EIDHS
Emerging Infectious Diseases
& Health Security

A Changing Landscape: How Response to a Pandemic can Impact Antimicrobial Resistance

FEBRUARY 1, 2022

fhi360
THE SCIENCE OF IMPROVING LIVES

Acronyms

AMR	Antimicrobial resistance
AMS	Antimicrobial stewardship
AMU	Antimicrobial use
GHS	Global health security
INGO	International non-governmental organization
LMIC	Low and middle-income country
NAP	National action plan
NGO	Non-governmental organization
OTC	Over the counter
WHO	World Health Organization

Executive Summary

Antimicrobial resistance (AMR) is a global public health threat with substantial human and economic impact.

Preliminary research on changes in antibiotic use throughout the COVID-19 pandemic raises grave concerns about increasing AMR. On 12-13 October 2021, FHI 360 convened a symposium of partners, funders, and stakeholders to develop a strategy for addressing AMR during pandemic settings. Leading experts and participants provided insights on the intersection between COVID-19 and AMR and potential global health impacts. This document is a proceeding of what was discussed and proposed for the future. The symposium was organized across four focal areas for addressing AMR in the face of pandemics, and these focal areas inform the framework presented in this report (*see Box. 1*). The symposium took place over two days and included participatory discussions using online platforms with rapid analysis of these discussions at the end of day one that were reported out on day two. The second day culminated in an overarching strategy, shown on page 10 in this report.

Contributors to the symposium identified key actions, drivers and outcomes needed to address AMR for each focal area, shown in Figures 1-4 of this report. Based on the analysis of participant contributions, experts identified critical cross-cutting factors to inform our overall AMR-focused pandemic response strategy. These factors include: the importance of addressing equity for improved outcomes in low and middle-income countries (LMICs) in AMR and pandemic responses, the need to engage stakeholders throughout the development and implementation of strategies to mitigate AMR while still being responsive to pandemic needs, and the need to leverage existing and build-out weak infrastructure – such as data collection systems, laboratory diagnostics and clinician education and training initiatives – to address and not further AMR during pandemics.

We aimed to advance the AMR/global health security (GHS) agenda by sharing knowledge from leading experts and synthesizing a framework for addressing AMR during pandemics. Findings from the symposium synthesizes leading expertise to advance use of evidence-based best practices to improve antimicrobial stewardship (AMS). Based on these findings, the symposium resulted in a call to action that highlights vital steps in addressing AMR, including: engaging stakeholders, strengthening laboratory capacity, enhancing public education, encouraging implementation of strong policies, developing standard treatment protocols, facilitating evidence-based prevention, and promoting innovation and adaptation (page 11). This call to action is urgent given the gravity of AMR in the face of the current COVID-19 global pandemic and can inform our approach to ensuring our global health in the face of future pandemics.

BOX1.
SYMPOSIUM FOCAL AREAS

1. Antibiotic use and misuse during the COVID-19 Pandemic: Implications for the future of AMR
2. The role and importance of laboratory diagnostic capabilities in mitigating AMR
3. The importance of integrating antimicrobial stewardship measures into the COVID-19 response
4. One Health: Zoonoses implications for AMR

Global Concerns of Increased Antimicrobial Resistance During a Pandemic

Antimicrobial resistance (AMR) is a global public health threat with substantial human and economic impact.

It occurs when bacteria, fungi, and parasites stop responding to and become resistant to antimicrobial medications. The World Health Organization (WHO) states that resistant bacteria, sometimes called superbugs, already claim 700,000 lives annually worldwide. If left unchecked, the death toll from AMR could reach 10 million per year by 2050, according to a recent United Nations 2019 report.[1] The World Bank estimates global AMR health care costs could increase by more than $1 trillion per year by 2050 degrading healthcare down to the patient level.[2, 3] Among individuals who were affected by drug-resistant infections, the risk for morbidity and mortality increased by two- and three-fold, respectively, compared to healthy individuals. The scale of AMR has increased rapidly in recent years, especially in countries where regulations that control antibiotic prescription and use in humans and animals are weak or nonexistent.

Researchers have started to explore how antimicrobial use has changed throughout the COVID-19 pandemic. Knight and colleagues report a marked increase in the use of antimicrobials during inpatient and outpatient treatment of COVID-19, with 70% of diagnosed patients receiving antimicrobials.[4] Comparatively, Boten and Prins reveal that in a population of patients with acute influenza caused by the virus H3N2, only about 17% of patients diagnosed with a respiratory infection received antibiotics.[5] Hospitalized patients with COVID-19 have been increasingly prescribed broad-spectrum antibiotics as the nature of the infections make it challenging to discern between COVID-19 symptoms and secondary bacterial infections. Chen and colleagues declare that in a disease unit in China, 71% of patients with COVID-19 were prescribed antibiotics, though only 1% of the hospitalized patients with COVID-19 had secondary bacterial infections that required antibiotic therapy.[6]

> *"We have reached the point where scientists are warning that we face one of the greatest threats to humankind: not only could many common infections become incurable, but a lack of effective antibiotics could effectively end much of modern medicine, since we rely on these drugs to keep us healthy during surgery and cancer treatment."*[7]

[1] The World Bank. (2016, September 18). By 2050, drug-resistant infections could cause global economic damage on par with 2008 financial crisis. https://www.worldbank.org/en/news/press-release/2016/09/18/by-2050-drug-resistant-infections-could-cause-global-economic-damage-on-par-with-2008-financial-crisis; World Health Organization. (2019a, April 29). New Report Calls for Urgent Action to Avert Antimicrobial Resistance Crisis. https://www.who.int/news/item/29-04-2019-new-report-calls-for-urgent-action-to-avert-antimicrobial-resistance-crisis; World Health Organization. (2019b, April 29). No Time to Wait: Securing the Future from Drug-Resistant Infections. https://www.who.int/docs/default-source/documents/no-time-to-wait-securing-the-future-from-drug-resistant-infections-en.pdfsfvrsn=5b424d7_6; World Health Organization. (2020, October 13). Antimicrobial Resistance. https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance

[2] By 2050, drug-resistant infections could cause global economic damage on par with 2008 financial crisis (worldbank.org)

[3] Dadgostar, P. (2019). Antimicrobial Resistance: Implications and Costs. Infection and Drug Resistance, Volume 12, 3903–3910. https://doi.org/10.2147/idr.s234610

[4] Knight, G. M., Glover, R. E., McQuaid, C. F., Olaru, I. D., Gallandat, K., Leclerc, Q. J., Fuller, N. M., Willcocks, S. J., Hasan, R., van Kleef, E., & Chandler, C. I. (2021). Antimicrobial Resistance and COVID-19: Intersections and Implications. ELife, 10. https://doi.org/10.7554/elife.64139

[5] Bonten, M. J. M., & Prins, J. M. (2006). Antibiotics in Pandemic Flu. BMJ, 332(7536), 248–249. https://doi.org/10.1136/bmj.332.7536.248

[6] Chen, N., Zhou, M., Dong, X., Qu, J., Gong, F., Han, Y., Qiu, Y., Wang, J., Liu, Y., Wei, Y., Xia, J., Yu, T., Zhang, X., & Zhang, L. (2020). Epidemiological and Clinical Characteristics of 99 Cases of 2019 Novel Coronavirus Pneumonia in Wuhan, China: A Descriptive Study. The Lancet, 395(10223), 507–513. https://doi.org/10.1016/s0140-6736(20)30211-7

[7] William Hall, Anthony McDonnell, Jim O'Neill. 2018. Superbugs: An Arms Race Against Bacteria. Boston, MA: Harvard University Press

Mismanaged use and overuse of antibiotics are known to contribute to increased levels of AMR. Hospitals in LMICs are particularly vulnerable to low compliance to best practices in antimicrobial stewardship due to scarce laboratory resources, limited health system capacity, systemic stress, and poor antibiotic control. Ghosh, Bornman, and Zafer highlight the need for LMICs to implement stronger antimicrobial stewardship programs, reporting the use of over-the-counter antibiotics has surged during the COVID-19 pandemic, with antibiotic self-medication at a rate of 33%.[8] In settings where the aforementioned challenges are present, the COVID-19 pandemic may have long-term consequences on the global emergence and acceleration of AMR; countries and their health systems need to act to address this global public health threat.

Developing an Antimicrobial Resistance Pandemic Response Strategy

On 12-13 October 2021, FHI 360 convened a symposium where partners, funders, and stakeholders gathered to provide expertise and thought leadership to develop a strategy to address the consequences of the intersection between COVID-19 and AMR. We sought to learn from leading experts, report these learnings to the global community, and deliver a call to action for combatting AMR, especially when confronting a pandemic. Global experts (*see Box 2*) provided a keynote address, plenary presentations, and led online focus group discussions in each of the identified focal areas. Participants totaled 197 people from over 38 countries across the globe. Several sectors were represented during the symposium, including government (66, 42.9%), nonprofit (26, 16.9%), academia (21, 13.6%), private/corporate (17, 11%), NGO (6, 3.9%), INGO (5, 3.3%), and others (13, 8.4%). Over half of all participants had at least ten years of relevant experience, and respondents contributed to collaborative discussions that informed the results included in this report. This document is a proceeding of what was discussed and ultimately proposed for addressing AMR in the face of the current and future pandemics (*see Box 3*).

BOX 2.

AMR PANDEMIC RESPONSE SYMPOSIUM KEYNOTE SPEAKER AND PANELISTS

Keynote Speaker:

Lord Jim O'Neill
PhD., Economist, Member of the Pan-European Commission on Health and Sustainable Development

Panelists:

Bradley Langford
BscPhm, PharmD, BCPS, Lead Pharmacist for Public Health Ontario's Antimicrobial Stewardship Program

Sabiha Essack
BPharm, MPharm, Ph.D., Professor in Pharmaceutical Sciences at the University of KwaZulu-Natal (UKZN); South African Research Chair in Antibiotics Resistance and One Health

Isidore Bonkoungou
Ph.D., Professor in Microbiology at the University Joseph KI-ZERBO in Burkina Faso

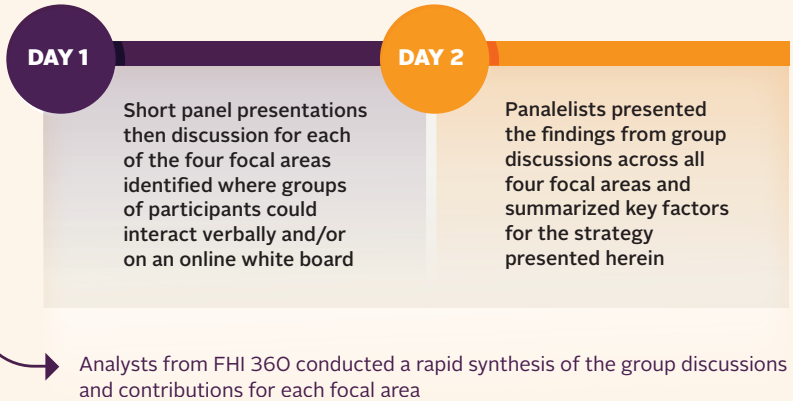
Thuy Doan
MD, PhD Professor and Clinical Scientist at University of University of California, San Francisco

[8] Ghosh, S., Bornman, C., & Zafer, M. M. (2021). Antimicrobial Resistance Threats in the Emerging COVID-19 Pandemic: Where

BOX 3.

FHI 360's Approach to Developing and AMR Pandemic Strategy

Convened 2-day symposium with an hour-and-a-half online conference including a keynote address



Analysts from FHI 360 conducted a rapid synthesis of the group discussions and contributions for each focal area

Based on this symposium, a strategy has been proposed for addressing AMR during pandemics supported by data, experiences, and observations during the COVID-19 global pandemic. Through this strategy, FHI 360 and our partners aim to: explain the need for a global health strategy to address the intersection of COVID-19 and AMR; advance the AMR/global health security (GHS) agenda by sharing knowledge from leading experts and synthesizing a framework for addressing AMR during pandemics; and provide thought leadership to advance use of evidence and best practices to improve AMS.

Implications of Antibiotic Use and Misuse during the COVID-19 Pandemic for the Future of Antimicrobial Resistance

Symposium participants discussed how antibiotic use and misuse during the COVID-19 pandemic has significantly impacted the future of AMR, particularly through off-label use of antibiotics to treat COVID-19. It is critical that deliberate misuse be prevented, and to do this the health sector must work closely with community members, public and private healthcare providers and facilities, policymakers, and traditional healers to reduce antibiotic misuse. Antimicrobial misuse should be addressed outside the context of COVID-19 as well as within the context of pandemic response. Laboratory capacity to diagnose viral and bacterial infections must be increased, along with much needed rapid AMR diagnostic capacity with advanced molecular characterization. These efforts need to be realistic, multi-level, and involve local actors and adhere to global standards. To ensure equity, stakeholders

from LMICs must set and lead their agendas and policies for addressing AMR. Specific outcomes discussed by the group, as well as the actions and drivers necessary to achieve these outcomes, are highlighted in Figure 1.

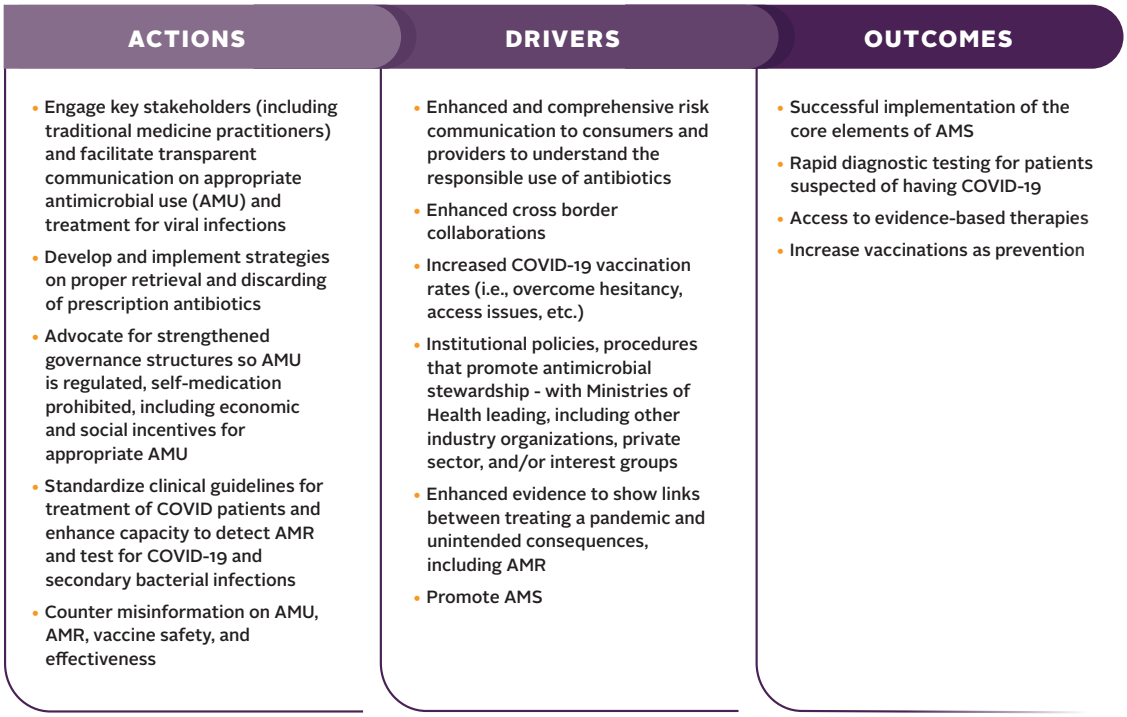


FIGURE 1. *Focal Area 1 Actions, Drivers and Outcomes to Reduce AMR*

The Role and Importance of Laboratory Diagnostic Capabilities in Mitigating AMR

As was noted during the discussion of antibiotic use and misuse, laboratory diagnostic capabilities play a vital role in mitigating AMR, using rapid detection techniques and molecular characterization to determine AMR. With potentially fatal illnesses, it is vital that clinicians are able to accurately diagnose and treat patients as early in the disease as possible. However, clinical practice guidelines for the proper use and application of therapeutics to address COVID-19 are unclear or under development in many facilities and health systems, especially for treatment of potential secondary bacterial infections. To achieve reliable, timely, and accurate diagnoses of microbial infections and AMR, symposium participants emphasized that we must: standardize approaches for diagnosing pathogens; build capacity and integrate human and animal health laboratory systems; and ensure laboratory diagnostics are available to broader stakeholders. Specific outcomes discussed by participants, as well as actions and drivers necessary to achieve these outcomes, are highlighted in Figure 2.

ACTIONS	DRIVERS	OUTCOMES
• Harmonize/standardize laboratory procedures and diagnostics • Engage relevant human and animal health authorities, regulatory bodies, and interest groups • Engage stakeholders through a collaborative process • Leverage existing resources and infrastructure from other disease areas and seek outside resources	• Capacity for surveillance in animal and human health; training, education, awareness raising • Fully functioning and adequate supply chains to support necessary laboratory diagnostic and surveillance needs • Necessary funding to support laboratory strengthening	• Rapid diagnostics to support clinical care decisions; molecular diagnostics that are valid and reliable; ability to isolate/detect depending on specimen source • Surveillance systems that integrate across human and animal, and include population, community, and environmental surveillance systems

FIGURE 2. *Focal Area 2 Actions, Drivers and Outcomes to Reduce AMR*

The Importance of Integrating Antimicrobial Stewardship Measures into COVID-19 Response in LMICs

Antimicrobial stewardship must be included at all levels of a healthcare system to effectively combat AMR; this is especially important in LMICs where surveillance systems may lack the ability to track and report AMR data in real time. Leadership and political will are essential to building capacity and buy-in for addressing AMR in pandemic responses at the local and global levels. Where resources are limited, coordination and collaboration are key factors that can help bolster efficiencies and prevent redundancies in AMR surveillance and stewardship measures. Symposium participants highlighted the unique opportunity to take advantage of the COVID-19 pandemic to develop more sustainable and integrated infectious disease diagnostic and surveillance systems by capitalizing on ongoing efforts to strengthen systems and increased awareness of the global nature of infectious diseases. Figure 3 outlines the outcomes that need to be achieved, as well as actions and drivers that can contribute to progress in this area.

ACTIONS	DRIVERS	OUTCOMES
• Develop, implement, and enforce policies on AMR • Harness political and regulatory will and partnerships to design solutions for LMICs • Develop and/or leverage and expand on existing collaborations and networks to address the issue comprehensively • Education about AMR and AMU for healthcare providers and community members	• Strong leadership • AMR Policies with clear and strong guidelines • Antimicrobial surveillance (AMS) included in the national action plan (NAP) • Resources: human, infrastructure, & operational • Technical capacity to develop and implement AMS programs	• Funded and sustainable stewardship and surveillance programs across the healthcare continuum from primary to tertiary care • Diagnostic stewardship to optimize the management of infection while minimizing resistance • Uninterrupted access to the needed category of antibiotics

FIGURE 3. *Focal Area 3 Actions, Drivers and Outcomes to Reduce AMR*

One Health: Zoonoses Implications to AMR

An effective One Health approach requires multi-sectoral collaboration spanning animal, human, and environmental health. Practitioners and policymakers need to shift the mentality that antimicrobials are a panacea solution and adopt more targeted practices to meet their needs and production demands. The need for judicious and appropriate AMU cuts across clinical practice guidelines for human and animal healthcare, as well as for industrial agricultural practices that often use antimicrobials as a prophylactic treatment to prevent bacterial, viral, and fungal infections in confined, large populations of livestock and fish. Inadequate diagnostic capabilities also limit efficiency within a One Health framework where there are varying degrees of capacity and lack of integration in surveillance strategies across human and animal health sectors. AMR needs to be addressed at a systems level – spanning human, animal, and environmental health. Figure 4 presents the key actions, drivers, and outcomes for this area.

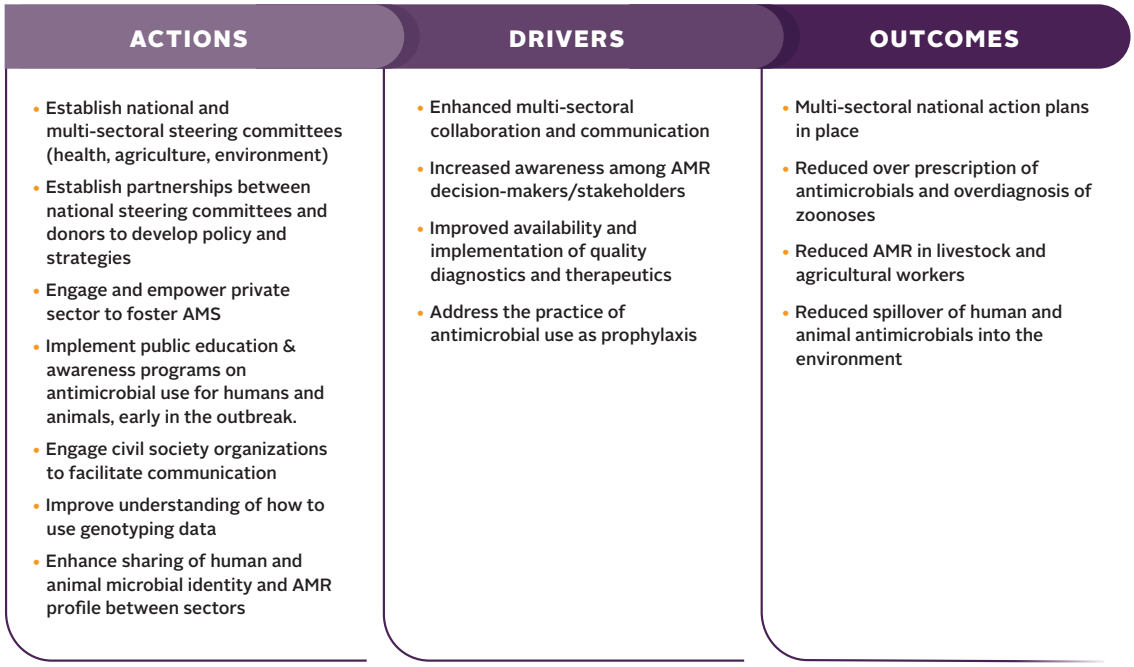


FIGURE 4. *Focal Area 4 Actions, Drivers and Outcomes to Reduce AMR*

Cross-cutting Issues in Addressing AMR in the Face of a Pandemic

The symposium highlighted how multisectoral collaboration and integration of antimicrobial stewardship and laboratory diagnostics across all levels of the health system, including human, animal, and environmental health, are crucial to reducing AMR. Use of antibiotics for viral infections and prophylactic administration of antimicrobials remains a persistent challenge despite evidence that it contributes to AMR; these norms need to be addressed with medical providers, patients, veterinarians, and animal caretakers. Specific to COVID-19, standardized protocols for AMR diagnostics and consistent guidelines on the use of antimicrobials for treatment of severe illness are needed. There is a need for equitable access to rapid diagnosis of AMR strains, particularly in LMICs—both for COVID-19 patients and in general. Pandemic infrastructure and response can be leveraged for strategies to reduce AMR — including funding, information sharing, supply chains, surveillance systems, and public and policymaker awareness. The AMR Pandemic Response Strategy (Figure 5) was designed by the symposium participants to incorporate these cross-cutting issues.

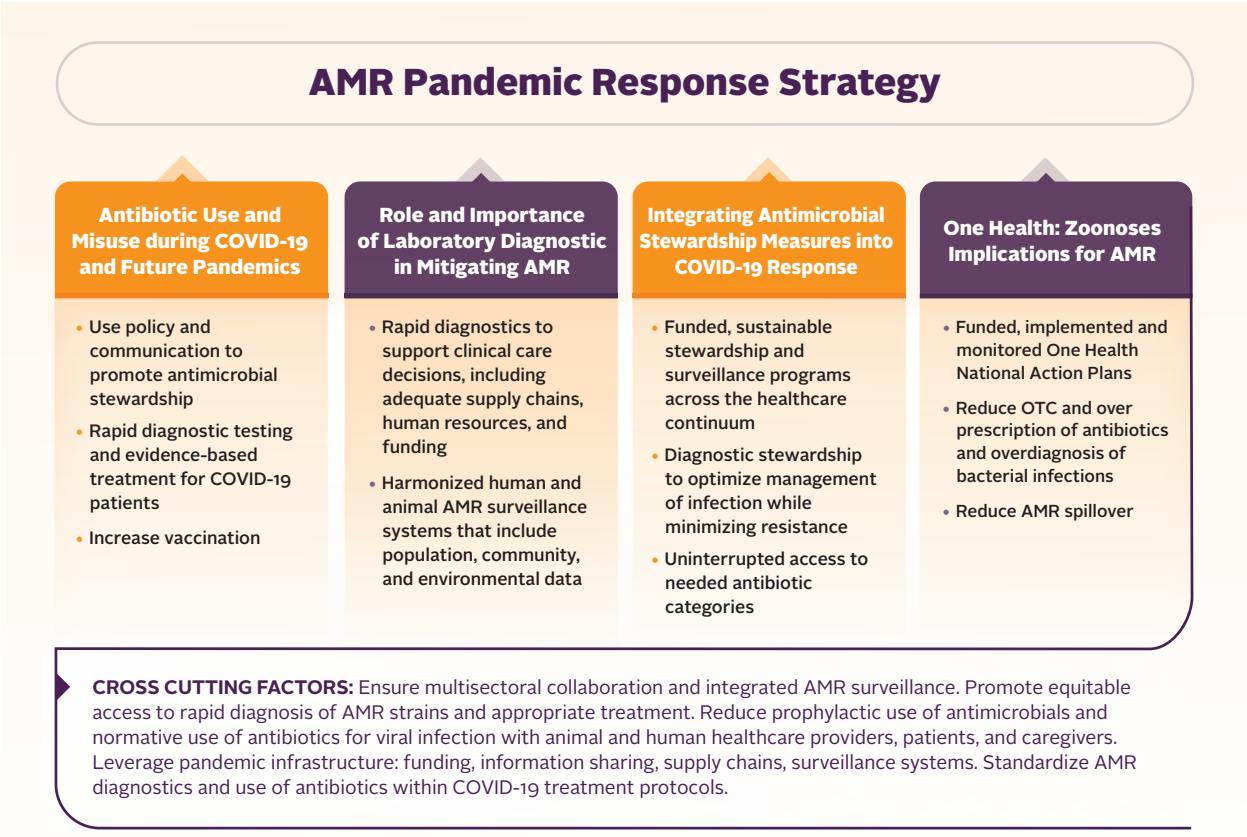


FIGURE 5. *AMR Pandemic Response Strategy*

Combatting Antimicrobial Resistance in Pandemic Settings: A Call to Action

The results of our symposium build on existing frameworks and expert input to inform a call to action. The steps outlined in our call to action are timely given the gravity of AMR in the face of the current COVID-19 global pandemic and can inform our approach to ensuring our global health in the face of future pandemics.

Call to Action Vital Actions Necessary to Combat AMR During a Pandemic

ACTION 1: Engage key stakeholders across and between borders to ensure transparency and collaboration across different types of medical practitioners and decision makers. Establish national public health priorities to combat AMR within pandemic responses.

ACTION 2: Strengthen laboratory capacity to detect, characterize, record, and report on AMR, as well as capacity to test for bacterial infections in both animals and humans, particularly in LMICs. Must simultaneously strengthen surveillance capacity and align mechanisms and metrics, including creating robust data reporting systems that can harmonize inputs from multiple systems and levels.

ACTION 3: Enhance public education and awareness programs on appropriate antimicrobial use for human and animals; counter misinformation using relevant communication platforms, including social media, mass-media, and inter-personal communications. Tailor strategies to target audiences with an eye to who are the key influencers and community leaders, including informal leaders.

ACTION 4: Encourage implementation of policies to reduce antibiotic misuse, including restricting over the counter sales and operationalizing systems for retrieval and discarding of unused medications; simultaneously boost economic and social incentives for appropriate antimicrobial prescribing and use. Initiatives should be evidence-based and led by local stakeholders. Must include private and public healthcare providers, as well as pharmacies and drug shops, traditional healers, farm suppliers, and veterinarians.

ACTION 5: Develop and disseminate standardized treatment protocols for pandemic diseases, including guidance on diagnosing and treating concomitant bacterial infection.

ACTION 6: Facilitate evidence-based prevention of pandemic diseases; for example, vaccinations, personal hygiene measures, and use of personal protective equipment. Prevention of primary infections negates risk of secondary bacterial infections. Efforts must address equitable access to preventive measures, as well as demand for preventive measures—including countering misinformation.

ACTION 7: Promote innovation and adaptation to better address AMR within pandemic situations, such as new classes of antimicrobials, vaccines, and diagnostic approaches, as well as innovations in delivery of services. Public-private partnerships and other collaborative fora may facilitate such innovations.

Emerging Infectious Diseases and Health Security, Infectious Diseases and Health Systems Department
359 Blackwell Street, Suite 200,
Durham, NC 27701, USA
O: +1.919.544.7040| www.fhi360.org

Janet Robinson, FIBS
Janet Robinson is the Portfolio Director of Emerging Infectious Diseases and Health Security at FHI 360 and is a leading expert on health systems strengthening and emerging infectious diseases.
jrobinson@fhi360.org

Pat Sadate-Ngatchou, PhD
Dr. Sadate-Ngatchou is the Program Director of Emerging Infectious Diseases and Health Security at FHI 360 and is an expert in combatting antimicrobial resistance and laboratory sciences.
psadate-ngatchou@fhi360.org

fhi 360
THE SCIENCE OF IMPROVING LIVES

EIDHS
Emerging Infectious Diseases & Health Security