workers and at primary care facilities.
- Organize communications and SBC campaigns among service providers on rational use of antimicrobial drugs in coordination with WHO, the Food and Agriculture Organization (FAO), the World Organization for Animal Health (WOAH), the United Nations Environment Programme (UNEP) and other partners.
- Strengthen the interpersonal communication skills of health providers and other relevant providers (e.g., pharmacists) to promote rational use of antibiotics.



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9. ROLES AND RESPONSIBILITIES WITHIN UNICEF

Listed below are the proposed roles for how different UNICEF Divisions, Programmes and Offices can strengthen ongoing efforts to combat AMR while also engaging in new ones. To effectively engage in new efforts and ensure sustainable work, it will be necessary to strengthen institutional capacities relevant for AMR such as developing skills and competencies of teams around AMR, ensuring minimum levels of human resource capacity in key country offices, and investing appropriately in the implementation of programmes at scale that can lead to improved policy and programming around AMR.

Various sections and divisions at the national, regional and headquarters levels have a role to play and will need to work in coordination to effectively respond to AMR. The health threat is directly relevant for the work of Supply Division; Division of Global Communication & Advocacy (GCA); Division of Data, Analytics, Planning and Monitoring (DAPM); Emergency Operations (EMOPS); Programme Division (PD), particularly Water, Sanitation and Hygiene (WASH) and Nutrition; and Health Programme Group (Immunization; Maternal, Newborn, Child and Adolescent Health (MNCAH), HIV/AIDS, Public Health Emergencies (PHE), and SBC). All are already engaged in activities directly or indirectly related to AMR, even where these activities are not explicitly labelled as such.

Country offices: At the frontline of the UNICEF AMR response are country offices, which play a critical role in strengthening national capacities to protect children from the growing threat. Each country office carries out UNICEF's mission through a unique programme of cooperation developed with the host government. Going forward, situation reports produced at the beginning of the programme cycle should include a situation analysis in each country to identify AMR-specific and AMR-sensitive areas of work that UNICEF can support at the national level. The analysis should also specify potential areas for future engagement where UNICEF has a comparative advantage in the national AMR response.

Situation reports ideally should inform the development of a five-year programme that includes practical ways to mitigate the impact of AMR on children and women. Countries that have recently completed this process without accounting for AMR should consider a desk review of the country programme of cooperation, the national action plan on AMR (where available), and the national action plan for health security (where available). Country offices should also assist governments in prioritizing investments for implementation of national action plans on AMR¹⁰¹ and advocate for inclusion of AMR-related activities in national plans and budgets.

Regional offices provide guidance and technical assistance to country offices to strengthen the AMR response. This includes, but is not limited to, the following types of support that could be enhanced and expanded to help drive more robust action against AMR:

- Technical assistance and information-sharing. Regional offices support implementation of the recommendations made in this guidance note, collect and analyse data, and share information and lessons learned with other countries in each region and across the organization.
- Leadership: Regional offices identify areas of common concern among countries and facilitate collective solutions such as data gathering and analysis of drug-resistance levels and drug consumption in children, procurement of quality-assured antimicrobials through SD, implementation of external quality assurance in laboratories involved in detection of AMR, and analysis of drug quality and efficacy.
- Coordination: Regional offices cooperate with stakeholders across sectors as well as regional institutions and programmes to ensure that AMR activities are integrated across partners, sectors and programmes, taking into account global, regional and national priorities.

Programme Group currently undertakes several areas of work that directly aim to address AMR, all of which could be expanded and enhanced in the future to help support more effective responses against AMR. They include providing global strategic and technical assistance on AMR through direct implementation of AMR-sensitive or AMR-specific activities and by increasing global sectoral and cross-cutting capacity related to AMR; influencing global policy relating to AMR; providing technical assistance on addressing AMR to UNICEF regional, country and field offices; shaping internal AMR policy and practice through monitoring and evidence capture, generation and dissemination; and managing UNICEF's engagement in key global AMR programme partnerships. In particular, the Health Programme Group will likely need to play a bigger and more prominent role in UNICEF's response to AMR.

Division of Global Communication and Advocacy could further leverage its extensive reach and network to raise awareness, educate and advocate around AMR issues affecting children on a global scale. The intended goal would be to reach millions of people through multiple approaches and channels, including traditional and social media, and to build an enabling environment for advocacy with decision makers and national governments to strengthen policies and regulations related to AMR.

Division of Data, Analytics, Monitoring and Planning should play a key role in monitoring the spread of AMR by supporting surveillance efforts; monitoring the progress of multisectoral efforts to address AMR; and contributing analytical support to UNICEF's response to AMR, particularly programmatic and communication efforts.

Supply Division is a global leader in the procurement and supply of quality vaccines, medicines, diagnostics and commodities to support disease prevention, diagnosis and treatment. Supply Division should work to shape markets for diagnostics and antimicrobials and engage with the industry sector to improve availability, affordability, acceptability and quality of diagnostics and antimicrobials.

ENDNOTES

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- 92 <https://www.fao.org/antimicrobial-resistance/quadripartite/who-we-are/en/>
- 93 <https://www.who.int/health-topics/antimicrobial-resistance>
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- 95 World Health Organization, Food and Agriculture Organization, World Organization for Animal Health. (2020) Technical brief on water, sanitation, hygiene (WASH) and wastewater management to prevent infections and reduce the spread of antimicrobial resistance (AMR). Retrieved from <https://www.who.int/publications/i/item/9789240006416>
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- 98 <https://www.unicef.org/reports/unicef-strategic-plan-2022-2025>
- 99 UNAIDS considers gay men and other men who have sex with men, sex workers, transgender people, people who inject drugs and prisoners and other incarcerated people as the five main key population groups that are particularly vulnerable to HIV and frequently lack adequate access to services.' [<https://www.unaids.org/en/topic/key-populations>]
- 100 Graham et al. BMC Public Health (2016) 16:897 DOI 10.1186/s12889-016-3541-8
- 101 <https://www.who.int/teams/surveillance-prevention-control-AMR/national-action-plan-monitoring-evaluation/library-of-national-action-plans>

