

A Global Call to Action to Fight Antimicrobial Resistance: IDSA and ESCMID Joint White Paper

Anurag N. Malani,¹ Mike Sharland,² Cornelius J. Clancy,³ and Robert Skov^{4,*}; on behalf of the IDSA and ESCMID executive boards

¹IDSA Public Policy and Advocacy Committee, Member, Trinity Health Michigan, Ann Arbor, MI, USA, ²ESCMID AMR Subcommittee Policy Officer, Pediatrics Infectious Diseases, City and St George's University of London, UK, ³IDSA Public Policy and Advocacy Committee, Member, University of Pittsburgh, Pittsburgh, PA, USA, and ⁴ESCMID President, Epidemiological Infectious Disease Preparedness, Statens Serum Institut, Copenhagen, Denmark

Keywords. antimicrobial resistance (AMR); carbapenem-resistant Enterobacterales; carbapenem-resistant *Acinetobacter*; One Health; WHO AWaRe antibiotic classification; water, sanitation and hygiene (WASH); United Nations General Assembly (UNGA); PASTEUR Act.

World leaders will convene this September at the United Nations General Assembly (UNGA) to tackle one of the greatest threats facing human health—antimicrobial resistance or AMR. This is an extraordinary opportunity to drive meaningful and urgently needed global change to reduce the impact of AMR through a One Health approach. AMR represents an escalating crisis that poses an imminent and severe threat to global health. The current pace of progress is insufficient and robust action is required so as not to undermine decades of advances in health.

With this commentary, the Infectious Diseases Society of America (IDSA) and European Society for Clinical Microbiology and Infectious Diseases (ESCMID) representing thousands of physicians, scientists, and other health care providers working in the area of infectious diseases and microbiology jointly issue an urgent call for the adoption of a political declaration with bold targets and practical steps to accelerate progress against AMR across human, animal, agricultural and environmental sectors and ensure accountability. It is critical that multilateral organizations and high-income countries provide the financing and technical assistance

necessary to support AMR efforts in low- and middle-income countries (LMICs).

The imperative for global action against AMR is clear. AMR is not a future problem—patients are already experiencing poor outcomes including death associated with these difficult-to-treat resistant infections. There were an estimated 1.27 million deaths directly attributable to bacterial AMR in 2019, with 20% of those deaths occurring in children under age 5 [1]. The COVID-19 pandemic worsened the burden of AMR by placing extreme pressure on hospitals and health systems, overcrowding health care facilities, decreasing resources for infection prevention and control, driving overuse of antibiotics early in the pandemic. For example, in the US, AMR infections caused by 7 key pathogens (carbapenem-resistant Enterobacterales, carbapenem-resistant *Acinetobacter*, *Candida auris*, methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant Enterococcus, ESBL producing Enterobacterales, and multidrug resistant *Pseudomonas aeruginosa*) increased by a combined 20% during the pandemic and remain above pre-pandemic levels [2].

It has been estimated that antibiotics have extended the human lifespan by more than 20 years, making their discovery one of the major scientific advances in the past century [3]. The impact of AMR on human health is tremendous given the central role of antibiotics in modern medicine. Organ transplantation; cancer chemotherapy; use of prosthetic joints, heart valves and other implantable devices; surgery and complex care have extended lives and improved quality of life, however, they also carry significant risks of infection, making antimicrobials essential to support this care. AMR is eroding much of this medical progress and for many populations very few treatment options for serious infections are now available. This threat is, however, not equally distributed but affects vulnerable populations in LMICs and women and children the most. To truly propel consequential, sustainable progress against AMR, the UN political declaration must include bold targets and be accompanied by robust financing. We urge all participants to

Published online 11 September 2024

Corresponding author at: Epidemiological Infectious Disease Preparedness, Statens Serum Institut, Copenhagen, Denmark Email address: RSK@ssi.dk (R. Skov).

Open Forum Infectious Diseases®

© The Author(s) 2024. Published by Oxford University Press on behalf of Infectious Diseases Society of America. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (<https://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact reprints@oup.com for reprints and translation rights for reprints. All other permissions can be obtained through our RightsLink service via the Permissions link on the article page on our site—for further information please contact journals.permissions@oup.com.

This article is being copublished by CMI Communications and Open Forum Infectious Diseases. Minor differences in style may appear in each publication, but the article is substantially the same in each journal. All rights reserved in respect of Open Forum Infectious Diseases © the Authors and in respect of CMI Communications © the Authors. Minor differences in style may appear in each publication, but the article is substantially the same in each journal. For permissions, please e-mail: journals.permissions@oup.com <https://doi.org/10.1093/ofid/ofae522>

agree on a global commitment to scale up action commensurate with the present threat of AMR, with the aim to reduce the global deaths caused by AMR by 10 percent by 2030. A comprehensive One Health approach to better identify, track, prevent and treat AMR infections will be required to achieve this goal. A One Health approach is necessary because antimicrobial use in animals, plants and the environment contributes to resistance with deleterious effects for health in each of these sectors, and resistant infections can easily spread across sectors.

Optimizing antimicrobial use and reducing overuse through stewardship and policy is essential to limit the development of resistance. In conjunction with expanding access to health professionals with stewardship expertise, we must also take concrete steps to educate and empower other health professionals, patients and the public on antimicrobial stewardship and to reduce the over-the-counter availability of antimicrobials. We recommend a target that 70% of all antibiotic use globally in humans should be from the Access group using the WHO AWaRe system. The Aware classification categorizes antibiotics according to their spectrum of activity and potential to develop resistance. Access group antibiotics are first or second choices, typically narrow spectrum and offer high therapeutic value with lower potential for resistance. We further recommend a global reduction in the quantity of antimicrobial use in the agri-food system by at least 30% by 2030 and the continued phasing out of the use of medically important antimicrobials for growth promotion. In addition, we recommend that all nations work with non-government experts to develop guidance for appropriate antimicrobial use in plant agriculture.

The best way to reduce antimicrobial use is to prevent infections in the first place through evidence-based strategies including water, sanitation and hygiene (WASH), vaccination and infection prevention and control standards in health care facilities. However, in a recent report it was estimated that 1 billion people visit health care facilities with inadequate or no WASH services [4]. In the decade prior to the COVID-19 pandemic, global immunization rates plateaued, and the pandemic led to dramatic setbacks in immunization coverage which have not yet rebounded. Globally in 2023 there were over 14 million children who had not received a single recommended vaccine [5]. Lower immunization coverage increases the risk of individual disease and outbreaks and related antimicrobial use, and we urge a global commitment to scale up immunization coverage in children with a target of reaching 14 million children with essential immunization services.

WHO has published guidelines on core components of infection prevention and control (IPC) at the national and acute care facility level. These guidelines were developed to help prevent infectious diseases threats, including AMR. The WHO core components guidelines include health professional training, healthcare associated infection surveillance, and thresholds for staffing and equipment. Unfortunately, a 2021 study found

that only 12.5% of countries have all core elements in place. In particular, while most countries have an IPC program and national guidelines, fewer have invested adequate resources in implementation and monitoring, particularly in low-income countries [6]. We recommend a commitment to scale up implementation of the WHO IPC guidelines to ensure that all nations have the core components in place.

As health care grows increasingly complex and outbreaks and pandemics become increasingly frequent, even with comprehensive and well-funded prevention efforts in place, it is not possible to prevent every infection. Unfortunately, the antimicrobials market is broken, as traditional financial models do not align with the unique properties of antimicrobials. Antimicrobials are the only class of medicine for which use in one individual impacts efficacy in the entire population. Clinicians must prescribe antimicrobials judiciously to preserve their effectiveness, thus limiting the ability of novel antimicrobial developers to earn a return on their investments through traditional sales models.

There are only 97 antimicrobials in the pipeline, and just 12 of those are considered novel. Furthermore, only 4 of these 12 are active against at least 1 pathogen identified as “critical” by WHO. There are also significant gaps with regard to products for children, oral agents for outpatient treatment, and agents capable of tackling rising resistance [7]. Given how few drugs in clinical development ultimately achieve regulatory approval, the slim pipeline is even more worrisome. The large majority of development continues to be driven by small biotech firms, as most large pharmaceutical companies have exited this space.

It is essential to rebuild our antimicrobial drug pipeline to ensure we can treat multidrug resistant infections, with a focus on developing a sustainable innovation ecosystem capable of delivering novel, clinically meaningful antimicrobials that target pathogens identified by WHO as the greatest threats. To achieve this goal, we must rethink how governments have paid for antimicrobials and advance new mechanisms that delink antimicrobial revenues from use and align with the key principles of innovation, stewardship and access. G7 leaders have repeatedly committed to this effort, but work remains to bring these concepts to fruition in many high-income countries and at a global scale. The UK and Sweden have taken a leadership role in this effort by implementing an antimicrobial subscription model. The US Congress is considering the bipartisan Pioneering Antimicrobial Subscriptions to End Upsurging Resistance (PASTEUR) Act, which will establish a subscription model in which the US government would enter into contracts with novel antimicrobial developers to provide set payments for a steady supply of novel antimicrobials, instead of paying for the volume of antimicrobials used.

Surveillance is critical to inform clinical, public health, research and policy decisions and to enable evaluation of interventions and must cover all sectors (human, animal, crops

and the environment). Since the 2016 UN High Level Meeting on AMR, important progress has been made in scaling up surveillance systems on AMR but work remains to strengthen surveillance capacities, including development and access to diagnostics, laboratory information systems and other infrastructure to support timely data sharing at national, regional and global levels.

To achieve sustainable AMR mitigation, it is essential that interventions against AMR be based on independent scientific evidence. Therefore, the development and evaluation of context-specific, evidence-based strategies and the ongoing measurement of the status of AMR mitigation must be subject to continuous scientific evaluation. Professional societies in infectious diseases and clinical microbiology have an important role both in developing the evidence base for future policy interventions in all key scientific areas of AMR, including optimal use of antibiotics, WASH, IPC and vaccines, and in creating guidelines informed by that evidence. ESCMID and IDSA strongly urge that an independent scientific panel for AMR mitigation (as for climate change) be established as part of the upcoming UN Declaration.

As the UN, the Quadripartite and country governments devise ways to tackle AMR with an integrated One Health approach, we strongly encourage them to work with our societies to help provide the scientific basis to guide this important work. Advancing effective solutions will require all of us, working in concert globally and advocating for change in our own countries, communities and institutions. Clinicians and scientists who specialize in infectious diseases and microbiology have a unique voice and a responsibility to use that voice on

behalf of our patients and public health. Many of our patients are already living and dying in the post-antibiotic era, and their future and the very future of modern medicine depend upon what we do next.

Notes

Potential of competing interest. The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Robert Skov reports a relationship with European Society of Clinical Microbiology and Infectious Diseases that includes: board membership.

If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. A. R. Collaborators, Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet* 399, 629-655 (2022).
2. Centers for Disease Control and Prevention, Antimicrobial Resistance Threats in the United States, 2021-2022. Centers for Disease Control and Prevention; 2024. <https://www.cdc.gov/antimicrobial-resistance/media/pdfs/antimicrobial-resistance-threats-update-2022-508.pdf>. Accessed on August 28, 2024.
3. M. I. Hutchings, A. W. Truman, B. Wilkinson, Antibiotics: past, present and future. *Curr Opin Microbiol* 51, 72-80 (2019).
4. Water, sanitation, hygiene, waste and electricity services in health care facilities: progress on the fundamentals. 2023 global report. Geneva: World Health Organization and the United Nations Children's Fund (UNICEF), 2023. <https://www.who.int/publications/i/item/9789240075085>. Accessed on August 28, 2024.
5. World Health Organization, Immunization coverage. Geneva: World Health Organization; 15 July 2024. <https://www.who.int/news-room/fact-sheets/detail/immunization-coverage>. Accessed on August 28, 2024.
6. E. Tartari et al., Implementation of the infection prevention and control core components at the national level: a global situational analysis. *J Hosp Infect* 108, 94-103 (2021).
7. World Health Organization, 2023 Antibacterial agents in clinical and preclinical development: an overview and analysis. Geneva: World Health Organization; 2024. <https://www.who.int/publications/i/item/9789240094000>. Accessed on August 28, 2024.