EXECUTIVE SUMMARY

# LEARNING FROM COVID-19 TO TACKLE ANTIBIOTIC RESISTANCE

**The unchecked growth of drug-resistant infections – which are increasingly hard to treat – is a silent pandemic with long-term consequences for global public health and the global economy. The COVID-19 pandemic has brought into sharp focus the impact of pandemics, in which more than a million people have died, trillions of dollars have been lost, expenditures cut and international efforts to achieve the Sustainable Development Goals put in jeopardy. There are vital lessons to learn from this tragedy. Now more than ever, governments have the opportunity to make robust and comprehensive investments into the way they prepare and respond to pandemics. This has the potential to translate into long-term, interlinked health and economic benefits for people and countries.**

This paper examines several lessons of the COVID-19 pandemic and how these lessons can be applied to a successful long-term response to antimicrobial resistance (AMR), with a focus on the development and use of diagnostics, vaccines and treatments - also known as medical countermeasures. The paper argues universal, equitable and affordable access to these vital health tools is a cornerstone of pandemic response.

Differences between AMR and fast-moving viral pandemics, such as COVID-19, have led to an artificial distinction between drug-resistant infections and viral pandemics. Yet the development and use of diagnostics, vaccines and treatment to counter the effects of drug resistance are an essential component of any pandemic response. Drug-resistant infections have some commonalities with fast-moving pandemics, for three interrelated reasons:

**DRUG-RESISTANT INFECTIONS ARE A SILENT PANDEMIC**. Drug-resistant infections spread rapidly through international travel and migration, though impacts are felt more slowly in well-resourced settings. The unchecked growth of drug-resistant infections is a silent pandemic with long-term implications for global health security.

**TIMELY ACCESS TO APPROPRIATE ANTIBIOTICS WILL BE AN IMPORTANT COMPONENT OF PREPAREDNESS AND RESPONSE TO FUTURE VIRAL PANDEMICS**. Although current evidence is mixed on the impact of bacterial co-infections or secondary infections upon morbidity and mortality of people with COVID-19, future pandemics could carry a significant risk of hospitalization and secondary bacterial infections. Therefore, health systems will require timely access to effective antibiotics and diagnostics.

**ANTIBIOTIC PRESCRIPTIONS INCREASE SUBSTANTIALLY DURING A VIRAL PANDEMIC AS EARLY EVIDENCE DURING COVID-19 HAS SHOWN.** This could have a long-term impact on the availability and use of antibiotics and potentially upon drug-resistance. Antibiotics are essential for a comprehensive response but are diminishing in value due to a natural process of resistance linked to their use. The use of antibiotics could increase in future pandemics, including an inappropriate use of antibiotics to treat viral infections, or to address co- or secondary bacterial infections.

The initial international response to COVID-19 has been criticised by many and has revealed 'a collective failure to take pandemic prevention, preparedness and response seriously and prioritise it accordingly', according to the Global Preparedness Monitoring Board (GPMB). COVID-19 has reinforced the importance of research, development, and supply of medical countermeasures to prevent and treat pandemic diseases.

This paper identifies lessons related to the development and supply of vital health tools to tackle COVID-19. It highlights how preparedness is possible even for a pandemic, through research and development of new treatments and vaccines; the critical importance of collaboration and international coordination to address a pandemic; and the significance and value of access to diagnostics, treatments and vaccines wherever needed.

During the COVID-19 pandemic, medical countermeasures have been lacking. In addition, traditional market incentives have neither been sufficient nor appropriate to ensure the timely development of new solutions on a global scale. Despite efforts to foster international cooperation and solidarity, many countries may no longer trust the 'international system' to promote timely, equitable and affordable access to the diagnostics, treatments and vaccines they need to tackle a pandemic. The lessons of the COVID-19 pandemic could help strengthen global health security as access to new vital health tools are developed.

Even as global health security-based responses are strengthened, there should be a recognition of the limits and risks associated with a narrow focus on global health security, including as it relates to the emerging pandemic of drug-resistant infections. Risks related to research and development and access to medical countermeasures, in the context of AMR, may include: priority-setting that is mostly focused on the needs of high-income countries; insufficient attention or exclusion of marginalised populations; and measures which could restrict equitable access to an effective countermeasure due to concerns, for example, that the use of a novel antibiotic will be too widespread and therefore accelerate drug resistance.

The challenge of ongoing and future pandemics will require an approach to pandemic preparedness and response for which global health security is one component. The recommendations of the UN Interagency Coordination Group on AMR provide a roadmap to apply a One Health framework. This will address not just AMR, but also other infectious disease pandemics of zoonotic origin - infectious diseases that spread between animals and people.

Ultimately, the initial lessons of the COVID-19 pandemic present an opportunity to improve the response to pandemics, including the silent pandemic of drug-resistant infections. This rests upon building an approach to AMR that acknowledges what global health security can contribute, as well as its limitations. This paper recommends five measures to strengthen domestic and global responses to AMR, focusing on the development and access to medical countermeasures.

## FIVE RECOMMENDATIONS TO STRENGTHEN DOMESTIC AND GLOBAL RESPONSES TO AMR

1. **Recognise and urgently address the silent pandemic of drug-resistant infections.**

2. **Invest in the development of medical countermeasures as a critical element of pandemic preparedness.**

3. **Ensure that access to diagnostics, treatments and vaccines for all is a cornerstone of pandemic preparedness and response.**

4. **Expand global cooperation across geographies and sectors and within a One Health framework.**

5. **Ensure low- and middle-income countries are equal partners in a comprehensive global response. Solutions that have been pioneered by such countries should be recognised and integrated into pandemic preparedness and response.**

# LEARNING FROM COVID-19 TO TACKLE ANTIBIOTIC RESISTANCE

## INTRODUCTION

The SARS-COV2 (COVID-19) pandemic has driven home the challenge of controlling pandemic diseases, and the consequences of pandemics upon human health and economic welfare.[1] While infection prevention and control measures have successfully reduced morbidity and mortality during the COVID-19 response, measures put in place to prepare for such threats, such as the development of new medical countermeasures (biomedical technologies that consist of treatments, diagnostics and vaccines) have proven to be insufficient.

While the COVID-19 pandemic has illustrated why a two-decade long effort to improve the global health security apparatus was necessary, there should be a reflection as to whether global health security can be adopted wholesale as the framework for pandemic preparedness and response. This includes tackling COVID-19 as well as future or ongoing pandemics, such as the pandemic of drug-resistant infections that are driven by antimicrobial resistance (AMR). Global health security may be too narrow and may present risks that can undermine its purpose. In addition, global health security does not address the broader causes of infectious diseases, including underlying environmental causes and the link of human pandemics with zoonotic diseases – infectious diseases that spread between animals and people.

Antimicrobial resistance occurs when microbes no longer respond to existing antibiotics. One driver of AMR is poor access to quality, affordable antibiotics, which results in both misuse and increased mortality. These are often inaccessible because of regulatory barriers or pricing. Drug-resistant infections, including those caused by tuberculosis and malaria, are estimated to be responsible for 700,000 deaths per year.[2] The health impact of AMR, already a public health crisis in low- and middle-income countries, is projected to increase exponentially over the coming decades, and could undermine achievement of several Sustainable Development Goals, including ending extreme poverty by 2030, reducing inequality, and ensuring the sustainability and security of food production and the livelihood of farmers.

### BOX 1: THE GROWING IMPACT OF AMR

Each year, an estimated 700,000 people die worldwide because of drug-resistant infections.[3]

In 2015, an estimated 214,000 newborn babies died due to infections resistant to first-line antibiotics.[4]

Serious bacterial infections (SBIs) lead to longer hospital stays, long-term disability and more preventable deaths, and a massive financial burden for health systems.

In the USA, 98,000 deaths every year are attributed to hospital infections, with an annual economic impact of about US$6.5 billion.[5]

50% of SBIs are resistant to multiple drugs.[6]

In 2015, in the European Union 670,000 people had drug-resistant infections and ~33,000 of these died. The highest burden was in babies under one year old, and adults over 65 years.[7] In 2018, total deaths in the U.S. due to AMR were re-estimated to >150,000 people.[8]

In low- and middle-income countries (LMICs), the situation is worse:

In 2019, in hospitals in Bangladesh, Columbia, Ghana, India, Lebanon, Nepal, Nigeria, Pakistan and Vietnam, death rates in patients with bloodstream infections due to carbapenem-resistant bacteria was 35% versus 20% in patients with drug-susceptible infections.[9]

In South Africa (2018), the bacterium most often found in blood, *Klebsiella pneumoniae*, is usually resistant to common antibiotics (~68% resistant to extended spectrum beta-lactams). One in 12 samples are also resistant to carbapenems (used to treat multi-drug resistant (MDR) infections).[10]

Like COVID-19, drug-resistant bacteria can infect anyone, of any age, in any country. Not only are drug-resistant infections already a pandemic, but during future viral pandemics, widespread access to antibiotics may be required if hospitalized patients suffer from bacterial co-infections. As early evidence has indicated during the COVID-19 pandemic, antibiotic prescriptions increase substantially during a viral pandemic. This could have a long-term impact on the availability and use of antibiotics and potentially upon drug-resistance.

This paper examines early lessons of the COVID-19 pandemic and how these can be applied to a successful long-term response to AMR, with a focus on the development and use of vital health tools needed as countermeasures. The paper argues that we know what is needed to counter the ongoing silent pandemic of drug-resistant infections and governments should take concrete steps to effectively tackle this growing crisis.

It highlights the critical importance of universal, equitable and affordable access to antimicrobials and diagnostics as a cornerstone of pandemic response. It recommends governments make large and long-term investments in medical counter-measures, as well as set terms and conditions that ensure these serve the public interest. Finally, the paper calls attention to the importance of global coordination and collaboration to secure our collective and individual well-being. Low- and middle-income countries should be included as part of the solution and reap the benefits of medical research and development in the face of ongoing and future pandemics. As we have seen during the HIV/AIDS and COVID-19 pandemics, these countries have devised and implemented successful local solutions and developed health tools that can strengthen the international response.

*Like COVID-19, drug-resistant bacteria can infect anyone, of any age, in any country.*

## A RECENT HISTORY OF GLOBAL HEALTH SECURITY

The concept of global health security is nearly two centuries old. It existed long before the term itself was coined, and focused largely on how to handle health risks, such as cholera, that crossed borders.[12] COVID-19 has highlighted that the world still relies on some of the health security measures that were used as early as the 14th century, when quarantines were adopted to prevent the spread of the bubonic plague.[13]

Global health security was integrated within the 21st century's global health architecture partly due to the HIV pandemic, the SARS outbreak of 2002 and concerns amongst some countries about a future flu pandemic.

Recently, the concept of and approaches to global health security have evolved, prompted by shortcomings in the response to health threats. An example is when the International Health Regulations (IHR) were revised in 2005, following the SARS outbreak. While new requirements provide a framework to enhance global health security, they do not safeguard access to goods and services for affected countries and do not protect the health security of individuals.[14] This became clear when Indonesia, as well as other countries, could not secure access to an avian influenza vaccine during the 2007 avian flu outbreak.[15]

The years before the emergence of COVID-19 saw an increase in funding,[16] the creation of at least one new entity to accelerate the development of vaccines against pandemic threats (the Coalition for Epidemic Preparedness Innovations), and the establishment of several frameworks and multi-stakeholder initiatives, such as the World Health Organization Research & Development Blueprint and the Global Health Security Agenda. It also prompted calls to expand global health security to account for and protect individual human security.[17]

With each successive outbreak (SARS, MERS, Ebola), governments have acknowledged the importance of pandemic preparedness and response. However, they have relied heavily on constructing a global health security apparatus, without introducing domestic investments and domestically-owned strategies, or aligning overseas development assistance where appropriate, to strengthen domestic capacity and complement an effective international system. The COVID-19 pandemic has also exposed other gaps and needs, including a lack of effective health tools that could be readily tested or adapted to address COVID-19.

A lack of medicines, vaccines and diagnostics was also a shortcoming of previous efforts against SARS, MERS, and until recently Ebola. Communities at the frontline of outbreaks also didn't have ready access to vital health tools. Today, global health security, or the protection from threats to health, is focused on four key interventions: (1) preventing and reducing the likelihood of outbreaks and other public health hazards and events (preparedness); (2) detecting threats; (3) responding rapidly and effectively, using multi-sectoral, national and international coordination and communication; and (4) the development and deployment of medical countermeasures, including vaccines, diagnostics, treatments and other health technologies.

## DRUG-RESISTANT INFECTIONS: A SILENT PANDEMIC WITHOUT BORDERS

AMR has been included within the global health security agenda for the last two decades and has featured in G20 discussions since 2016. In 2019, WHO named AMR as one of the 10 most urgent global health threats.[18] Despite this, political action and financial investments to tackle this growing crisis have fallen short. The private sector's disinvestment in AMR, particularly for the development of new countermeasures, has not been compensated by public investment, leaving a critical gap.

AMR is a focus of global health security because it threatens the health and economic interests of societies, including critical procedures that underpin modern medicine. In fact, AMR should be viewed as an insidious pandemic of drug-resistant infections. It is one pandemic among many, all that have exacted a heavy toll upon humanity over the last century and across human history (See Box 2).

## BOX 2: THE MANY FACES OF PANDEMICS

WHO has defined a pandemic as 'the worldwide spread of a new disease.'[19] A broader definition of a pandemic is 'an epidemic occurring worldwide, or over a very wide area, crossing international boundaries and usually affecting a large number of people.'[20] The last one hundred years is book-ended by two major viral pandemics, the 1918 Spanish flu and COVID-19, with several flu pandemics in the intervening years. Over the last century, the international community has also faced several other types of pandemics that have different origins and consequences.

Cholera has re-emerged, even though effective and affordable treatments and vaccines, as well as successful public health strategies, have been available for decades. Cholera's re-emergence is coupled with weak health systems devastated by natural disaster, conflict and a lack of collective political will to invest in measures – such as safe drinking water and access to effective vaccines – that are proven to work.[21]

A defining pandemic of the 21st century is the HIV/AIDS pandemic, which has led to the deaths of over 30 million people. A comprehensive international response to address the HIV/AIDS pandemic was delayed until more than twenty years after its discovery. The response to HIV/AIDS is distinct since it has been and will be sustained for decades. It has reshaped healthcare systems and emphasised the need to protect the human rights of people affected by or at risk of HIV. It requires an intersectoral response that touches on education, housing, food security, and other basic human necessities, and has generated a worldwide movement to support access to affordable and appropriate medicines for people living with HIV or at risk of the disease. Many effective strategies to tackle HIV, such as task shifting, have been identified, refined, and mainstreamed by endemic countries and have been integrated into models of care worldwide. These domestic innovations and solutions have been strengthened by international cooperation to develop and deploy effective antiretroviral medicines and diagnostics.

Antimicrobial resistance is already killing many people. New drug-resistant infections will emerge and spread in the future. Decades of underinvestment to tackle AMR, including disinvestment by the public and private sectors in the development of diagnostics, treatments and vaccines, has left health systems unprepared to prevent or treat such infections. Investing in AMR efforts has the potential to shape a better future and bring life-changing health and economic benefits to people and countries across the world.

There are differences between AMR and fast-moving viral pandemics such as COVID-19.

COVID-19, while presenting huge challenges, could be brought under control within a few years through infection prevention and control, improved clinical management in hospitals, testing, treatments and vaccines.

AMR requires a long-term, sustained response, including resources, political will, and coordination across multiple sectors, from reforms to health systems and food systems as well as improved infection prevention and control and long-term research and development efforts.


*Access to appropriate antibiotics will be a vital component of preparedness and response in future pandemics.*

Drug-resistant infections share some similarities with fast-moving pandemics. Treating drug-resistant infections is an essential component of any pandemic response.

Drug-resistant infections are a silent pandemic. Drug-resistant infections spread rapidly through international travel, migration, and supply chains. AMR may get insufficient attention from policymakers because there is low awareness, because it is poorly understood, and because of insufficient surveillance, which translates into a lack of data on the spread of resistant infections, morbidity, and mortality. Major gaps in data, particularly in low- and middle-income countries, have made it nearly impossible to reliably estimate AMR's global impact.[22]

Even as the spread of AMR is 'fast-moving', the impacts are often felt (or acknowledged) more slowly. This is because:

a) high-income countries may still have some effective antibiotics that can be used appropriately and in a timely manner to treat specific drug-resistant infections;

b) some countries have better infrastructure that reduces the spread of AMR within the environment and through the food system; and

c) some countries may be unable or unwilling to monitor and measure the public health impact of AMR.

Drug-resistant infections can be distinguished from other pandemics, such as COVID-19, in that the socioeconomic disparities between countries translates directly into less serious short-term impacts in well-resourced countries, and more serious impacts in poorly resourced countries. Poorly resourced countries may not have the diagnostic capacity, antibiotics or means to meet international standards for infection prevention and control in clinical settings and management of AMR in all sectors.

*Treating drug-resistant infections is an essential component of any pandemic response.*

Access to appropriate antibiotics will be a vital component of preparedness and response in future pandemics. Although there is limited data on bacterial co-infections and secondary infections in people with COVID-19, future pandemics could carry a significant risk of hospitalization and secondary bacterial infections, and therefore health systems will require timely access to both antibiotics to treat these infections and other therapeutics and diagnostics.[23]

Two studies from China and the United States point to significant morbidity and mortality for COVID-19 patients associated with bacterial co-infections,[24,25,26] whereas a meta-analysis of thirty studies of ICU and non-ICU COVID-19 patients in five countries (China, Singapore, Spain, Thailand and the United States) found only 7% had bacterial infections.[27] These may reflect differences in healthcare facilities.

Access to antibiotics remains a major challenge in most low- and middle-income countries for several reasons, including that many antibiotics are not registered with national drug regulatory authorities, and are often unaffordable.[28] Efforts are needed to accelerate equitable global access to important antibiotic treatments while ensuring they are used responsibly to maximize the number of patients successfully treated for bacterial infections.

Antibiotic prescriptions increase substantially during a viral pandemic, as early evidence during COVID-19 has shown. There has been widespread treatment of COVID-19 patients with existing antibiotics due to the lack of available countermeasures.

This has recently been changing, with evidence of the ineffectiveness of antimicrobials to treat this infection and the availability of other therapeutic options.[29] A U.S. multicentre study reported 72% of COVID-19 patients received antibiotics even when not clinically indicated.[30]

Multiple antibiotics were also tested for efficacy against COVID-19 in formal clinical research settings and ad-hoc studies. For example, as of September 2020, ClinicalTrials.gov shows 252 COVID-19 records contained 'hydroxychloroquine' and 112 contained 'azithromycin', a common antibiotic for the treatment of bacterial infections.' This has raised concerns about the potential for increasing the number of drug-resistant infections.[31] Such use of antibiotics will take place in future pandemics, whether to treat a viral infection or to address co- or secondary bacterial infections


*COVID-19 has clearly shown that a single country cannot solve the challenges of a fast-moving pandemic on its own.*

## EARLY LESSONS OF THE COVID-19 PANDEMIC

The COVID-19 pandemic, like the 1918 flu pandemic, is an all-encompassing, global economic, political, and social crisis for which 'health' is just one rationale for government investment. COVID-19 has reinforced the importance of development, testing, and deployment of treatments, vaccines, and diagnostics to prevent and treat pandemic diseases. The lessons of the COVID-19 pandemic are both a cause for hope and concern. This paper identifies five initial lessons related to the development and access to medical countermeasures to tackle COVID-19.

### LESSON 1: INVESTMENTS IN PREPAREDNESS ARE NECESSARY, AND COST-EFFECTIVE FOR A PANDEMIC, INCLUDING RESEARCH AND DEVELOPMENT OF NEW TREATMENTS AND VACCINES.

The 2020 annual report of the GPMB notes the 'COVID-19 pandemic will trigger the biggest hit to global economic growth since World War II, with economic costs in the order of tens of trillions of dollars over the next five years.' Even if investments in preparedness run into the billions, it would 'take 500 years to spend as much on investing in preparedness as the world is losing due to COVID-19.'[32]

### LESSON 2: COLLABORATION AND INTERNATIONAL COORDINATION ARE CRITICAL TO ADDRESS A PANDEMIC.

COVID-19 has clearly shown that a single country cannot solve the challenges of a fast-moving pandemic on its own. This includes the identification and development of new medical countermeasures to prevent, test and treat; understanding how the virus is evolving; the execution of worldwide clinical trials in countries with active outbreaks; and the production of adequate supply to meet the needs of all. Without the flexibility to conduct clinical trials in countries where the pandemic is intensifying, it will be difficult to test health tools in a timely manner.[33]

### LESSONS 3: MEDICAL COUNTERMEASURES HAVE NOT BEEN AVAILABLE BECAUSE TRADITIONAL MARKET INCENTIVES ARE NEITHER SUFFICIENT NOR APPROPRIATE TO ENSURE THEIR TIMELY DEVELOPMENT ON A GLOBAL SCALE.

Since most pandemics are uncertain events that may never occur, or will materialise when unexpected, the normal incentives that are intended to promote the development of new medicines, vaccines, and diagnostics within the 'free market' are not sufficient to encourage companies to prevent, anticipate or respond without the active intervention and support (especially financial resources) of governments.[34,35]

*Regional efforts should be welcomed to ensure countries can meet their own needs and ensure there is equitable access to medical supplies worldwide.*

**LESSON 4: EQUITABLE AND AFFORDABLE ACCESS TO MEDICAL COUNTERMEASURES IS AN ESSENTIAL ELEMENT OF A COMPREHENSIVE AND EFFECTIVE PANDEMIC RESPONSE.**

Equitable access to these vital health tools has become a major challenge during the pandemic. Efforts to encourage coordination and collaboration to facilitate equitable access to countermeasures have been undermined repeatedly. This may be due to two factors: (a) anticipated or actual scarcity of supply, whether for personal protective equipment (PPE), treatments, testing equipment and tests, and future vaccines and (b) the financing of new vaccines and treatments primarily by a small number of largely high-income countries, which has allowed them to secure privileged access to new countermeasures.

As the GPMB noted in its 2020 report, there was an 'absence of a pre-established multilateral agreement to share limited countermeasures', which in its estimation will threaten to 'prolong the (COVID-19) pandemic'.[36] At the outset of the pandemic (and even now for many countries for diagnostics and treatments), there was no pooled procurement facility to pool demand for countermeasures, improve sharing of limited supply and encourage balance between supply and demand. Breakdowns of coordination and collaboration have impacted access to everything from PPE,[37] to oxygen,[38] while many countries may face delays waiting for access to new treatments, diagnostics, and vaccines approved during COVID-19.[39] The introduction of the COVAX Facility, a global risk-sharing mechanism for pooled procurement and equitable distribution of eventual COVID-19 vaccines, has been a major international effort to attempt to overcome this problem.

**LESSON 5: INEQUITABLE ACCESS TO MEDICAL COUNTERMEASURES CAN UNDERMINE THE TRUST MANY COUNTRIES HAVE IN THE 'INTERNATIONAL SYSTEM'.**

The challenges of access to countermeasures during the COVID-19 pandemic could also mean governments turn inwards as a protective measure against the shortcomings and inequities of cooperation. Even if there is greater cooperation, it will conflict with inward looking approaches for countries that do not want to fully rely upon or do not trust the 'international system'. Thus, countries may rely on shortened supply chains,[40] including end-to-end production within a country, to meet domestic needs. They may also introduce regional approaches to pandemic response, production, supply and pooling of demand, such as the recently established Africa Medical Supplies Platform.[41] These kind of regional efforts should be welcomed to ensure that countries can meet their own needs and ensure there is equitable access to medical supplies worldwide. Where possible, such efforts should be aligned with or integrated into global mechanisms that ensure equitable access.

## STRENGTHENING GLOBAL HEALTH SECURITY WHILE ACKNOWLEDGING ITS LIMITATIONS AND RISKS

The lessons of the COVID-19 pandemic hold the promise of strengthening global health security, including responses such as the development and access to new health tools. This may include a conception of 'health' in more comprehensive terms, through raising global awareness and a focus on maintaining good public health measures including infection prevention and control and hand hygiene, rather than just managing outbreaks, epidemics, and pandemics. An expansion of global health security could also mean addressing national-level needs, since the pandemic is as much about how governments assess 'external threats' as to how they manage their own response.

Yet even as global health security-based responses are strengthened, there should be a recognition of the narrowness and limits of applying a global health security approach to the emerging pandemic of drug-resistant infections. In short, the challenge of ongoing and future pandemics will require an approach to pandemic preparedness and response for which global health security is only one component.

The recommendations of the UN Interagency Coordination Group on AMR produced a roadmap to apply a One Health framework,[42] which simultaneously addresses the health, environmental, and agricultural aspects of AMR. In fact, a wider cross-sectoral approach may also be important to tackle other infectious disease pandemics. COVID-19 is linked to broader causes of infectious diseases, including underlying environmental causes[43] and the link of human pandemics with zoonotic diseases.[44] Investments that mitigate and address AMR, introduced through a One Health approach, could also improve preparedness and response to other pandemics.

The global health strategy of the German government identifies the wider applicability of a One Health approach. Its October 2020 strategy states:

*'The most suitable course of action is the One Health approach, which is based on the cross-sectoral, integrated management of health risks. This interdisciplinary approach focuses on the complex relationships between human and animal health and the protection of the environment. It is vital to consider these human-animal-environment links as they help us to understand where health risks originate, how climate change may affect our health and what effective measures we can take to prevent future pandemics, tackle antimicrobial resistance, control neglected tropical diseases associated with poverty and improve food security.'* [45]

### BOX 3: RISKS ASSOCIATED WITH GLOBAL HEALTH SECURITY FOR R&D AND ACCESS TO COUNTERMEASURES FOR AMR

Priority setting guided by global health security could lead governments that are the largest payers for research and development to focus only on microbes that have a negative public health impact on those countries, as opposed to microbes that may have the largest public health impact globally but whose impact is largely localised to low- and middle-income countries. The WHO Priority Pathogen List (Global Priority List of Antibiotic-Resistant Bacteria to guide research, discovery, and development of new antibiotics) is widely credited for identifying and prioritising unmet needs according to global public health importance and offers a common set of priorities for all countries.

A global health security framework can also relegate affected populations, such as migrants, refugees, community sex workers and men who have sex with men, as people who 'carry disease' and as a threat, instead of considering them as people in acute need.[46] A global health security approach may ignore or exclude populations who are not considered a threat because they are not mobile, but who are highly vulnerable (children, the elderly), or are confined (in hospitals and prisons).

The relegation of these populations is exacerbated by the lack of engagement with non-governmental organisations and community-based organisations in health security-led responses. This has consequences for research and development priorities, if governments, for instance, don't support the development of formulations that are needed in most low- and middle-income countries and for vulnerable populations in high-income countries. Furthermore, governments with a security-based mindset may choose to protect their investments and prioritise their own needs, and therefore advocate for policies that distort the careful balance between promoting antimicrobial stewardship and ensuring access to those in need. For example, this could result in policies that mandate strict controls to avoid using new antibiotics in low- and middle-income countries due to concerns about drug resistance. Paradoxically, this could impede global control efforts of a specific infection.

*The impact of COVID-19, along with its lessons, presents a turning point to improve the response to pandemics, particularly the silent pandemic of drug-resistant infections.*

## FIVE RECOMMENDATIONS TO STRENGTHEN THE INTERNATIONAL RESPONSE TO AMR

The impact of the COVID-19 pandemic, along with its lessons, presents a turning point to improve the response to pandemics, particularly the silent pandemic of drug-resistant infections. We recommend five concrete measures that would strengthen domestic and global responses to AMR:

### 1. RECOGNISE AND URGENTLY ADDRESS THE SILENT PANDEMIC OF DRUG-RESISTANT INFECTIONS.

Unlike COVID-19, where governments and scientists are still learning about the disease and constantly adjusting the international response, with AMR there is the ability and knowledge to prepare now. The drug-resistant microbes are known, and the potential economic and health impacts of AMR over the next 30 years have been estimated.

Without increased investments, governments cannot respond to AMR and will also be unable to provide appropriate antibiotics during a future pandemic. Without such investment, the people as well as the governments will have to contend with negative socioeconomic impacts and costs. Appropriate preparedness should also include health and surveillance systems to prevent, detect and treat emerging drug-resistant infections, including appropriate surveillance during a pandemic. The scale of drug resistance is not known due to inadequate surveillance capacity in many countries.

There is also a need for the development of new diagnostics, medicines and vaccines that will serve as countermeasures that may not be needed extensively today but will be required in the future. Following decades of underinvestment, investments are also required in basic science and research for AMR, to ensure that governments are better prepared.

## 2. INVEST IN THE DEVELOPMENT OF MEDICAL COUNTERMEASURES AS A CRITICAL ELEMENT OF PANDEMIC PREPAREDNESS.

Solutions exist to tackle the drug-resistant infections pandemic, mortality can be reduced, and the societal and economic costs seen with COVID-19 can be avoided by investing in preparedness to develop new health tools. This could cascade into long-term public health returns and economic gains. Substantial and sustained financial, scientific, and public health investments, relative to the pandemic of drug-resistant infections, need to be made. Public funding needs to be accompanied by significant private investment, provided that it can be aligned to global health priorities.

## 3. ENSURE THAT ACCESS TO DIAGNOSTICS, TREATMENTS AND VACCINES FOR ALL IS A CORNERSTONE OF PANDEMIC PREPAREDNESS AND RESPONSE.

No countermeasure will work if people cannot access it or if rationing prevails. Undermining access erodes public confidence in national and international interventions and could reduce the cooperation between countries to respond effectively to a pandemic, as well as develop and manufacture countermeasures. COVID-19 has been a wake-up call to countries – wealthy, poor, large and small – that the existence of any effective new medicine, diagnostic or vaccine in the midst of a public health crisis will not necessarily be available to those who need it most.

Governments can strengthen domestic capacity to participate fully in globally coordinated R&D efforts, improving upon historically low levels of funding and insufficient support from international health agencies. As it relates to AMR, governments can consider several recommendations to ensure fair and equitable access. This can include resurrecting agreements, such as the Development and Stewardship Framework; ensuring international and domestic supply chains are reliable and robust; and stockpiling critical countermeasures needed for both the sudden onset of a viral pandemic like COVID-19 or to tackle the long-term and silent pandemic of drug-resistant infections.

**4. EXPAND GLOBAL COOPERATION ACROSS GEOGRAPHIES AND SECTORS AND WITHIN A ONE HEALTH FRAMEWORK.**

To support both the development of and access to existing and new countermeasures particularly for AMR, governments should expand cooperation and co-ordination with all stakeholders: across geographies; between the private and public sectors; and within a One Health framework, recognising the importance of connecting the health of people to both the health of animals and our shared environment.

AMR will require improved collaboration and coordination to ensure that the best diagnostics, treatments and vaccines are selected for development; understand the evolution of resistance in different settings; and efficiently test vaccines and treatments (in high-burden countries). No country can or should act alone to develop new countermeasures to prevent and respond to drug-resistant infections.

Other substantial, coordinated initiatives could also help to drive progress. This could include strategies to:

- Pool funding by governments, for example via contributions to WHO's recently launched AMR Multi-Partner Trust Fund (launched by WHO, FAO and OIE), to make National Action Plans a reality, especially in countries with inadequate domestic resources.
- Expand not-for-profit global partnerships such as the Global Antibiotic Research and Development Partnership (GARDP) to develop and introduce new antibiotics that are necessary for preparation and response, including products adapted for use in low- and middle-income countries.
- Create a facility that can pool demand and procure new and important old antibiotics and diagnostics as well as balance supply and demand.
- Establish regulatory mechanisms and collaboration that while not sacrificing quality, safety and efficacy, will promote greater coherence and facilitate development.

*AMR will require improved collaboration and coordination to ensure that the best diagnostics, treatments and vaccines are selected for development.*

**5. ENSURE LOW- AND MIDDLE-INCOME COUNTRIES ARE EQUAL PARTNERS IN A COMPREHENSIVE GLOBAL RESPONSE. SOLUTIONS THAT HAVE BEEN PIONEERED BY COUNTRIES SHOULD BE RECOGNISED AND INTEGRATED INTO PANDEMIC PREPAREDNESS AND RESPONSE.**

Many low- and middle-income countries have built impressive domestic strategies and solutions in the face of the HIV pandemic while also addressing other outbreaks and epidemics over the last few decades. Many of these countries are now responding successfully to COVID-19. The solutions, strategies and innovations of these countries must be respected and promoted. Countries also need to look for new solutions as a hedge against scarcity and rationing of new medical tools. These include countries that lack raw materials and manufacturing capacity, those that do not have significant purchasing power on the open market (which can include small, high-income countries), and poor countries which must rely on development assistance and philanthropy to bolster health expenditure and pandemic response.

## CONCLUSION

There are risks associated with relying on the current global health security framework to address pandemics. Governments should consider global health security, in the aftermath of COVID-19, as one part of a wider framework of pandemic preparedness and response. The One Health framework that guides the response to AMR could provide a wider, intersectoral strategy to prevent and prepare for pandemics of the future. Governments should also recognize preparedness is a shared responsibility and can only be successful if solutions work for the public and are available to all.

These considerations also apply to the development and introduction of new medical countermeasures. Efforts to coordinate the global response to the COVID-19 pandemic took a while to get underway. Many governments now recognise that access is a key issue in the pandemic response. It is therefore essential to strengthen and sustain recent efforts to expand supply and ensure equitable access to lifesaving medicines and medical supplies that maximise global public health impact.

The consequences of COVID-19, which could be felt for years to come, should make it both economically viable and politically necessary for governments to address ongoing and future pandemics. The COVID-19 pandemic has illustrated the need to strengthen AMR surveillance and healthcare infrastructure, as well as ways to ensure worldwide, equitable access to antimicrobials, diagnostics, and vaccines.[47]

AMR requires a long-term investment and is an opportunity for governments to find a collective approach to global health that is fair to all; that prioritises coordination, partnership and solidarity; that takes a multisectoral and multilateral approach; and that satisfies public health needs and human life over economic and political considerations. Achieving this would cascade into lasting and life-saving benefits for people and countries across the world.

*It is essential to strengthen and sustain recent efforts to ensure equitable access to lifesaving medicines and medical supplies.*

## GLOSSARY

**Antimicrobial resistance** - antimicrobial resistance (AMR) occurs when bacteria, viruses, fungi and parasites change over time and no longer respond to medicines making infections harder to treat and increasing the risk of disease spread, severe illness and death. (source: World Health Organization)

**Antibiotic resistance** - antibiotic resistance is the ability of bacteria to change in a way that makes antibiotics ineffective. (source: Wellcome)

**Drug-resistant infections** – term used to describe illnesses that have been caused by resistant microbes, resulting in an infection that is much harder – or potentially impossible – to treat. (source: Wellcome)

**Countermeasures** – the term 'medical countermeasures' refers to life-saving medicines and medical supplies that can be used to diagnose, prevent, protect from, or treat conditions associated with chemical, biological, radiological, or nuclear threats, emerging infectious diseases, or a natural disaster. (source: US Centers for Disease Control and Prevention)

**One Health** – 'One Health' is an approach to designing and implementing programmes, policies, legislation and research in which multiple sectors communicate and work together to achieve better public health outcomes. The areas of work include food safety, the control of zoonoses (diseases that can spread between animals and humans, such as flu, rabies and Rift Valley Fever), and combatting antibiotic resistance (when bacteria change after being exposed to antibiotics and become more difficult to treat). (source: World Health Organization)

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