The antimicrobial resistance cube: a framework for identifying policy gaps and driving action

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WHO has summarised its commitment to Universal Health Coverage (UHC) with the UHC cube diagram,[1,2] a globally recognised visual representation of policy choices to promote UHC and prioritise investments in health-care interventions. Inspired by the concept of the UHC cube, we propose a streamlined framework for policy makers, academics, and civil society to examine a country's response to antimicrobial resistance (AMR)—the AMR cube. The AMR cube integrates three essential dimensions: One Health contexts, interventions, and resources, each representing a critical aspect of combating AMR.

The first dimension, One Health contexts, reflects the One Health approach by acknowledging the interconnectedness of human, animal, and environmental health.[3] It also considers the range of different contexts relevant to treatments and infection prevention within human settings (eg, hospital care, primary care, and long-term care), animal settings (eg, terrestrial livestock, aquaculture, and companion animals), and environmental settings (eg, wastewater systems and processing, intensive farming, and effluent from the pharmaceutical industry and health-care facilities). The One Health framework emphasises the dynamic interactions among these contexts, encouraging a coordinated response to tackle AMR holistically.[4] However, there is a need for quantification of the relative importance of these different pathways in driving AMR across the One Health spectrum to support prioritisation of interventions. This will require the development of robust surveillance systems that take an integrated One Health approach, research that examines cross-contamination and transmission dynamics between AMR reservoirs across diverse contexts, and advance modelling exercises that synthesise evidence to map the emergence and dissemination of AMR both presently and in the future.

The second dimension, interventions, emphasises surveillance, prevention, diagnosis, and treatment as the cornerstone strategies for combating AMR. Surveillance systems provide a crucial foundation for evidence-based decision making.[5] By monitoring AMR trends, these systems identify emerging threats, evaluate the effectiveness of interventions, and guide policy adjustments.[6] Prevention focuses on reducing the incidence of infections through access to clean water, sanitation, and hygiene (WASH), infection prevention and control programmes, vaccination programmes, antimicrobial stewardship, and public awareness campaigns. Improved sanitation, hygiene, and access to clean water prevent the spread of infectious diseases among human and animal populations, particularly in low-resource settings.[7,8] Infection prevention and control programmes in health-care facilities involve actions such as improved hand hygiene, isolation of infected patients, and screening of incoming patients.[9] Infection prevention and control programmes in agricultural settings involve actions such as biosecurity measures, improved husbandry methods, and decontamination of equipment, vehicles, and clothing. Vaccines are important in curbing infections in human and animal health settings, significantly reducing the need for antibiotics.[10] Antimicrobial stewardship ensures the judicious use of antibiotics by implementing guidelines and educating prescribers of antimicrobials including health-care providers and veterinarians.[11] Diagnostics are fundamental to strengthening both surveillance and treatment across One Health settings, including investment in rapid diagnostic tests, which can

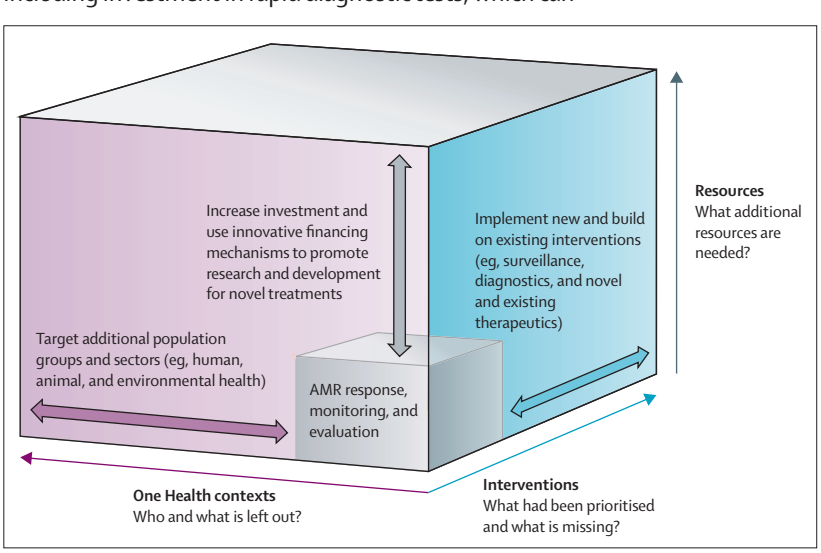

Figure: **The antimicrobial resistance cube**
The arrows highlight gaps and guide necessary expansions in each dimension. AMR=Antimicrobial resistance.

ensure that local treatment decisions are made based on empirical data.[12] Treatment strategies emphasise equitable and sustainable access to both existing and novel antimicrobials while combating the proliferation of counterfeit and substandard drugs.[13] Although access to antibiotics must be prioritised to save lives, the only way to make access sustainable is through research and development creating new antibacterial treatments which requires investment in research and development and innovative financing mechanisms.

The third dimension, resources, highlights the investments and systemic support required to sustain AMR responses sustainably and equitably across different populations using the most effective interventions. This includes funding, infrastructure, and capacity and capabilities. Strengthened laboratory infrastructure, networks, and quality control are essential for accurate and timely diagnostics, guiding appropriate treatment decisions and minimising unnecessary antibiotic use.[14] An appropriately trained workforce is also required, such as infection prevention and control nurses, infectious disease physicians, microbiologists, laboratory technicians, veterinarians, and environmental health officers, to implement and monitor effective interventions to respond to AMR.[15] Funding is also required to promote equitable access to antimicrobials and addresses disparities in health-care delivery, ensuring that marginalised populations can obtain the treatments they need.[16] Resources also encompass investments in research and development to innovate diagnostics, new antibiotics and vaccines, and alternative therapies such as phage treatment or immunotherapies.[17] Innovative financing mechanisms, including push and pull incentives, mobilise resources to support these efforts. Push incentives, such as direct grants and funding, can reduce the costs of research and development of novel antimicrobials.[18] Pull incentives, such as financial rewards linked to research and development results, reimbursement reforms, and regulatory changes, are also needed to create viable markets for antimicrobials. However, global collaboration is needed to promote alignment of eligibility and evaluation criteria for push and pull incentives including targeting priority pathogens that display increasing resistance to currently available antibiotics.[19]

The simplified structure of the AMR cube retains key policy elements while emphasising clarity (figure). In the One Health context, the question of who or what is left out prompts stakeholders to focus on equity and inclusivity across sectors and population groups, ensuring that vulnerable populations, such as rural communities and marginalised groups, are not excluded from AMR initiatives.[20] For interventions, the question about priority allows for the gaps in implementation to be identified, such as underutilised prevention measures, insufficient treatment protocols, or inadequate surveillance networks. For resources, the question about additional resource encourages innovative approaches to financing, capacity building, and research and development for novel treatments through global collaboration.

Once investment candidates have been identified with the AMR cube, policy makers need to examine the relative trade-offs between investment in different interventions based on evidence related to potential reductions in the health and economic burden of AMR. Although substantial evidence exists for specific interventions such as stewardship initiatives,[21] infection prevention and control programmes,[22] public awareness campaigns,[23] research and development for new treatments against Gram-negative bacteria,[24] and biosecurity and WASH initiatives,[7] there have been few attempts to estimate the comparative relative effectiveness and cost-effectiveness of different interventions that aim to reduce AMR in diverse contexts. Such a review could be recommended by the proposed Independent Evidence Panel for AMR, alongside efforts to model the relative importance of different transmission pathways in the emergence and spread of AMR.[25] A quantitative One Health model would facilitate understanding relative cost-effectiveness and trade-offs.

The AMR cube can serve as a strategic tool for shaping and driving effective policy responses to AMR. By presenting a clear and structured framework, it enables policy makers to identify policy gaps and allocate resources. The cube also facilitates cross-sectoral collaboration by fostering dialogue between the health, agriculture, and environmental sectors, reducing policy silos and promoting coordinated efforts. Moreover, the cube emphasises equity, ensuring that underserved populations are included in AMR strategies and that resources are allocated where they are most needed. By incorporating research and development into its

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resources structure, the cube can drive innovation in diagnostics, treatments, and alternative therapies, while encouraging international cooperation and regional collaborations to harmonise policies and share resources.

The simplicity of the AMR cube makes it a tool for advocacy, policy making, and education. By presenting AMR challenges and solutions in a clear and structured manner, the cube facilitates engagement with diverse stakeholders, including policy makers, health-care providers, and the general public. By focusing on three core dimensions—One Health contexts, interventions, and resources—the AMR cube provides a roadmap for action.

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*Elias Mossialos, Kevin Outterson, Sally Davies, Michael Anderson

e.a.mossialos@lse.ac.uk

LSE Health, Department of Health Policy, London School of Economics and Political Science, London WC2A 2AE, UK (EM, MA); School of Law, Boston University, Boston, MA, USA (KO); Trinity College, University of Cambridge, Cambridge, UK (SD); Health Organisation, Policy, Economics (HOPE), Centre for Primary Care and Health Services Research, The University of Manchester, Manchester, UK (MA)

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