



OPEN ACCESS

This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

University of Texas Health Science Center at Houston Texas, USA

Correspondence to:
Elkin V. Lemos-Luengas,
lemoselkin4@gmail.com

Additional material is published online only. To view please visit the journal online.

Cite this as: Lemos-Luengas EV. Beyond Antibiotics: A Global Perspective on Combating Antimicrobial Resistance Through One Health and Innovative Technologies. Premier Journal of Public Health 2024;1:100006

DOI: <https://doi.org/10.70389/PJPH.100006>

Received: 27 August 2024

Revised: 4 October 2024

Accepted: 5 October 2024

Published: 18 October 2024

Ethical approval: N/a

Consent: N/a

Funding: No industry funding

Conflicts of interest: N/a

Author contribution:
Elkin V. Lemos-Luengas –
Conceptualization, Writing –
original draft, review and editing

Guarantor: Elkin V. Lemos-Luengas

Provenance and peer-review:
Commissioned and externally
peer-reviewed

Data availability statement:
N/a

Beyond Antibiotics: A Global Perspective on Combating Antimicrobial Resistance Through One Health and Innovative Technologies

Elkin V. Lemos-Luengas, MD, PhD

ABSTRACT

Antimicrobial resistance (AMR) is a global problem that has been emerging and threatens much of the progress in modern medicine over the past centuries. Drawing on the One Health methodology, which recognizes the connections between human, animal, and environmental health, this paper considers how the AMR problem is understood from the different angles (“silos”) of the disciplines involved in the fight against AMR and how we can merge different perspectives to find solutions. It explores the main drivers of resistance and the related economic losses, highlighting some of the innovative approaches in the field, such as CRISPR/Cas9 and nanotechnology, and understanding the causes of resistance through an empirical hypothesis that suggests multidimensional ways to tackle the problem collaboratively. Therefore, this paper calls for the international community’s united action to protect health systems and economies at a global level through education and informed use of antimicrobials.

Keywords: Antimicrobial resistance, One Health, CRISPR/Cas9, Nanotechnology, Global health

Introduction

The Imminent Crisis of Antimicrobial Resistance: A One Health Perspective on Innovative Solutions

Modern medicine has seen breakthroughs in life and longer lifespans to undo this stiff resistance due to excessive antimicrobial drug use and misuse, which is pushing microbes to evolve new ways of dodging human medicine. It is a new generation of resistant pathogenic microbes that is turning some of the things that were meant to be treatable into a potentially lethal scenario. The threat of antimicrobial resistance (AMR) was prominently named one of the most important challenges to global health, placing it on the World Health Organization’s (WHO) list of the top 10 threats to the survival of humanity.¹ And as a result, antibiotic-resistant infections have grown, as have the economic and financial costs that accompany them. The steep increase of AMR is expected to lead to 10 million people’s deaths in 2050.² The possibility of a world in which a routine operation and simple infections return to be life-threatening is no more a dystopian fantasy than the current one. And it is coming sooner than we think – this is something we need to start paying attention to now.

In this paper, we articulate a detailed overall response to AMR that draws upon a One Health framing. One Health recognizes that human, animal, and environmental health are inextricably intertwined and that the causes and consequences of AMR span across

fields. We explore the interplay of incentives leading to resistance, not the least inappropriate antimicrobial use in health care and agriculture, and the ecological impacts of antimicrobial pollution. Additionally, the paper shows how new technologies, such as CRISPR/Cas9 gene editing and targeted nanotherapies, can transform how we combat AMR. Finally, the paper addresses how the concepts of holistic connectivity and joint, cross-sectoral action may serve as an inspiration and a future direction for mitigating the AMR crisis and securing global health for generations to come.

AMR: A Global Health Challenge

The Unfolding Crisis: Scope and Magnitude of AMR

It represents the biggest public health threat facing the globe now, and the threat of undoing the fruits of 20th-century medicine may be realized with a ticking back of the clock to a pre-antibiotic “dark age.” One problem that does persist with medicine is that of AMR. However, while we celebrate the curative powers of antimicrobial medicine and the new antibiotic drug, and changing what was once dubbed as “miracle drugs,” “wonder drugs,” “magic bullets,” or “panaceas,” we have grown up to realize that cure is no longer a sure thing, and many infections pose a risk of relapse. It changed the ability to treat infections and permitted life-saving surgery and organ transplantation and now complex cancer treatment where otherwise it would not have been allowed. Modern life would be impossible without them. The problem of AMR, however, according to surviving doctors born in the Victorian era, is considered to be one of the biggest and most neglected challenges to global health security, which could undo the fruits of 20th-century medicine, roll back the gains of civilization, and return us to a pre-antibiotic dark age.

A crisis of epic proportions faces us. As good an overall measure of the human impact of AMR as any study was published in 2016 in *the Lancet*: The authors of the paper calculated that, in 2019, AMR caused 1.27 million deaths around the world. This is an even higher figure than those found for HIV/AIDS and malaria.³ They were stark reminders that we were not talking of some distant future threat but of a present reality and its devastating implications. But who knows, if this trend continues, by 2050, the world could have its very own zombie apocalypse. This is when the WHO projects AMR will kill an estimated 10 million people annually and take its place as the leading cause of death, surpassing even cancer.³

Besides its human cost, AMR is an economic time bomb: The recently published World Bank report

predicts that AMR can be expected to lead to a worldwide economic recession as dramatic as the global financial crisis of 2008, with a disproportionate impact on low- and middle-income countries.⁴ It is estimated that by 2030, antimicrobial resistance (AMR) will push an additional 24 million people into extreme poverty, further exacerbating global health inequalities. One example is an infection caused by multidrug-resistant *Acinetobacter baumannii*, which has developed resistance to all available last-resort antibiotics, including last-generation carbapenems (see Figure 1). This graph was created using data from the ATLAS Platform (ATLAS Surveillance, 2020–2022).

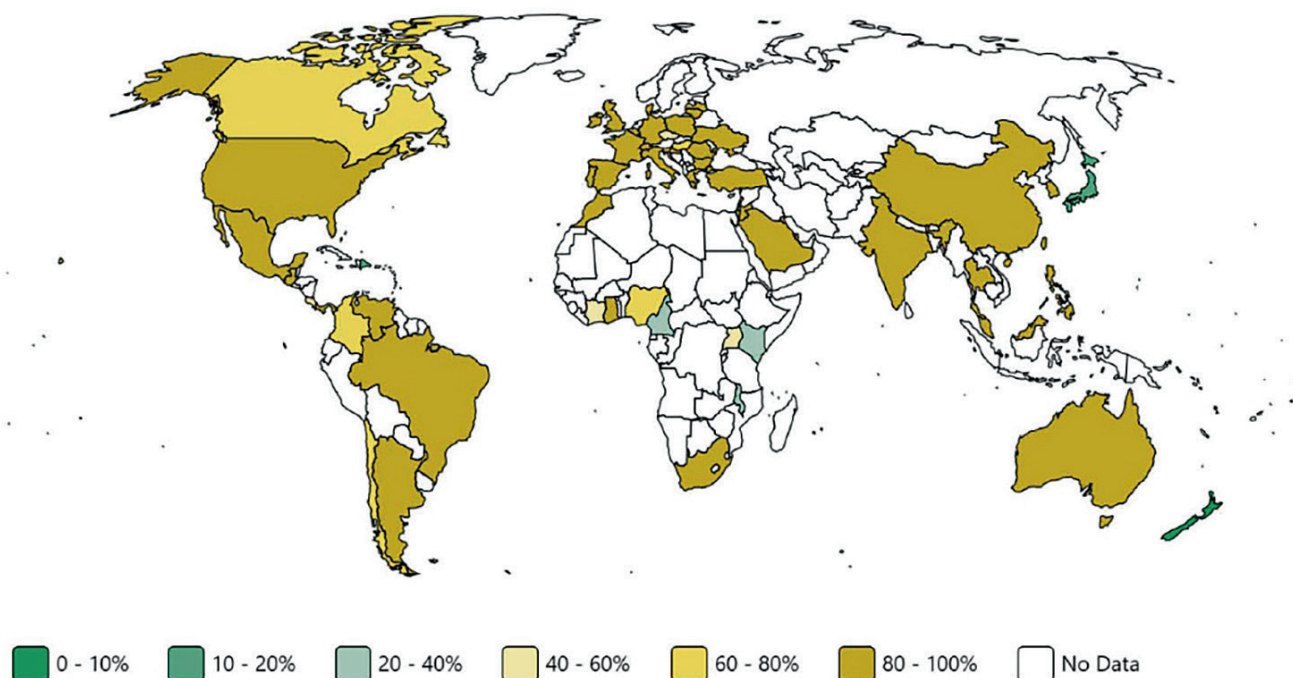
Fuelling the Fire: Drivers of AMR

Although biological mechanisms may be quite complex, the primary causes are also in many ways all too often deeply interlinked with human behavior and practice.⁵

Overuse and Misuse of Antimicrobials: The single most important cause of AMR worldwide is the misuse of antimicrobials in human and animal health.^{6,7} This includes unnecessary prescription of antibiotics – often for viral infections where antimicrobials are

neither needed nor effective to treat and cure – that allow resistant bacteria to continue to spread. Indeed, a Pew study published in 2023 in *JAMA Network Open* revealed that nearly a third of antibiotic prescriptions in the US were inappropriate.⁸ This issue is further compounded by using antimicrobials as growth promoters and prophylactic agents in livestock and aquaculture, creating a reservoir of resistant bacteria that can transfer to humans.⁹

Lack of Infection Prevention and Control: Inadequate infection prevention and control measures in healthcare settings and communities contribute to the spreading of resistant organisms.¹⁰ This includes insufficient hand hygiene practices, improper sterilization of medical equipment, and inadequate sanitation infrastructure, particularly in resource-limited settings. A study by Casalini *et al.* demonstrated the positive impact of bundled interventions on quality-of-care indicators for *Staphylococcus aureus* bacteremia, highlighting the importance of a multifaceted approach to infection control.¹¹ As outlined in Table 1, such an approach will be key to how we respond to these and other drivers to slow the spread of AMR and preserve the effectiveness of antimicrobials for future generations.



Report Date: August 26th 2024, 20:21:31

The clinical significance of in vitro activity is unknown.

ATLAS Surveillance. 2020-2022. ATLAS platform.
<https://atlas-surveillance.com>

Fig 1 | Global trends in *Acinetobacter baumannii* resistance to Carbapenems (2020–2022) using CLSI 2024 (M100-ED34) breakpoints, including all data sources and MDR phenotypes

Table 1 | Key Drivers Fueling Antimicrobial Resistance and Their Impact on Global Health.

Driver	Description	Impact on AMR
Overuse and Misuse of Antibiotics	Excessive use of antibiotics in healthcare settings and agriculture, often without proper diagnosis or prescription.	Accelerates the development of resistant bacteria by increasing selective pressure, allowing resistant strains to thrive and multiply. Misuse includes using antibiotics for viral infections or not completing prescribed courses.
Lack of New Antibiotics	Insufficient investment in the development of new antibiotics due to economic challenges and regulatory hurdles.	Limits the availability of effective treatments for resistant infections, forcing reliance on older, less effective drugs. The slow pipeline of new antibiotics makes it difficult to keep pace with the evolving resistance patterns.
Poor Infection Control and Sanitation	Inadequate hygiene practices, sanitation, and infection control in healthcare facilities and communities.	Facilitates the spread of resistant bacteria within hospitals and the community, increasing the likelihood of outbreaks. Poor sanitation and overcrowded living conditions, especially in low-resource settings, exacerbate the spread of infections and resistant strains.
Agricultural Practices	Use of antibiotics in livestock and aquaculture to promote growth and prevent disease, often in sub-therapeutic doses.	Contributes to the emergence of resistant bacteria that can be transmitted to humans through food consumption, direct contact with animals, or environmental contamination (e.g., water and soil).
Global Travel and Trade	Increased movement of people, animals, and goods across borders.	Facilitates the global spread of resistant bacteria, making it challenging to contain outbreaks. Resistant strains that emerge in one region can quickly spread to others, complicating efforts to control AMR at national and international levels.
Suboptimal Surveillance and Data Sharing	Inadequate tracking and sharing of data on resistance patterns and antibiotic use across countries.	Hinders the ability to monitor trends, implement effective interventions, and respond to emerging threats. Limited surveillance, particularly in low-resource settings, means that resistant strains can spread unchecked, and global efforts to combat AMR lack crucial data.
Inequitable Access to Healthcare	Disparities in access to quality healthcare, leading to delayed treatment and the use of substandard or counterfeit antibiotics.	Increases the likelihood of improper antibiotic use and the persistence of infections, contributing to the development and spread of resistance. In low-income countries, lack of access to effective antibiotics leads to overuse of older, less effective ones, further driving resistance.
Environmental Contamination	Release of antibiotics, resistant bacteria, and pharmaceutical waste into the environment through industrial and healthcare effluents.	Contaminates water sources and soil, creating reservoirs of resistant bacteria that can be transmitted to humans and animals. Environmental AMR hotspots, such as wastewater treatment plants, are breeding grounds for resistant bacteria, which can spread to the broader environment and food chain.
Human Behavior and Public Awareness	Lack of understanding and awareness about the appropriate use of antibiotics among the public and healthcare providers.	Leads to overprescribing, self-medication, and demand for antibiotics for non-bacterial infections. Public health campaigns to educate both the public and healthcare professionals about AMR and appropriate antibiotic use are crucial to slowing resistance development.

- World Health Organization (WHO). (2020). *Antimicrobial resistance: Global report on surveillance*. World Health Organization.
- Centers for Disease Control and Prevention (CDC). (2019). *Antibiotic resistance threats in the United States, 2019*. U.S. Department of Health and Human Services.
- Laxminarayan R., Matsoo P., Pant S, Brower, C., Röttingen J. A, Kluginan K., & Davies S. (2016). *Access to effective antimicrobials: A worldwide challenge*. The Lancet, 387(10014), 168–175.
- World Bank. (2017). *Drug-resistant infections: A threat to our economic future (Vol. 2): Final report* (English). Washington, D.C.: World Bank Group.

The Economic Imperative: Costs and Consequences of Inaction

The economic burden associated with AMR is large and multi-faceted, transcending immediate healthcare expenditure implications to affect productivity, economic growth, and global security. The failure to tackle this crisis is dire, affecting individuals, health systems, and the global economy.

The economic burden of AMR is large and multi-stakeholder; it goes beyond immediate healthcare costs to include foregone economic productivity and impediments to economic growth and global security. The failure to tackle this crisis has dire consequences for individuals, health systems, and the global economy.¹² This is further compounded by exorbitant

healthcare costs related to the treatment of resistant infections, longer hospital stays, and increased morbidity and mortality – all threatening the sustainability of health systems and the economies relying on them.¹³ It also predicts that the long-term economic impact of AMR will increase rapidly and, if the present trends continue, will incur a death toll of 10 million people per year by 2050. In this regard, the important need for policy responses cannot be overemphasized in the battle to prevent this crisis from growing and to ensure a brighter future for all.¹⁴

Direct Costs: The financial strain of AMR is first felt within healthcare systems grappling with the increased costs of treating drug-resistant infections. More extended hospital stays, often required for patients battling

resistant pathogens, significantly burden hospital resources and contribute to rising healthcare expenditures.¹⁶ This is further compounded with the usage of more expensive last-resort antibiotics, which are also often related to a higher level of toxicity and side effects. A 2022 Clinical Infectious Diseases study concluded that the annual cost of treating antibiotic-resistant infections in the US alone exceeded \$4.6 billion.¹⁵ However, this only scrapes the tip of the iceberg.^{16,17} In addition to direct healthcare costs, the overall economic implications of AMR include lost productivity due to illness and early death and significant economic costs associated with increased morbidity and mortality in the workforce, which could result in loss of gross domestic product (GDP) and a national security threat.^{13,17,18}

Indirect Costs: The true economic cost of AMR is much broader than just the cost incurred within the walls of the hospital; it affects individuals, communities, and national economies. Lost productivity due to prolonged illness and premature death is an enormous but generally invisible cost. The World Bank estimates that in 2050, AMR could lead to a loss of \$3.4 trillion in global GDP.¹⁹ This economic fallout will be projected upon low- and middle-income countries, compounding existing inequalities and blocking development. Moreover, the threat of untreatable infections can upset global trade and tourism, as the fear of contagious outbreaks curtails travel or disrupts trade. This situation is only worsened by the fact that the economic consequences of AMR typically result in increased premiums by insurance companies and higher healthcare costs passed on to consumers, which, in the end, further straddles families and communities with financial burdens.¹³ In addition to the fact that infections resistant to treatment are increasing the financial burden on healthcare budgets, the development of new antibiotics and other therapies to treat resistant infections represents a significant investment with a great risk for sponsors in view of the many market dynamics and regulatory challenges. In addition, these antibiotics offer no immediate financial returns in a high-risk environment.²⁰ In this way, tackling the economic aspects of AMR is not just a healthcare issue but also an imperative global economic issue, and it needs collective action and investment at international, national, and community levels to avert potential collapse, thus safeguarding public health systems for future generations. As the costs of inaction mount and threaten global stability, this will also show the need for innovative financing mechanisms since the public and private sectors will have to come together to prioritize research and development for new antimicrobial agents, similar to the strategies used in other critical areas of public health.^{4,13,17,21} However, the rapid growth of AMR without timely intervention and investment in antimicrobial stewardship jeopardizes decades of medical progress and puts us at risk of a world where routine procedures may become life-threatening, making it necessary to radically reconsider certain policies and strategic investments in

order to avert this impending crisis and secure a more prosperous and sustainable future. Concomitantly, the economic implications of AMR go beyond the health sector and will pervade the global workforce, as the emergence of resistant infections is marked by lost productivity and increases in rates of absenteeism, and, therefore, further the problems of economies in recovering from the COVID-19 pandemic. Furthermore, the potential of AMR to cause drastic disruptions of the health workforce and general economic status should underline the urgent need for integrated approaches that include increased public awareness, education about the responsible use of antimicrobials, and robust strategies for the prevention of infection at all levels to avert these wide-ranging effects and ensure the health and general well-being of human beings, communities, and nations. The multiple effects of AMR on health systems, economies, and individual lives emphasize the need for immediate global action, including work towards sustainable strategies to prevent and manage AMR and to drive innovation in antibiotic development, including campaigns to raise awareness for the responsible use of antimicrobials, all of which will ensure the continued effectiveness of these major medical breakthroughs.^{17,22-24}

Current Challenges in Combating Resistance

Effectively addressing AMR requires a multifaceted approach that tackles the complex interplay of factors contributing to its rise. Here are some key challenges (Table 1): transgressive antibiotic use in health care – overtreatment, i.e., prescribing more antibiotics than needed and for longer than required, is another major factor in the creation of resistance. This is most prominent in using antibiotics for viral infections for which they are ineffective. The problem has been exacerbated by the need for rapid diagnostic tools to identify a bacterial infection promptly and the inability to discriminate between bacteria and viruses without appropriate rapid testing. This leads to the empirical use of antibiotics until test results are known. Lack of effective and appropriate antibiotics in many healthcare settings hampers efforts to achieve optimal antibiotic use and maintain susceptibility.

Agricultural Use and the Breeding of Resistant Bacteria: The widespread and non-selective use of antimicrobials for growth promotion and prevention of diseases in animals for food production has created a huge reservoir of resistant bacteria that can transfer uncontrolled to humans via food and the environment.^{5,25} Although in some countries the legislation on the use of antibiotics in animals has been restricted for this purpose, a lack of coordination and proper enforcement of these regulations at a global level persists.⁹

Environmental Impact of AMR: Pollution and Spread: The non-therapeutic release of antimicrobial residues and resistant microorganisms into the environment via sewage from hospitals, manufacturing of drugs and antibiotics, and agricultural runoff, among others, add to the dissemination of AMR.¹

These effluents can contaminate water reservoirs, soils, and animals, leading to a pathway for resistant microorganisms to enter into the food chain and infect humans. New One Health approaches integrating environmental surveillance and mitigation measures to human and animal health interventions are helping mitigate this challenge.²⁴

One Health: A Unified Approach to Antimicrobial Stewardship

The fact that human, animal, and environmental health are also intertwined shows the need for a truly One Health perspective to take account of these connections and maximize the chances of tackling AMR. The One Health concept is based on the understanding that to address AMR we need to bring together all sectors working to improve health outcomes for humans, animals, and the environment.

Principles and Goals of One Health

At a basic level, One Health recognizes the intricate interconnectedness of health for humans, animals, and our environment, and the mutuality of their well-being.²⁶ The methodological approach is underpinned by transdisciplinary collaboration and information-sharing among health scientists, veterinarians, ecologists, policymakers, and communities to mitigate or alleviate shared health threats, such as AMR.²⁷ By maximizing the health of humans, animals, and our environment, One Health aims to achieve the optimal health outcomes for all stakeholders.

Education and Training in Antimicrobial Stewardship across Sectors

A critical pillar of the One Health approach is fostering a culture of responsible antimicrobial use across all sectors. This requires comprehensive education and training programs tailored to different target audiences. Healthcare professionals need ongoing education on evidence-based prescribing guidelines, infection prevention and control measures, and the importance of antimicrobial stewardship.²⁸ Similarly, veterinary experts require training on prudent antimicrobial use in animal care, emphasizing reduced unnecessary antibiotic use in livestock and aquaculture.²⁸ Public awareness campaigns can empower individuals to make informed decisions about antibiotic use and understand their role in mitigating AMR.

Policy Changes to Foster Collaboration and Responsible Use

This can be achieved through effective policy interventions that create an enabling environment for responsible utilization of antimicrobials, such as framing and enforcing regulations on antimicrobial use in human and animal health, incentivizing and accelerating research and development of new antibiotics and alternatives, and strengthening surveillance to monitor the emergence and spread of resistance organisms.²⁴ Given the globalization of AMR, global collaboration becomes imperative to approach

these issues in a unified manner. For example, the WHO's Global Action Plan on Antimicrobial Resistance provides a roadmap for joint action and resource-sharing among nations.²⁹

Following a One Health approach and incorporating these holistic strategies will move us closer to a future where antimicrobials are still valuable tools for safeguarding human and animal health.

Beyond Antibiotics: Exploring Innovative Solutions

Since the anti-infective drugs we already have are becoming less effective with each passing year, we must urgently look for new ways of treating bacterial infections. New treatment options and new technologies should be an integral part of the fight against AMR.

Research into Alternative Treatment Options

Scientists are actively investigating a range of promising alternatives to conventional antibiotics:

Antimicrobial Peptides (AMPs): These small proteins are found ubiquitously in nature. They are broad-spectrum antimicrobials and so would help address the problem of antibiotic resistance.³⁰ Because of the multivalent action of AMPs on their bacterial targets, it is difficult for resistance to occur.

Phage Therapy: In this strategy, viruses that infect and kill bacteria (bacteriophages) are utilized against bacterial infections. This therapy loses out by a hair because it still depends on antibiotics to get rid of bacterial exotoxins. However, the virus/bacteria combination is a potential response to multidrug-resistant infections, and, in theory, allows for targeted elimination of only the bad bacteria.³¹

Anti-virulence Strategies: Unlike the anti-bacterial approaches described above, these therapies do not kill bacteria, but rather impair pathogenic bacteria by disarming their virulence factors so that they are no longer harmful to the host,³² an approach that could reduce antibiotic selection for resistance.

The Role of Advanced Technologies

Cutting-edge technologies are revolutionizing the development of new antimicrobial agents:

CRISPR/Cas9: This revolutionary gene-editing tool holds immense potential for combating AMR. CRISPR/Cas9 can be used to develop highly specific antimicrobials that target essential genes in resistant bacteria, potentially overcoming existing resistance mechanisms.³³

Nanotechnology: Nanoparticles offer a versatile platform for delivering antimicrobial agents with enhanced efficacy and targeted delivery. Nanoparticle-based therapies can improve drug solubility, enhance penetration into bacterial biofilms, and reduce off-target toxicity.^{12,34}

Engaging Stakeholders for Sustainable Change

The fight against AMR is not only for healthcare professionals and scientists to take up but also involves all stakeholders working together – from public education to patient engagement to cross-sector collaboration towards sustainability of change.

The Importance of Public Education in Combating AMR

The role of public awareness-raising in promoting appropriate antimicrobial use and limiting the occurrence and spread of AMR cannot be underestimated. Responsible practices should be promoted through microbial-ecology-based educational campaigns concentrating on:

Value and Threat: Why antibiotics are precious and how AMR poses a threat.

Ensuring Appropriate Antibiotic Use: Enlightening people on what illnesses require antibiotics and the need to stick to professionals' instructions.

Preventing Infections: Stressing the importance of handwashing, vaccination, and other sources of infection, reducing the demand for antibiotics.

The WHO offers some valuable resources and guidance for public awareness campaigns relating to AMR.³⁵

Engaging Patients in Discussions About the Appropriate Use of Antimicrobials

In addition to establishing behavioral protocols to mitigate the development of resistance, healthcare professionals must educate patients about the proper use of antimicrobials:

1. **Open Communication:** Discuss the pros and cons of antibiotic treatment (e.g., side effects, risk of resistance).
2. **Conditional Consent:** Share information about the potential for potential resistance to antibiotics with your child.

Shared Decision-Making: Involving patients in decisions about antibiotic use, considering their preferences and values.

"Adherence": Focus on the emphasis of the necessity of completing the course of antibiotics, irrespective of symptom improvement.

The Need for Collaboration across Sectors: Health care, Agriculture, and Environment

Addressing AMR requires a One Health approach that fosters collaboration across sectors:

Health care: Develop antimicrobial stewardship, enhance infection prevention and control, and incorporate judicious prescribing.⁵

Agriculture: Cutting antimicrobial use in livestock and aquaculture, introducing biosecurity to stop pathogen spread, and developing alternative growth promoters.⁵

Environment: Recovering and mitigating antimicrobial residues in the environment, finding ways to improve sanitation and hygiene, and increasing appropriate waste management pathways.⁵

Ethical Considerations in the Age of AMR

Our current crisis of AMR presents an entire matrix of ethical conundrums, much beyond the clinical-therapeutic sphere. We have a collective responsibility

to address these dilemmas justly and ethically – to ensure that we not only pursue the best treatments but also prioritize them in a way that is fair to all.

Balancing Individual and Collective Interests

Perhaps, one of the greatest ethical challenges going forward will be how to accommodate individual patient interests with the need to preserve the effectiveness of antimicrobials for the community. On the one hand, a necessary response to drug resistance is to restrict antibiotic use. However, it can still be a wrench when there is an individual patient who might possibly benefit from the use of an antibiotic (even if the indication is debatable). This highlights the fact that we also need more fine-tuned ethical frameworks, which are able to help us guide decision-making in the face of uncertainty. They will have to weigh up potential benefits for the individual when a patient treatment option becomes available, against the possibility that such use will compromise future treatment options for us all.³⁶

Access and Equity

The overall ethical complexity of the situation is deepened by the unequal distribution of the burden of infectious diseases and access to health care across the globe. High-income countries are grappling with overprescribing and healthcare-associated infections, while low- and middle-income countries often suffer from poor availability of existing antimicrobials, thus perpetuating an undertreatment vicious cycle that leads to increased resistance.³⁷ Both equitable distribution of existing antimicrobial therapies and shared collaboration to foster access to new antimicrobials are crucial, especially in light of healthcare infrastructure inequalities and affordability concerns. This again requires international collaboration and researching of resources to enable the distribution of new therapies in scenarios where access to healthcare systems is not guaranteed.

Stewardship and Responsibility

The appearance of AMR brings home the need for stewardship – for all of us to use antibiotics responsibly. This includes individual stewardship of using antibiotics as directed by your healthcare provider and taking full courses prescribed (yes, even if you start to feel better), and the stewardship of healthcare providers to prescribe antibiotics judiciously and to ensure proper stewardship for their patients.³⁸ The stewardship responsibilities of the agricultural community include a reduction in the use of antimicrobials in livestock and in sustainable farming practices that reduce the spread of resistant organisms.³⁸

Research and Innovation

Ethical issues figure prominently in the development of new antimicrobial therapies. The desperate need to discover new treatments must be balanced with the need for appropriate development and clinical uses – access to new drugs around the world, reducing

clinical trials conducted in developing countries, and maintaining transparency in research funding and data sharing.³⁹

Addressing the Knowledge Gap

Public education has a place in the ethical response to AMR, too. Broadening societal awareness of the problem, its implications if nothing is done, and the value that might be gained through collective action promotes responsible antimicrobial use and supports AMR mitigation policies.⁴⁰

There are no simple answers to the ethical challenges posed by AMR. Resolving these issues calls for continuous discussion, interdisciplinary collaboration, and the development of a social justice agenda. By bringing ethical reflection to bear on policy development, research, and clinical practice, we might someday achieve the goal of a world where antimicrobial therapies continue to protect human health.⁴⁰

Conclusion: Charting a Path Towards a Post-Antibiotic Future

The possibility of a post-antibiotic apocalypse, where treatable infections start to kill again, becomes a grave reality. Despair is not an option. The problem of AMR is daunting, but not insurmountable. Our best response will be a broad, multifaceted one that blends scientific innovation with public engagement and global solidarity. In this way, we can forge a future where antimicrobial therapies continue to be part of modern medicine.

Key Takeaways from Our Exploration of AMR

AMR is also an endemic global health problem, exacerbated by a perfect storm of antibiotic overuse and misuse, poor infection control, and the paucity of new drug antibiotics.

The costs of doing so are huge: Hundreds of millions of lives, trillions of dollars of economic activity and, most importantly, massive disruption to society.

There are no silver bullets – we need a multi-pronged approach: AMR demands an approach that encompasses antimicrobial stewardship, infection prevention, new drug development, international collaboration, and public education.

Innovative solutions are key: Maintaining our capacity to produce novel antimicrobial therapies, such as phage therapy and AMPs, and the development of novel technologies, such as CRISPR/Cas9 and nanotechnology, are of utmost importance.

It is important to emphasize public awareness: Training the public about the need for judicious antibiotic use, hand and cough hygiene, and the significant threat posed by AMR will help cultivate a culture of stewardship.

No more declaring an end to communism. We must work together globally. AMR does not respect national boundaries, and we need international collaboration on discovery, surveillance, and policy to tackle this shared menace.

What is needed now is a collective awareness of the threat posed by AMR, a willingness to learn, a spirit of cooperation, and momentum. Governments, care providers, equestrian athletes, industry leaders, researchers, and civilians have all invested heavily in the preservation of these medicines that save lives. Sustainability demands a holistic, One Health approach also mindful of the connection between human, animal, and environmental health. Our response must recognize the shared burden – and take collective action – before it is too late.

The post-antibiotic future is not written but one that we can help shape. If we act boldly, collaboratively, and with mutual responsibility, we can help ensure that our critical weapons in the battle against infectious disease remain with us for the coming decades.

References

1. Salam MA, Al-Amin MY, Salam MT, Pawar JS, Akhter N, Rabaan AA, et al. Antimicrobial resistance: a growing serious threat for global public health. *Healthcare*. 2023;11(13):1946.
2. McKibbin WJ, Fernando R. Global macroeconomic scenarios of the COVID-19 pandemic. *SSRN Electron J*. 2020. Available from: <https://doi.org/10.2139/ssrn.3547729>.
3. Murray CJL, Ikuta KS, Sharara F, Swetschinski L, Robles Aguilar G, Gray A, et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet*. 2022;399(10325):629–55.
4. Ahmed SMS, Aleem A. Drug-resistant infections: a threat to our economic future. Washington, DC: World Bank; 2017 Mar. Available from: <https://openknowledge.worldbank.org/handle/10986/26707>.
5. Arnold KE, Laing G, McMahon BJ, Fanning S, Stekel DJ, Pahl O, et al. There is a need for One Health systems-thinking approaches to understand the multiscale dissemination of antimicrobial resistance. *Lancet Planet Health*. 2024;8(2):e124–e33.
6. Brown T, Lee JY, Guzman A, Fischer MA, Friedberg MW, Chua K-P, et al. Prevalence and appropriateness of in-person versus not-in-person ambulatory antibiotic prescribing in an integrated academic health system: a cohort study. *PLOS ONE*. 2023;18(7):e0289303.
7. Kurdi A, Al Mutairi N, Baker K, M-Amen K, Darweesh O, Karwi H, et al. Impact of COVID-19 pandemic on the utilization and quality of antibiotic use in the primary care setting in England, March 2019–March 2023: a segmented interrupted time series analysis of over 53 million individuals. *Exp Rev Anti-infect Therapy*. 2024;1–12.
8. Hamilton A, Poleon S, Cherian J, Cosgrove S, Laxminarayan R, Klein E. COVID-19 and outpatient antibiotic prescriptions in the United States: a county-level analysis. *Open Forum Infect Dis*. 2023;10(3):OFID 1–OFID 9.
9. Okaiyeto SA SP, Chen C, Ni JB, Wang J, Mujumdar AS, Zhang JS, et al. Antibiotic-resistant bacteria in food systems: current status, resistance mechanisms, and mitigation strategies. *Agric Cult Commun*. 2024;2:100027.
10. Cocker D, Birgand G, Zhu N, Rodriguez-Manzano J, Ahmad R, Jambo K, et al. Healthcare as a driver, reservoir, and amplifier of antimicrobial resistance: opportunities for interventions. *Nat Rev Microbiol*. 2024;22(7):636–649.
11. Casalini G, Pagani C, Giacomelli A, Galimberti L, Milazzo L, Coen M, et al. Impact of a bundle of interventions on quality-of-care indicators for *Staphylococcus aureus* Bacteraemia: a single-centre, quasi-experimental, before–after study. *Antibiotics*. 2024;13(7):646.
12. PACCARB. A United Front: Collaborative Global Leadership To Combat Antimicrobial Resistance: A Report with Recommendations. U.S. Department of Health and Human Services; 2024.
13. Ouakrim DCA, Cecchini M, Plachouras D. The health and economic burden of antimicrobial resistance. In: Press CU, editor. *Challenges to Tackling Antimicrobial Resistance*. Cambridge University Press, 2020.
14. De Kraker MEA, Stewardson AJ, Harbarth S. Will 10 million people die a year due to antimicrobial resistance by 2050? *PLOS Med*. 2016;13(11):e1002184.

- 15 Ku JH, Bruxvoort KJ, Salas SB, Varley CD, Casey JA, Raphael E, et al. Multidrug resistance of *Escherichia coli* from outpatient uncomplicated urinary tract infections in a large United States Integrated Healthcare Organization. *Open Forum Infectious Diseases*. 2023;10(7):ofad287.
- 16 Thorpe KE, Joski P, Johnston KJ. Antibiotic-resistant infection treatment costs have doubled since 2002, exceeding \$2 billion annually. *Health Aff*. 2018;37(4):662–9.
- 17 Dadgostar P. Antimicrobial resistance: implications and costs. *Infecti Drug Resist*. 2019;12:3903–10.
- 18 Lemos EV, De La Hoz FP, Alvis N, Einarson TR, Quevedo E, Castañeda C, et al. Impact of carbapenem resistance on clinical and economic outcomes among patients with *Acinetobacter baumannii* infection in Colombia. *Clin Microbiol Infect*. 2014;20(2):174–80.
- 19 Poudel AN, Zhu S, Cooper N, Little P, Tarrant C, Hickman M, et al. The economic burden of antibiotic resistance: a systematic review and meta-analysis. *PLOS ONE*. 2023;18(5):e0285170.
- 20 Kadri SS. Key takeaways from the U.S. CDC's 2019 antibiotic resistance threats report for frontline providers. *Crit Care Med*. 2020;48(7):939–45.
- 21 Naylor NR, Atun R, Zhu N, Kulasabanathan K, Silva S, Chatterjee A, et al. Estimating the burden of antimicrobial resistance: a systematic literature review. *Antimicrob Resist Infect Control*. 2018;7(1):1–17.
- 22 Jasovsky D, Littmann J, Zorzet A, Cars O. Antimicrobial resistance threatens the world's sustainable development. *Upsala J Med Sci*. 2016;121(3):159–64.
- 23 Mantravadi PK, Kalesh KA, Dobson RCJ, Hudson AO, Parthasarathy A. The quest for novel antimicrobial compounds: emerging research, development, and technologies trends. *Antibiotics*. 2019;8(1):8.
- 24 McEwen SA, Collignon PJ. Antimicrobial resistance: a One Health perspective. *Microbiol Spectrum*. 2018;6(2):521–47.
- 25 Walsh TR. A one-health approach to antimicrobial resistance. *Nat Microbiol*. 2018;3(8):854–5.
- 26 Léger A, Stärk KDC, Rushton J, Nielsen LR. A One Health evaluation of the University of Copenhagen Research Centre for control of antibiotic resistance. *Front Vet Sci*. 2018;5:00194.
- 27 Velazquez-Meza ME, Galarde-López M, Carrillo-Quiróz B, Alpuche-Aranda CM. Antimicrobial resistance: One Health approach. *Vet World*. 2022;743–9.
- 28 Sjöberg AM, Fellman CL, Destefano IM, Langfitt SM, Stein MR, Kwong M, et al. One Health interprofessional stewardship to combat antimicrobial resistance. *Nat Med*. 2023;29(3):512–3.
- 29 World Health Organization FaOotUN, United Nations Environment Programme, and World Organisation for Animal Health. Implementing the global action plan on antimicrobial resistance WHO; 2023—200 p.
- 30 Macnair CR, Rutherford ST, Tan M-W. Alternative therapeutic strategies to treat antibiotic-resistant pathogens. *Nat Rev Microbiol*. 2024;22(5):262–75.
- 31 Dave R, Banerjee D. Bacteriophage therapy: a refurbished age-old potential strategy to treat future antibiotic and multidrug-resistant bacterial infections. *Braz J Microbiol*. 2024;55(3):3043–3049.
- 32 Tran S, Lebreuilly L, Cormontagne D, Samson S, Tô T, Dervyn R, et al. An anti-virulence drug targeting the evolvability protein Mfd protects against infections with antimicrobial-resistant ESKAPE pathogens. *bioRxiv*. 2024. Available from: <https://doi.org/10.1101/2024.01.22.576688>.
- 33 Pandey P, Vavilala SL. From gene editing to biofilm busting: CRISPR-CAS9 against antibiotic resistance—a review. *Cell Biochem Biophys*. 2024;82:549–560.
- 34 Singh C, Mehata AK, Priya V, Malik AK, Setia A, Suseela MNL, et al. Bimetallic Au–Ag nanoparticles: advanced nanotechnology for tackling antimicrobial resistance. *Molecules*. 2022;27(20):7059.
- 35 Darcovich ACB, Jaka B, Liauw F, Balasa G, Kariuki J, Lawal M, et al. Meaningful engagement of patients, survivors and carers in addressing antimicrobial resistance. World Health Organization (WHO); 2019.
- 36 Parsonage B, Hagglund PK, Keogh L, Wheelhouse N, Brown RE, Dancer SJ. Control of antimicrobial resistance requires an ethical approach. *Front Microbiol*. 2017;8:2124.
- 37 Pokharel S, Adhikari B, Johnson T, Cheah PY. Interventions to address antimicrobial resistance: an ethical analysis of key tensions and how they apply in low-income and middle-income countries. *BMJ Glob Health*. 2024;9(4):e012874.
- 38 Kelbrick M, Hesse E, O'Brien S. Cultivating antimicrobial resistance: how intensive agriculture plows the way for antibiotic resistance. *Microbiology*. 2023;169(8):001384.
- 39 Fletcher S. Understanding the contribution of environmental factors in the spread of antimicrobial resistance. *Environ Health Prevent Med*. 2015;20(4):243–52.
- 40 Huang Z, Tang WE, Guo H, Natarajan K, Lee TH, Yeo TW, et al. An evidence-based serious game app for public education on antibiotic use and antimicrobial resistance: protocol of a randomized controlled trial. *JMIR Res Protocols*. 2023;12:e45833.