



ANTIMICROBIAL RESISTANCE, FUELED BY THE COVID-19 PANDEMIC

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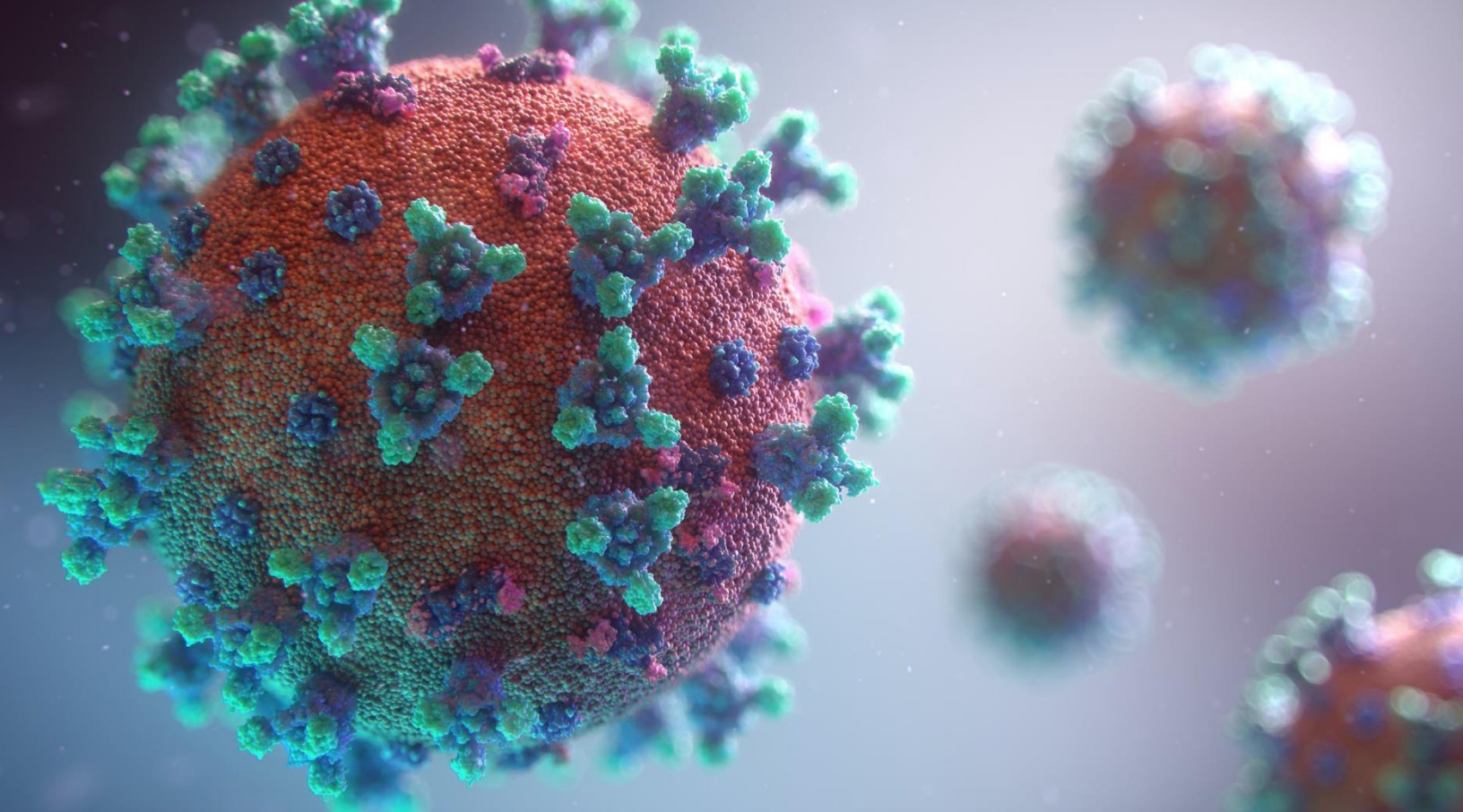
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Preface

Long before the COVID-19 pandemic, antimicrobial resistance (AMR) was recognized as a major global emergency causing around 700,000 deaths each year. AMR is projected to cause 10 million deaths a year by 2050 (1). It threatens the effective treatment of an ever-increasing range of infections caused by bacteria, parasites, viruses, and fungi, resulting in prolonged illness and increased mortality which are often felt hardest by the most vulnerable populations.

AMR is accelerated by the overuse and misuse of antimicrobial drugs such as antibiotics, antivirals, and antifungals. Worldwide, more than half of all antibiotics are prescribed, distributed, or sold inappropriately. Antibiotics can be purchased without a prescription in 80% of the countries in the Americas (2).

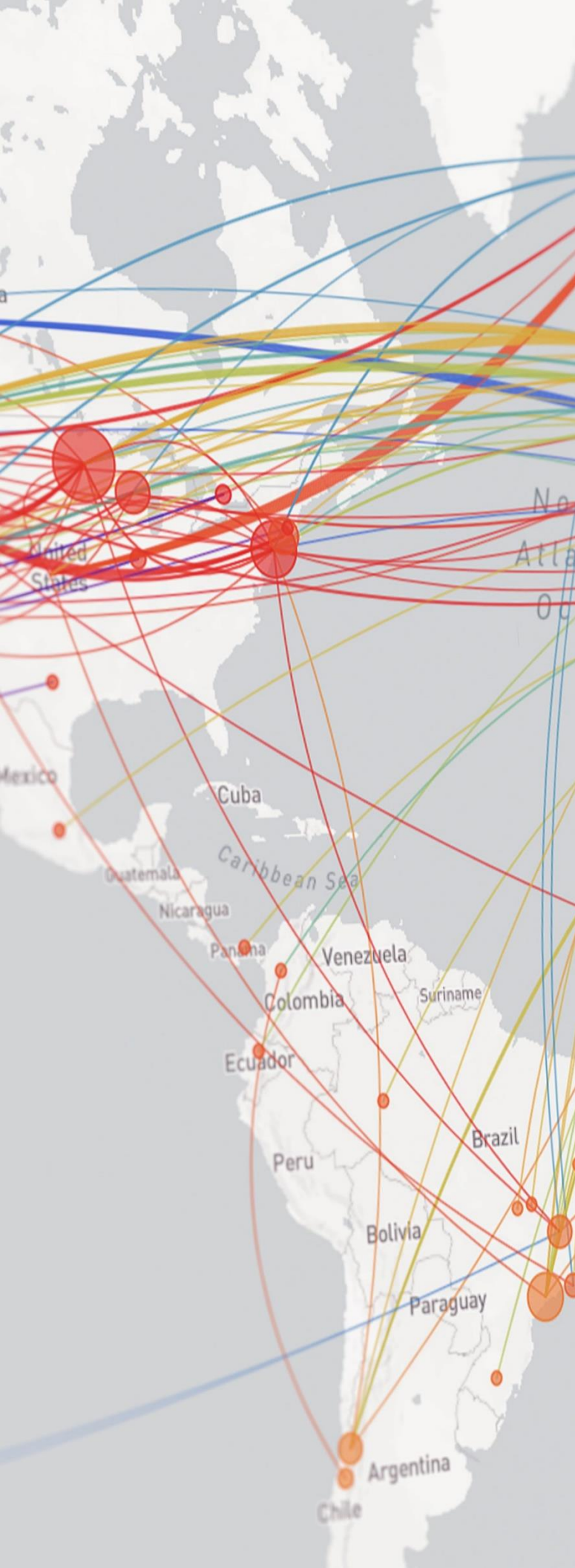
With the advent of the COVID-19 pandemic, AMR continues to gain ground, fueled by an increase in the use of antibiotics to treat COVID-19 patients. This may be explained by the increased antibiotic use due to concerns about bacterial co-infections and difficulty differentiating between COVID-19 and bacterial infections early in the pandemic, disruptions to infection prevention and control practices in overwhelmed health systems, and diversion of human and financial

resources away from monitoring and responding to AMR threats. Moreover, AMR is likely to have caused more COVID-19 deaths, as secondary bacterial infections can worsen the outcome of severe and critical COVID-19 illness.

With more than 93 million COVID-19 cases and 2 million COVID-19 deaths, the Region of the Americas is the most severely affected WHO Region to date. Particularly in Latin America and the Caribbean, healthcare capacity is exceeded, resources are exhausted, and poverty and inequalities are on the rise in every country (see Figure 1).

As AMR becomes exacerbated by the COVID-19 pandemic, it is more urgent than ever to prioritize efforts toward its containment. We must ensure that resources are allocated to preventing, detecting, and responding promptly to the emergence and spread of new multidrug-resistant pathogens. We must invest in optimizing antimicrobial prescribing and use, and advocate for research and development in infection diagnostics and treatment. And we must continue to monitor the impact of the COVID-19 pandemic on AMR epidemiology in the Region of the Americas.

The COVID-19 pandemic in the Americas



Two years after the emergence of SARS-CoV-2, the COVID-19 pandemic continues to have severe health effects and serious implications for economic growth and social development in the Americas. It is the most affected WHO Region thus far, with more than 93 million confirmed cases and over 2 million deaths. This represents 38% of global COVID-19 cases and 45% of global COVID-19 deaths (Figure 1) (3). The Region's highest numbers of deaths to date have been in the United States of America, Brazil, Mexico, Peru, Colombia, and Argentina.

According to the Economic Commission for Latin America and the Caribbean (ECLAC), we are potentially facing "a new lost decade" (4). The course of the COVID-19 pandemic in the Americas remains uncertain as surges in cases in the first half of 2021, coupled with vaccine hesitancy and shortages, continue to pose a challenge.

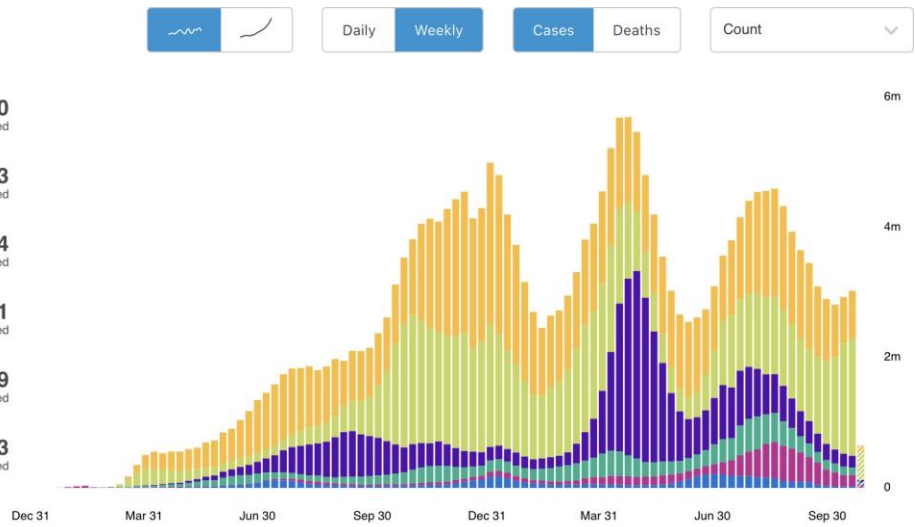
In this demanding context, poverty, extreme poverty, and inequality are on the rise in every country in Latin America and the Caribbean (4). In 2020, Latin America and the Caribbean witnessed the worst economic contraction since 1900, with GDP falling by 6.8% (5). The pandemic has disproportionately affected vulnerable population groups and their capacity for response, including women, migrants, children and adolescents, older adults, rural populations, informal workers, indigenous and Afrodescendant populations, and persons with disabilities. ECLAC has estimated an increase in poverty of at least 4.4% in 2020 compared to 2019, bringing the total number of people living in poverty to 214.7 million (over a third of the population of Latin America and the Caribbean) (4).

Figure 1. COVID-19 epidemiological situation per WHO Region as of November 2021. Source: [World Health Organization](https://www.who.int).

Situation by WHO Region

Americas	93,711,700 confirmed
Europe	77,231,883 confirmed
South-East Asia	44,005,474 confirmed
Eastern Mediterranean	16,382,071 confirmed
Western Pacific	9,465,219 confirmed
Africa	6,154,163 confirmed

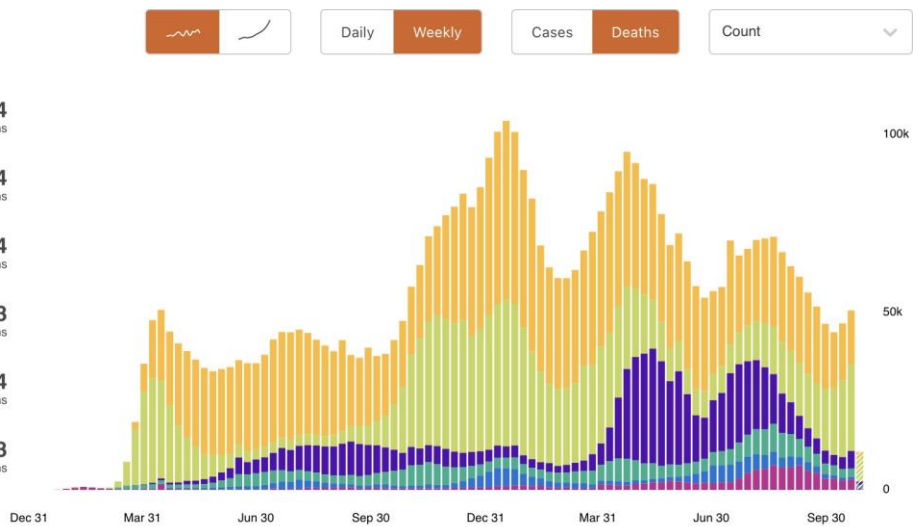
Source: World Health Organization
 Data may be incomplete for the current day or week.



Situation by WHO Region

Americas	2,296,114 deaths
Europe	1,432,224 deaths
South-East Asia	693,814 deaths
Eastern Mediterranean	301,753 deaths
Africa	150,704 deaths
Western Pacific	130,233 deaths

Source: World Health Organization
 Data may be incomplete for the current day or week.



An aggravating context for AMR

While most countries in the region had made significant progress since 2015 in developing and implementing National Action Plans on AMR under a One Health approach, the COVID-19 emergency deprioritized planned activities and diverted human and financial resources that had been contributing to AMR surveillance and response activities, channeling them instead to the COVID-19 response (6).

The COVID-19 pandemic has put an enormous strain on healthcare systems across the region by increasing the demand for healthcare professionals and the need for beds in intensive care units and respiratory support such as ventilators, among others. The prolonged emergency has exhausted resources and disrupted infection prevention and control practices, which in turn has led to increased infections in healthcare settings (7, 8). While antimicrobial prescribing and use increased especially among COVID-19 patients, antimicrobial stewardship programs have not necessarily

been reinforced as part of the emergency response. Moreover, resources for AMR laboratory surveillance, the best available source of information to accurately assess the impact of COVID-19 on AMR epidemiological trends, have also been diverted to the COVID-19 response (9-11).

Finally, with the surge in demand for antimicrobials such as those for the treatment of rare fungal infections that have become more common as a consequence of the pandemic, some countries have faced difficulties in accessing antimicrobials due to shortages or to regulatory implications for the incorporation of new drugs. [PAHO's Strategic Fund](#), which facilitates procurement of essential medicines, has helped countries of the Region to gain access to high quality and effective medicines. Another economic repercussion of the rise in AMR is the potential higher cost of new antimicrobial treatments.

Healthcare-associated infections have increased during the COVID-19 pandemic, due to overwhelmed healthcare capacity and changes in routine infection prevention and control practices, including limited availability and reuse of gloves and gowns, and modified cleaning and disinfection procedures (7, 8).



Overcrowded healthcare facilities have faced a rise in the number of invasive procedures associated with the use of antibiotics, steroidal anti-inflammatory and other immunomodulatory drugs (9).



COVID-19 patients in intensive care share underlying diseases and risk factors associated to bacterial and fungal infections, such as corticosteroid therapy, chronic respiratory diseases, intubation/mechanical ventilation, and immunoinflammatory response (7, 10-12).



The use of antibiotics in SARS-CoV-2 patients during the COVID-19 pandemic has exceeded the incidence of secondary infections and coinfections, suggesting inappropriate and excessive prescribing.



The rate of antibiotics usage in hospital care (94%–100%) was much higher than the reported incidence of secondary infection (10%–15%)(8, 14).



While just 7% to 8% of hospitalized patients and 14% of ICU patients had secondary infection (sepsis, hospital pneumonia), 72% of patients received broad spectrum antibiotics (14).

The alarming and rising impact of COVID-19 on AMR

Drug-resistant pathogens can cause outbreaks in healthcare settings, further complicating the clinical management of COVID-19 patients and the public health response to the pandemic. Indeed, increases in bacterial and fungal infections associated with COVID-19 have been reported as well as overall increases and geographic spread of “superbugs” such as those resistant to carbapenem, a drug of last resort for a variety of different bacterial infections.

It is crucial that countries sustain AMR surveillance and continue to reinforce infection and control practices that are essential to the COVID-19 response and to countering other infectious threats. They must prioritize antimicrobial stewardship and advocate for research and development for new antimicrobial drugs. Indeed, the clinical pipeline of new antimicrobials is dry. In 2019, WHO identified 32 antibiotics in clinical development that address the WHO list of priority pathogens, of which only six were classified as innovative. Furthermore, a lack of access to quality antimicrobials remains a major issue. Antibiotic shortages are affecting countries of all levels of development.

The increasing burden of AMR

- The pandemic has contributed to increases in infections caused by multidrug-resistant pathogens that are directly associated with worse clinical outcomes, longer hospital stays, excess mortality, and an increasing burden and cost on healthcare infrastructure (15) (Figure 2).
- Increased antibiotic use has accelerated the loss of activity of routine treatment drugs such as carbapenems, a class of highly effective antibiotic agents commonly used for the treatment of severe or high-risk bacterial infections, and alternative drugs such as colistin, used as a last-resort treatment for multidrug-resistant Gram-negative infections.
- The cost of AMR to national economies and their health systems is significant, as it affects the productivity of patients or their caretakers through prolonged hospital stays and the need for more expensive and intensive care.

A rise in bacterial and fungal infections associated with COVID-19 and the emergence of AMR (only the tip of the iceberg)

- **Increases in fungal infections** such as COVID-19-associated pulmonary aspergillosis, invasive candidiasis (e.g., caused by *Candida auris*) and mucormycosis have been reported in COVID-19 patients leading to severe illness and death (12, 13, 16). Early diagnosis and

monitoring for antifungal resistance are key to reducing death in patients with severe COVID-19 fungal infections.

- The region has recorded overall **increases in multidrug-resistant organisms** affecting human health, particularly in common carbapenem-resistant Gram-negative pathogens that can lead to healthcare-associated infection outbreaks (17, 18) (Figure 3).
- Bacterial strains harboring multiple carbapenemase genes, which confer **carbapenem resistance**, have been detected in several countries in the region.
- The **geographic spread of certain types of carbapenemase** such as the oxacillinase-48 (OXA-48) and New Delhi metallo- β -lactamase-1 producers (NDM) to non-endemic or non-previously affected areas has been observed.

Many COVID-19 patients with severe acute respiratory syndrome require admission to an intensive care unit (ICU) for invasive ventilation and are at significant risk of developing a secondary, ventilator-associated pneumonia (19).

In a study conducted in dedicated COVID-19 care units in a hospital in Maryland, USA, during May–June 2020, the spread of multidrug-resistant Gram-negative bacteria was accelerated among patients by factors such as critical illness, high antibiotic use, double occupancy of single rooms, and modified infection prevention practices (20).

The COVID-19 pandemic has brought about substantial challenges to the implementation of infection, prevention and control (IPC) programs in the Region of the Americas. A meeting of key experts from the Region held in March 2019 that reviewed advances in the organization and structure of IPC programs; the development and implementation of guidelines; education and training; surveillance of health care-associated infections; and monitoring, evaluation, and reporting of results, highlighted the need to strengthen IPC programs at the national and local levels, through the allocation of budget and personnel (21). Throughout the pandemic, PAHO has published evidence-informed guideline recommendations for infection control and prophylaxis and treatment of COVID-19 patients, taking into account the latest available evidence and emphasizing the prudent and appropriate use of antimicrobials (22, 23).

Figure 2. Overview of the impact of the COVID-19 pandemic on antimicrobial resistance. Source: [PAHO AMR Special Program](#). More widely-reported AMR outbreaks and novel pathogens are only the tip of the iceberg, with the increased spread of multidrug-resistant organisms and the higher burden of AMR often overlooked.

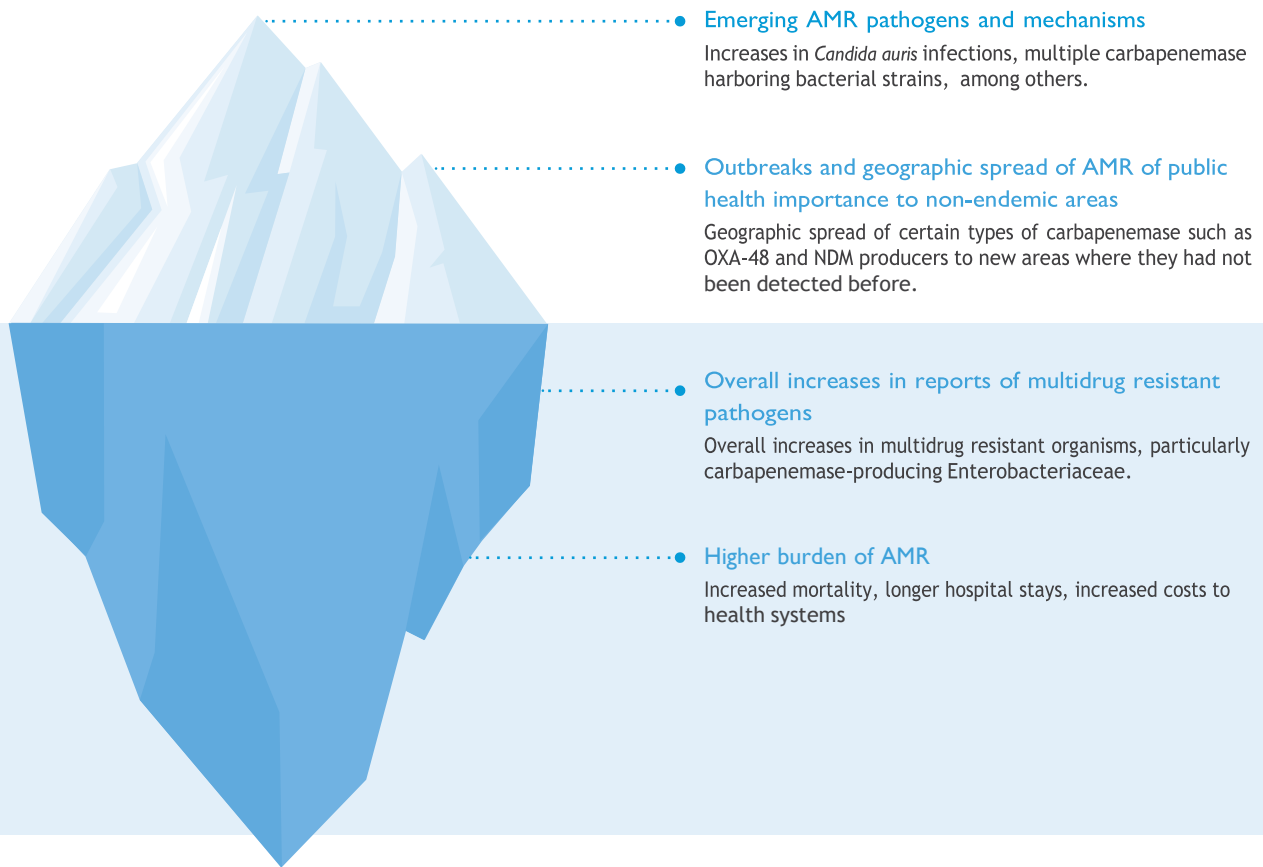
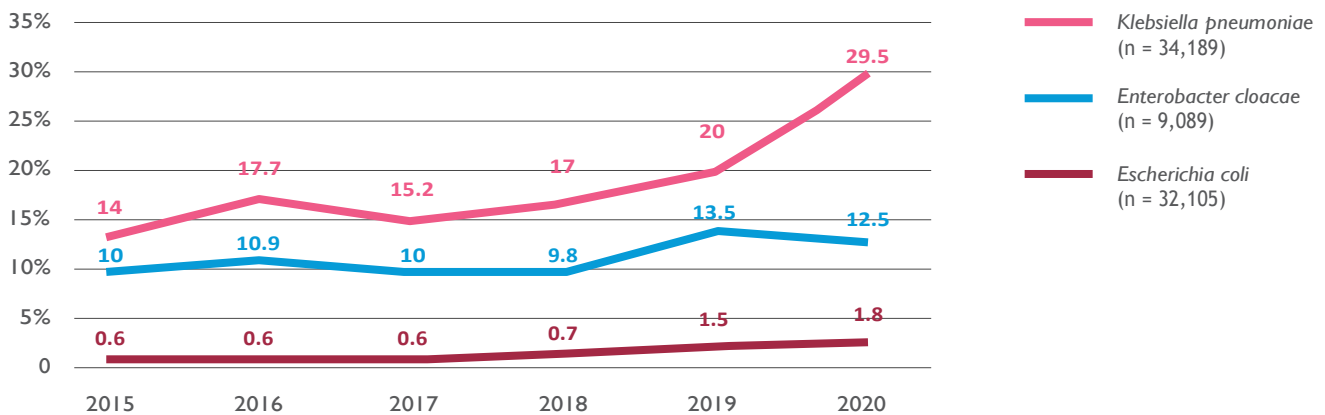


Figure 3. Proportion (%) of Enterobacterales bacteria non-susceptible to Imipenem (carbapenem), Argentina, 2015-2020. Source: Unpublished data. Courtesy of Ministry of Health, Argentina.



Key public health actions to address AMR in the context of COVID-19

AMR is a global public health and societal issue requiring urgent action. The continuing emergence of AMR may hinder the achievement of many Sustainable Development Goals (24). Without effective tools for the prevention and adequate treatment of drug-resistant infections and improved access to existing and new quality-assured antimicrobials, the number of people for whom treatment is failing or who die of infections will increase (25).

Key public health actions that are particularly relevant in the context of COVID-19 are aligned with the WHO global and regional action plans on AMR and take note of the recommendations of the Interagency Coordination Group on AMR (25–27). These actions include prioritizing the AMR response, preventing the emergence and spread of AMR, monitoring the impact of the COVID-19 pandemic, and continued investment in preserving and developing antimicrobials and AMR response.

Prioritize AMR response

- Increase awareness about AMR risk and urgency to address it **as part of the COVID-19 response**.

Prevent AMR emergence

- Strengthen **antimicrobial stewardship** programs and activities in inpatient and outpatient settings, to ensure appropriate use of antimicrobials.

Stop AMR spread

- Strengthen **AMR surveillance and early detection** of emerging AMR and novel resistance mechanisms, in line with the International Health Regulations.
- Reinforce **infection prevention and control practices** and take swift action to control healthcare-associated infections and AMR spread.

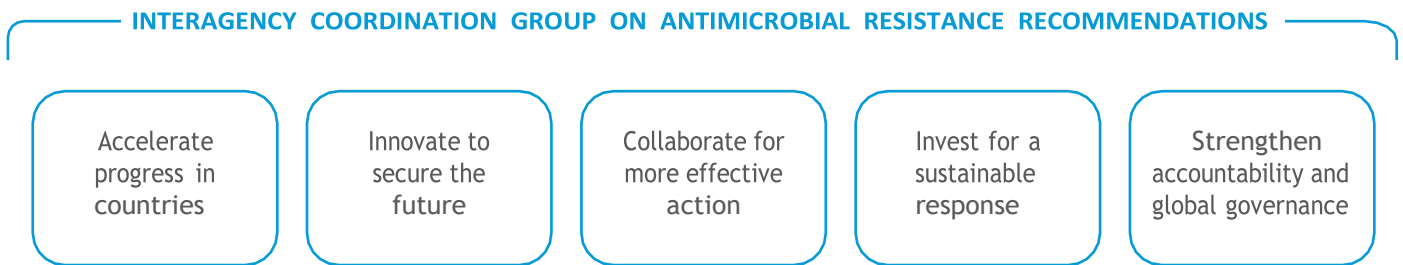
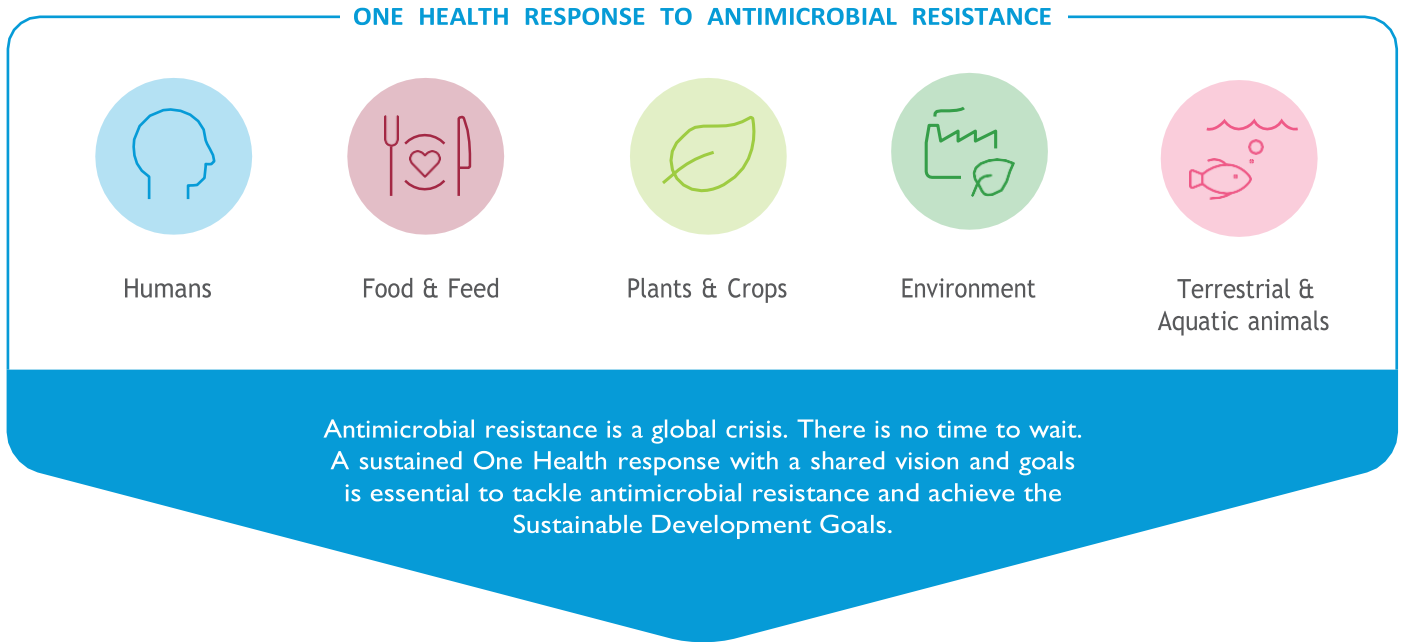
Understand and assess the impact of COVID-19 on AMR

- **Leverage COVID-19 and AMR surveillance data** to assess the impact of the pandemic on AMR epidemiological trends. The public health community should explore ways to evaluate the impact of current COVID-19 policies and programs on AMR.
- **Disseminate** as widely as possible and in a timely manner any new available evidence and knowledge about AMR in the context of the COVID-19 pandemic, to inform clinical and public health practice.

Prepare for the future

- Continue strengthening the public health response to AMR through the implementation, monitoring and evaluation of **National Action Plans on AMR (6, 26, 27)**, with emphasis on better integrating antimicrobial resistance surveillance, infection prevention and control, and antimicrobial stewardship programs.
- **Integrating AMR surveillance and infection prevention and control programs** can facilitate the early detection of new AMR threats and prompt rapid implementation of effective containment measures, in line with the International Health Regulations.
- The pandemic offers an opportunity to **invest in infection prevention and control and build resilient antimicrobial stewardship programs** that can withstand future pandemics.
- Link AMR activities to existing public health plans and consider **including key actions of the AMR response in pandemic preparedness plans**.
- **Adopt a “One Health” multidisciplinary and multisectoral approach** to addressing zoonotic diseases, AMR, food safety, and other health threats at the human-animal-environment interface in line with the recent PAHO One Health policy (28).
- **Advocate for research and development to address AMR.** The current clinical pipeline of antimicrobials is insufficient and may still require years of development before new tools in the preclinical pipeline can be used. Additionally, those may not target the most dangerous drug-resistant bacteria.

Figure 4. One Health, Interagency AMR Coordination Group recommendations and the Sustainable Development Goals.
 Source: [World Health Organization](#).





AMR is a growing global health emergency aggravated by the ongoing COVID-19 pandemic. With increases in the use and misuse of antimicrobials, resources deployed away from antimicrobial stewardship, and deteriorating economic conditions, AMR remains a significant threat requiring urgent prioritization and action.

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