"Fit for Purpose?" Assessing the Ecological Fit of the Social Institutions that Globally Govern Antimicrobial Resistance

Isaac Weldon and Steven J. Hoffman

Antimicrobial resistance (AMR) is a natural process where microbes develop the ability to survive the antimicrobial drugs we depend upon to treat and prevent deadly infections, such as antibiotics. This microscopic evolution is further propelled by human activities, where each use of an antimicrobial drug potentially induces AMR. As microbes can spread quickly from animals to humans and travel around the world through humanity's global circuits of movement, the use of any antimicrobial drug has potentially global consequences. As human-induced AMR occurs, mortality and morbidity increase due to increasingly or sometimes completely ineffective antimicrobial treatments. This article considers AMR as a product of the evolving and complex interplay between human societies and invisible microbial worlds. It argues that as a political challenge, AMR requires robust institutions that can manage human–microbial interactions to minimize the emergence of drug resistance and maximize the likelihood of achieving effective antimicrobial use for all. Yet, current governance systems for AMR are ill-equipped to meet these goals. We propose a conceptual paradigm shift for global AMR governance efforts, arguing that global governance could better address AMR if approached as a socioecological problem in need of sustainable management rather than solely as a medical problem to be solved. In biodiversity governance, institutions are designed to fit the biological features of the ecosystems that they are attempting to manage. We consider how a similar approach can improve global AMR governance. Employing the concept of ecological fit, which is defined as the alignment between human social systems and biological ecosystems, we diagnose 18 discrepancies between the social institutions that currently govern AMR and the ecological nature of this problem. Drawing from lessons learned in biodiversity governance, the article proposes five institutional design principles for improving the fit and effectiveness of global AMR governance.

Introduction

Antimicrobial resistance (AMR) is a natural, evolutionary process hastened by human activity. It occurs when microbes, including disease-causing bacteria, evolve to evade the antimicrobial drugs we rely on to treat them, such as antibiotics. This biological process gives rise to the creation of new, mutated microbes that cause drug-resistant infections. As a result, existing antimicrobial drugs—which are among the most effective treatments in modern medicine—become ineffective. In other words, AMR transforms previously curable infections into untreatable and often deadly diseases.

AMR can occur whenever antimicrobials are used, and the same antimicrobials are still widely used across many sectors of activity, including in human health, animal health, and agricultural settings. Microbes, including resistant ones, spread easily across humans, animals, and the environment, and travel around the world through humanity's global circuits of movement. Global governance has not sufficiently risen to meet this challenge. Almost a century's worth of human antimicrobial use in the absence of adequate mitigation and adaptation strategies has now accelerated AMR to the point of a global crisis: over 1.27 million people died from AMR in 2019 (Murray et al. 2022).

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Like many of today's greatest challenges, mitigating the threats posed by AMR requires new ideas and practices for governance (Denyer Willis and Chandler 2019). The inability of prevailing policy practices to sufficiently address the emergence and reemergence of mutated zoonotic and resistant disease variants, as well as the uneven global realities that they create, suggests a problem with the way that global health challenges are conceived. Thus, it is argued, a paradigm shift is needed to reconceptualize the objects, subjects, and methods of global health governance before even attempting to craft global health institutions that are more effective at achieving their stated goals. Otherwise, old conceptions in global health governance will continue to yield miscalculations and failures; reproduce class, race, and gender inequities; and deepen unjust and lingering colonial power relations. This is a conclusion increasingly recognized after several governance failures during the COVID-19 pandemic (Assefa et al. 2021; Büyüm et al. 2020; Fukuda-Parr, Buss, and Ely Yamin 2021; Wenham, Eccleston-Turner, and Voss 2022), which can also be applied to the governance of AMR.

The challenge is that AMR is not just another health problem to be solved. Nor is it just another technocratic challenge in need of scientific innovation to maintain existing human ways of life (Hinchliffe, Butcher, and Rahman 2018). Rather, it is an enduring global phenomenon caused by the innate ability of microbes to adapt and develop resistance to human intervention (Wallinga, Rayner, and Lang 2015). From this perspective, AMR represents a socioecological problem that demands robust institutions capable of managing the array of human behaviors with the potential to shape the human–microbial nexus (Jørgensen et al. 2020; Léger et al. 2021). To maximize the likelihood of achieving sustainable antimicrobial use for all, strategies to improve AMR governance should, therefore, aim to minimize the ways that human activities conflict with the natural tendencies of microbial life as these two interlinked worlds continue to evolve into the future.

Guided by this alternative conceptualization of AMR, new insights can be generated by considering how well global institutions align with the ecological characteristics of the problem, including the geographical scope, temporal scales, and natural tendencies of complex microbial ecologies. This concept of "ecological fit" emerges from the understanding that ecological systems have various unique qualities, and the institutions that govern them should be tailored to accommodate those unique qualities —much like a key that is designed to fit a specific lock (Epstein et al. 2015). Put differently, it shifts the question from asking whether AMR institutions can achieve their stated objectives (i.e., "are they fit for purpose?") to instead ask whether they are suited to the problem that they govern (i.e., "do they fit the challenge of AMR?"). Gaining insight into how well global health institutions fit the biophysical features of the problems they are meant to govern could significantly improve the likelihood of creating more effective and "fit-for-purpose" global health institutions.

This article adopts a socioecological perspective to examine the ecological fit between the social institutions governing AMR and the ecological nature of the problem. It begins by reviewing emerging ecological scholarship to frame AMR as an enduring, intersectoral, and widespread problem inextricably linked to other ecological processes. Next, drawing on research conducted in a complementary study (Weldon, Yaseen, and Hoffman 2022), it adopts the concept of the regime complex for AMR governance, which is defined as the array of global institutions converging around the problem, to frame the current social systems that govern human behavior around the challenge. By systematically comparing the logics of AMR governance with the ecological features of the problem, this article identifies 18 spatial, temporal, threshold, and cascading misfits. While not a comprehensive list, the results of this investigation illustrate how the concept of ecological fit can unlock new perspectives on recurring global health governance challenges. Finally, because the concept of ecological fit has been used extensively in biodiversity and ecosystems governance research, this article proposes five institutional design principles for AMR governance arising from lessons learned in those settings.

Part 1: Adopting a Socioecological Perspective to Investigate AMR

The socioecological perspective emphasizes the dynamic and complex relationships among people and their environments, both social and physical (Folke 2016). It can unlock new ideas for conceptualizing problems and identifying their dynamic causes, while generating solutions to address today's complex and interlinked global challenges, including AMR.

The perspective begins by observing that individuals exist within human social systems that are embedded in natural environments and ecosystems. Following this observation, it aims to contend with the interdependencies across these spheres (Wallinga, Rayner, and Lang 2015). In contrast to this large scope, however, prior research has historically privileged one set of systems and relationships at the expense of the other, focusing on only the social or the ecological. For example, Arild Underdal (2001) outlines a theory that suggests that problem structure and institutional problem-solving capacity are two independent variables that determine regime effectiveness. But these factors, while important, only pertain to human institutions and their normative understandings of the problem at hand. The socioecological perspective, on the other hand, grapples with the relationship between human social systems, including their various institutional and

normative aspects, and the biophysical characteristics of ecosystems (Folke 2016).

By emphasizing the interlinkages between human social and natural ecological systems, the socioecological approach provides a greater awareness of the shared material, planetary, and biospheric reality in which human institutions operate, and which human activity partly constitutes, compared to other human-centric political science and public health approaches. This advantage allows for investigations across AMR's multiple interdependent facets, encompassing both human and biological dynamics of the problem.

Prior research that emphasizes the ecological nature of AMR has identified at least four important socioecological characteristics (Green 2020; Ventola 2015; Wallinga, Rayner, and Lang 2015). Specifically, AMR is simultaneously (1) a widespread intersectoral problem; (2) a global and local—or "glocal"—problem; (3) a long-enduring process that, because it is caused by the innate evolutionary ability of microbes, is unlikely to ever truly be "solved"; and, finally, (4) a problem that is interlinked with other complex problems, such as the emergence of zoonotic disease, climate change, and biodiversity loss—all of which also have the potential to accelerate AMR. Table 1 expands on each of these characteristics in turn.

A starting point for considering how these socioecological interdependencies play out in global politics is Robert Cox's (1981) conception of the "three domains" present within any world order. These are the global political economy, the interstate system, and the global ecosystem. For Cox, "these three components are both autonomous in having their inherent dynamics, and, at the same time, interdependent with each other. Contradictions are generated within each of the three spheres, and contradictions arise in the interrelationships among the three" (1981, 161). When put in these terms, the socioecological approach essentially focuses on the contradictions that arise in the relationship between prevailing systems of human behavior (i.e., the global political economy and the interstate system) and the biosphere (i.e., the global

Table 1
Ecological Characteristics of Antimicrobial Resistance

Ecological characteristic	Explanation	Manifestation as a social challenge
1. Widespread and intersectoral	Microbes are all around us and AMR can occur anytime spontaneously or when an antimicrobial is used. Resistant pathogens can travel quickly across species and around the world, meaning no individual, community, or region may remain unexposed to the resistant pathogen (Weldon, Rogers Van Katwyk, et al. 2022).	AMR cuts across social boundaries, including sectoral, jurisdictional, and regional divides.
2. Glocal (global + local)	Microbial ecologies can be very localized. Microbes can live in small colonies in specific ecologies, and their capacity to travel on their own is limited. But their scale can be globalized through humanity's global circuits of movement (Rubin 2019).	AMR links individual actions with small microbial colonies and large global human communities.
3. Long enduring	Microbes have a natural adaptive potential to evolve and evade antimicrobial agents and drugs (Jørgensen et al. 2020). The innate potential for microbes to evolve is not likely to go away (Staupe-Delgado and Rubin 2023; Ventola 2015).	AMR can never truly be "solved." So long as we use antimicrobial interventions, we will have to contend with the inevitable evolutionary challenge of resistance.
4. Interlinked with other challenges	AMR is one of many interlinked planetary challenges. For example, zoonotic pandemics increase the volume of antimicrobials consumed (Knight et al. 2021). Meanwhile, adverse health events due to climate change put pressure on already fragile healthcare and food systems, increasing the likelihood of infectious disease and consumption of antimicrobials (Burnham 2021).	The causes and consequences of AMR are embedded in overlapping planetary systems, accelerated by human activity. There is no single cause, but many interlinked causal chains across various sectors of human activity.

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ecosystem). In doing so, it endogenizes that which would appear to be exogenous to approaches that only look at human activity.

As Cox's ideas aptly suggest, the relationship among human and microbial domains is historically specific and dialectical—determined in part by the prevailing forms of social organization, technological capacities, and material realities of the time (R. Cox 1981). The configuration of these domains, moreover, is not fixed, but rather changes over the long run through various historical processes (e.g., changing material capabilities, ideas, and social forces, though the relative importance of which is a major source of debate). In a time of overlapping planetary crises, the critical need to understand how the current configuration of these domains emerged, and the ways that it may be changing, must be balanced against the need to address and mitigate the urgent problems that exist within it (Hoffman, Bakshi, and Rogers Van Katwyk 2019). But conversely, those who adopt problem-solving approaches to confront these urgent problems must be aware of how assumptions about the fixity of the current configuration can embody ideologies associated with conserving it. Indeed, while Cox critiques problem-solving approaches that are unquestioning of the changing orders in which they operate, he notes that critical problem-solving perspectives can emerge "with a normative choice in favor of a social and political order different from the prevailing order" (R. Cox 1981, 130).

Cox's ideas are useful because they emphasize how patterns of human activity cannot be separated from, nor should they be considered autonomous from, the global ecosystem. This kind of thinking can foster the conception that culture is somehow separable from nature and lead to fallacies associated with thinking about "nature as something to be controlled by culture" (Agathangelou 2016; Latour 2004). Instead, a better way to conceptualize the relationship is to see human activity as occurring within specific material ecosystems. These ecosystems, together with human activity, constitute one interdependent and complex planetary system (Gill and Benatar 2019; Rockström et al. 2009a; 2009b). In this system, there is a growing acceptance that human activity is the single biggest driver of change—in what is now defined as "the Anthropocene"—but, importantly, the full effects and outcomes of those changes are not entirely under human control (Malhi 2017; Rockström et al. 2009a).

When deployed to investigate AMR, the socioecological perspective directs attention to the way that microbes form part of the natural ecological basis that orders human social relations. Since the discovery of effective antimicrobials in the early twentieth century, societies have formed systems that critically depend upon them to function (Chandler 2019). Antimicrobials have attained such an important role in modern societies that they operate like invisible infrastructure, enabling more productive food, labor, and healthcare systems. But this dependency, characterized by deeply engrained structures and practices that incentivize antimicrobial use for quick fixes for productivity, abundance, and profits, has generated a wide range of human activities that affect microbial adaptive behaviors (Denyer Willis and Chandler 2019). Specifically, these human activities precipitate biological change and accelerate microbial evolution toward drug resistance. AMR, in turn, undermines our social orders that rely upon antimicrobials to provide medical care and avoid more costly investments in sanitation and hygiene.

Put another way, AMR is a problem of interacting worlds. The discovery of antimicrobials enabled a shift in the relationship between human societies and invisible microbial ecologies (Green 2020). New human social orders were built around the ability to artificially affect microbes, making them more conducive for specific kinds of human activity (e.g., antimicrobials are most often used to reduce the likelihood and consequence of infection in animal farming operations and increase overall agricultural productivity [Van Boeckel et al. 2015]). The increasing failure of antimicrobials, though, now reveals the extent to which our social orders are precariously based upon effective antimicrobial drugs as ecology-transforming tools. This precariousness, moreover, manifests as social problems arising from drug resistance, including higher morbidity and mortality, reduced productivity, and declining agricultural yields from drug-resistant diseases (World Bank 2017). And with increasing calls to address the social structures and incentives that shape human behavior around antimicrobial use (Chandler 2019; Denyer Willis and Chandler 2019; Weldon, Rogers Van Katwyk, et al. 2022), there is an emerging normative project to achieve a new human–microbe relationship that reduces the rate at which human activity induces microbial evolution. In explicit terms, it requires a political order that pursues a more harmonious configuration among human governance institutions and microbial life to maximize the sustainability of effective antimicrobials for current and future generations.

Growing recognition of the significant findings generated by more holistic perspectives is fostering academic projects that aim to grapple with the ecological nature of today's interlinked health challenges, including AMR. There have even been journals established to consider these projects (e.g., see *Lancet Planetary Health*). Yet, there remains a need to apply this perspective to investigate the relationship between these challenges and the social institutions that govern them.

Part 2: Existing Governance Systems for AMR

As described in depth in a complementary study, AMR is currently governed by a global regime complex (Weldon, Yaseen, and Hoffman 2022). Regime complexes have

emerged as a defining feature of global governance in the twenty-first century (Alter and Raustiala 2018). They are defined as arrays of international regimes that converge around the same issue in global politics. As such, they represent the informal, formal, and legal architectures that structure existing human institutions in the current conjuncture. Although these architectures are evolving, their present, historically contingent form represents the socioecological niche into which resistant pathogens are currently emerging (Hruschka and Henrich 2013). Thus, investigating the regime complex for AMR governance in its current form can illuminate the various ways that the existing landscape of human institutions enables and accelerates microbial evolution and spread.

Indeed, the regime complex for AMR governance provides a systematic framework to understand the social order by which AMR governance takes place. But to fully understand the regime complex for AMR governance and its relevance to this article's socioecological perspective, it is first helpful to discuss the concept of an international regime and the evolution in regime theory that led to the emergence of the concept of regime complexes.

International regimes are often defined, using Stephen Krasner's seminal definition, as

> "sets of implicit or explicit principles, norms, rules, and procedures around which actors' preferences converge in a given area of international relations. Principles are beliefs of fact, causation, and rectitude. Norms are standards of behavior defined in terms of rights and obligations. Rules are specific prescriptions or proscriptions for action. Decision-making procedures are prevailing practices for making and implementing collective choice. (1982, 186)

Since Krasner introduced the idea of an international regime in 1982, scholars have used the concept to analyze the global governance of specific issues and domains, including money, trade, the environment, health, and nuclear technology (Gottemoeller 2015; Lakoff 2017; Ruggie 1982; Young 2011). There are, however, some important limitations that arise when employing the concept of an international regime to understand the dynamics of global governance systems, which many scholars began to identify in the late 1990s and early 2000s (Aggarwal 1998; Oberthür 2002; Rosendal 2001; Stokke 1997; Young 1996). Specifically, there was a recognition of at least three major limitations that prevent regime analysis from accurately capturing how global governance takes place. First, global issues are usually interdependent as the boundaries of one issue flow fluidly into others (Keohane and Nye 2000; Raustiala and Victor 2004). Second, issues are rarely if ever solely governed by a discrete regime. There may be one regime that features more prominently in certain discourses, but in the same way that problems blur into one another, so too do the social systems that emerge to govern them. Third, the international system evolves in a path-dependent way,

meaning that new regimes are always created and are shaped in a system already densely populated by other regimes. They cannot and do not start *tabula rasa*, but instead must connect, relate to, and interact with other regimes, which often causes overlap (Alter and Raustiala 2018).

Following these observations, Kal Raustiala and David Victor argued in 2004 that rather than being governed by discrete individual regimes, global issues are usually governed by regime complexes, which are defined as arrays of three or more international regimes with overlapping membership and conflicting principles, norms, rules, and procedures (Morin and Orsini 2013; Morin et al. 2017; Orsini, Morin, and Young 2013). And unlike investigating a single international regime, regime complex research necessarily starts by recognizing the densely populated, sometimes nebular, and path-dependent trajectory of the global political system, where regimes do not emerge, exist, or operate in isolation (Keohane and Victor 2011).

Thus, the idea of regime complexes aligns nicely with the socioecological perspective. Both share a commitment to see the interdependence of complex issues and note that these issues give rise to functionally interdependent social systems. Based on this understanding of regime complexes, it is possible to map the existing regime complex for AMR governance, including the various principles, norms, rules, and procedures across the elemental international regimes that comprise it.

The Anatomy of the Regime Complex for AMR Governance

The far-reaching nature of AMR makes it simultaneously a human health, animal health, agricultural, environmental, developmental, and trade issue, with no single global institution poised to comprehensively address it (Rogers Van Katwyk, Weldon, et al. 2020; Weldon, Yaseen, and Hoffman 2022). Instead, there are at least seven elemental international regimes coalescing in what can be identified as a textbook example of a global regime complex. These are (1) the human health security regime, (2) the humanitarian biomedicine regime, (3) the animal health regime, (4) the agriculture regime, (5) the trade regime, (6) the development regime, and (7) the environment regime (table 2).

Some of these elemental regimes have evolved with highly institutionalized agreements containing fully spelled-out expectations and behaviors. For example, the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPs) under the auspices of the World Trade Organization (WTO) espouses a set of principles, norms, rules, and procedures that formally structures part of the international trade regime. The International Health Regulations (IHR) under the auspices of the World Health

Table 2
The Regime Complex for AMR Governance[3]

Elemental regime	Principles	Norms	Rules	Procedures
1. Human health security	• Human health and security are linked. • Antimicrobials are essential to health security. • AMR is a threat to health security. • Global health preparedness is possible through international cooperation. • Early warning systems are paramount for global health preparedness. • Economic health is inextricably tied to population health.	• State sovereignty. • State responsibility for population health and health security. • Improving global health is a matter of protection against self-risk. • Information sharing. • Health interventions should minimize the impact on trade and travel.	• International Health Regulations (IHR). • Maintain core capacities to monitor and respond to emerging public health threats, including AMR. • Notify the WHO (IHR Article 6) and mount public health responses to emerging health threats (IHR Article 13). • Resolutions of World Health Assembly (WHA). • The Global Action Plan on Antimicrobial Resistance. • UN Resolution A/71/L.2. (2016 Political Declaration of the High-Level Meeting of the General Assembly on Antimicrobial Resistance). • Reserve new and critically important antimicrobials for human use only.	• Multilateral decision making at the WHA. • IHR Annex 2 on the reporting and declaration of a Public Health Emergency of International Concern (PHEIC).
2. Humanitarian biomedicine	• Access to essential medicines including effective antimicrobials is a human right. • Human suffering can be alleviated with medical intervention. • Human suffering demands an urgent and immediate response outside the framework of state sovereignty.	• Individual health is the unit of analysis. • State centricity (following but sometimes undermining local and state-level regulations). • Human right to health for all. • Improving global health is a moral obligation.	• Universal Declaration of Human Rights (UDHR). • Geneva Convention.	• United Nations Office for the Coordination of Humanitarian Affairs (OCHA). • World Food Programme. • Médecins Sans Frontiers (MSF). • International Committee of the Red Cross (ICRC).
3. Animal health	• Human health can be protected by protecting animal health.	• State sovereignty.	• World Organization for Animal Health (WOAH; formerly OIE) Framework. • Rules and resolutions of WOAH.	• Multilateral decision making at the WOAH.

(Continued)

TABLE 2 (*Continued*)

Elemental regime	Principles	Norms	Rules	Procedures
			• Sanitary and phytosanitary measures (SPS) of the World Trade Organization (WTO). • Terrestrial Animal Health Code. • Aquatic Animal Health Code. • Manual of Diagnostic Tests for Aquatic Animals. • Manual of Diagnostic Tests and Vaccines for Terrestrial Animals.	
4. Agriculture	• Food security and food justice demand that all people have physical and economic access to safe and nutritional food. • Antimicrobials are an important tool that can promote food security.	• Food systems should be sustainable, productive, and efficient. • Promotion of human, animal, and plant life and health. • State sovereignty.	• Food and Agriculture Organization of the United Nations (FAO) Constitution. • Resolutions of the FAO. • International Plant Protection Convention. • FAO Commission on Plant Genetic Resources and its Global System for the Conservation and Utilization of Plant Genetic Resources.	• Multilateral decision making at the FAO.
5. Trade	• Intellectual property rights promote progress and transparency for innovation. • Liberalized trade contributes to health. • Nondiscrimination in trade.	• Free trade and global capital flows. • State sovereignty and the enshrined right to protect human health. • Measures to reach other policy objectives should minimize impact on trade. • Private property rights.	• The Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) of the WTO. • The Agreement on the Application of Sanitary and Phytosanitary Measures (SPS). • The Agreement on Technical Barriers to Trade (TBT).	• Ministerial meetings. • WTO dispute resolution mechanisms. • Voluntary and compulsory licensing.
6. Development	• Access to medicine, including effective antibiotics, is a human right.	• Health for all is crucial for generating	• Convention on Biological Diversity (CBD) and its Nagoya Protocol on Access and Benefit Sharing.	• CBD Conference of the Parties.

(*Continued*)

TABLE 2 (*Continued*)

Elemental regime	Principles	Norms	Rules	Procedures
	• Development depends upon access to certain health rights. • Development improves health and health security.	and improving labor markets. • Sustainable development and SDGs. • State sovereignty over natural resources.	• United Nations Conference for Trade and Development BioTrade Initiative.	• United Nations Development Programme (UNDP).
7. Environment	• Environmental health is essential for human health. • Common but differentiated responsibilities. • AMR in the environment poses risks to environmental and human health.	• Sustainable development. • Precautionary principles to potential degradation. • Benefits from biodiversity and environmental conservation should be shared. • Universal access to basic and common biological and plant genetic resources. • State sovereignty.	• Thousands of multilateral environment agreements (MEAs). • Some MEAs are focused on specific species, e.g., the 1946 Convention on Whaling and the 1979 Bonn Convention on the Conservation of Migratory Species. • Some MEAs seek to protect specific areas or ecosystems, such as the 1971 Ramsar Convention on Wetlands and the 1991 Madrid Protocol on the Antarctic. • Some are about specific substances or types of substances, e.g., Basel, Rotterdam, and Stockholm Treaties on hazardous waste. • Convention on Biological Diversity and its Cartagena Biosafety Protocol. • Resolutions of the UNEP.	• Multilateral decision making through the United Nations Environment Programme (UNEP).

Organization (WHO), which are the legally binding rules that govern how states respond to infectious disease outbreaks, are another example of these kinds of formal rules.

Elemental regimes may also contain formally established agencies devoted to the implementation of desired goals and plans. For example, the Food and Agriculture Organization (FAO), which is the United Nations' agency for ending hunger and promoting nutrition, forms part of the global agricultural regime. Alternatively, behavior in an international regime may be guided by a looser arrangement of principles, norms, rules, and procedures. Such is the case for the humanitarian biomedicine regime, where many principles, norms, rules, and procedures guide actor behavior, but do not emanate from specific formalized agreements. Rather, these structures have been shaped historically through informally codified behaviors and sporadic international agreements.

There are several instances of overlapping and sometimes conflicting principles, norms, rules, and procedures across the regime complex for AMR. These overlaps and conflicts, moreover, have been found to have both positive and negative consequences. For example, synergistic overlaps include the shared commitment of human health security and trade regimes to minimize the impact of policy interventions on trade (Hoffman, Weldon, and Habibi 2022).

However, other aspects of the trade regime have previously obstructed the achievement of global health goals (Barlow et al. 2017), especially the principles, norms, rules, and procedures around intellectual property, investment, and financing for new medicines. For instance, some studies have found that regulations adopted and implemented through the international trade regime have previously prevented the adoption of health regulations (Mercurio 2017). Moreover, the trade regime places a significant emphasis on the importance of intellectual property rights as a means to enhance health innovation. In addition to this emphasis, specific regulations outlined in TRIPs are designed to support this principle. However, it has been observed that these measures have historically presented an impediment to the fundamental principle of providing access to medicine, which is advocated by both development and humanitarian biomedicine regimes as an essential human right (Motari et al. 2021). Indeed, the belief that intellectual property rights improve innovation has proven especially ineffective in stimulating research and development for new antimicrobials, which is a market with unique challenges (Kesselheim and Outterson 2011). Yet, attempts to address these obstacles and move beyond traditional market systems for antimicrobials has previously conflicted with the economic interests of powerful actors, such as pharmaceutical firms, their shareholders, and the states in which they operate (Lopert and Gleeson 2013).

Amid growing calls to reevaluate the priorities of global health governance, there remains a need to determine whose interests and which principles, norms, rules, and procedures prevail when elemental regimes interact with conflicting perspectives and aims. Similarly, where there are calls to identify and transform the suite of human behaviors that threaten the sustainability of antimicrobial therapy, there remains a need to identify and transform these governance institutions to better align with the ecological nature of AMR.

Part 3: Assessing the Ecological Fit of AMR Governance Systems

With an understanding of both the ecological characteristics of AMR (table 1) and the social systems that currently govern it (table 2), it is now possible to consider the ecological fit across these domains. The concept pertains to how well social institutions fit with the problem at hand (Young 2002). Specifically, it is defined as "the congruence or compatibility between ecosystems and institutional arrangements created to manage human activities affecting these systems" (Young 2002, 20).

The concept of ecological fit has been used extensively to explain governance challenges in biodiversity and ecosystems management (Galaz et al. 2008), where research has shown how institutions are likely to fail if they do not fit the problems that they are trying to govern (Epstein et al. 2015). Some research in global health has identified a similar theme of misfits between the dynamics of emerging health threats and existing institutions of global health governance. For example, Steven Hoffman and Sarah Silverberg (2018) note several political and technical barriers that prevent the IHR from responding to infectious disease outbreaks promptly, signaling a temporal incongruity between the rules of global health governance and the rate of infectious disease spread. Yet, none have systematically analyzed the full range of misfits or their consequences.

Operationalizing the Concept of Ecological Fit

We follow a relatively simple process to operationalize the concept of ecological fit for application to AMR governance. Specifically, we adopt what Graham Epstein and colleagues (2015, 36) describe as a straightforward process of "characterizing the attributes of the ecological problem and then comparing these to the attributes of governing institutions." Much has been written about theoretical and practical challenges associated with measuring fit (M. Cox 2012; Epstein et al. 2015; Vatn and Vedeld 2012), which has produced many different approaches and methods. For instance, any assessment of the fit between a problem and the institutions that govern it at least partially depends on a socially constructed and historically specific understanding of the problem and its corresponding

Table 3
Summary of Ecological Misfits in AMR Governance

Type of misfit	Misfits in AMR governance
1. **Spatial misfits:** Institutional jurisdiction is too small or too large to cover or affect the ecological system that it seeks to govern.	1. The global movement of people and microbes transcends national jurisdictional borders. The global problem of AMR governance demands a global response, but the international system is built on state sovereignty, which contradicts the realities of interconnectedness (Wenham, Eccleston-Turner, and Voss 2022). 2. Uneven spatial distribution of needs, capabilities, and responsibility to respond, including access to antimicrobials (Laxminarayan et al. 2016). 3. There is a wide range of national circumstances with little information or evidence on specific needs across settings. Places with historical barriers to access face high burdens of disease and AMR, and prioritize improving access, whereas other settings with a low burden of disease but historically high access face AMR, but their priority is conservation. There is no one size fits all (Léger et al. 2021). 4. Individuals around the world consume antibiotics daily, but governance only occurs in centralized locations, driven by some (powerful) individuals.
2. **Temporal misfits:** Institutions are formed too early or too late to affect the problem; institutions miscalculate the timespan of an ecological process, for example, when responses happen too fast, too slow, or take too short or too long a time to have a positive effect.	5. Innovation, driven by IP rights, is not fast enough to replenish the depleting stock of effective antimicrobials (Kesselheim and Outterson 2011). 6. Historically, declarations of PHEICs can be slow, caused by political and technical delays (Hoffman and Silverberg 2018). 7. The rate at which microbes evolve and travel is far greater than the global capacity for change and response—including the sum of our past efforts to combat AMR. 8. The IHR are event-focused and are reactive as opposed to process-focused and aimed at prevention. Even discourses about preparedness can miss opportunities for transformation to mitigate risk and prevent potential future outbreaks (Kamradt-Scott 2011).
3. **Threshold misfits:** Institutions cannot prevent, fail to recognize, or cause abrupt shifts in biophysical systems; institutions fail to provide adequate response contingencies, fail to initiate action, or fail to provide buffers against mechanisms that lead to irreversible shifts in ecosystems.	9. Use and dependence on antimicrobials are themselves threshold problems (Living with Resistance Project 2018). Antimicrobials are used to paper over shortcomings, instead of investing in better systems to promote health (Denyer Willis and Chandler 2019). Yet this leads to overdependence on a technology inherently moving toward a threshold as any use potentially leads to resistance. This points to the need for the regime complex to focus on social transformation and prevention. 10. Insufficient global surveillance means it is difficult to determine where thresholds are, how far away we are from them, and how quickly we are approaching them (Wernli et al. 2017). 11. Collective action framing can cause overfocus on some aspects (e.g., common-pool resource framing misses access problems). 12. Access, conservation, innovation, and prevention for AMR governance are interdependent, and focusing on some of these priorities but not others can cause negative threshold effects (Hoffman and Outterson 2015). 13. It is unclear whether certain contingencies apply to AMR and across elemental regimes (e.g., whether a PHEIC can be declared if a threshold is crossed and an untreatable disease emerges from AMR).
4. **Cascading misfits:** Institutions trigger or are unable to buffer the "effects between or among biophysical and/or social and economic systems" (Galaz et al. 2008).	14. No cross-sectoral contingency plans. 15. Zoonotic outbreaks, such as COVID-19, drive antimicrobial usage up (Knight et al. 2021). 16. Targeting antimicrobial usage in agriculture may undermine food security (World Bank 2017). 17. Use in many sectors around the world is contributing to AMR spillover in the environment (Singer et al. 2016). 18. Various unmeasured or unaccounted social equity considerations.

institutions. Someone with a different understanding of these matters could diagnose other important aspects of fit and misfit. Exactly what "fit" looks like, moreover, will also change as human institutions, microbial ecologies, and their relationship evolve. Furthermore, while the metaphor of a key and lock can be helpful, it is important to not necessarily see the "lock" and "key" as separate; as noted above, a more appropriate socioecological framing would see social systems as embedded in the global biosphere. These challenges notwithstanding, the benefit of adopting this simple approach is that it provides a replicable method, while demonstrating the power of the concept and its potential when applied to the global health governance of AMR.

Prior research in biodiversity governance, ecosystems management, and systems dynamics theory suggests that four different kinds of misfits can occur between institutions and the problems they seek to address (Epstein et al. 2015; Galaz et al. 2008; Rockström et al. 2009a). These are (1) spatial, (2) temporal, (3) threshold, and (4) cascading misfits (table 3). Through a theory-driven analysis, we use qualitative analytical reasoning guided by principles of similarity-matching to systematically evaluate the fit between the ecological characteristics described in part one with the governance attributes described in part two (Epstein et al. 2015). Each governance attribute across the regime complex was considered in relation to the overarching ecological characteristics of AMR. In doing so, the analysis identifies, categorizes, and elucidates 18 spatial, temporal, threshold, and cascading misfits in global AMR governance (table 3).

1. Spatial Misfits. Spatial misfits occur when the jurisdiction of a governance arrangement is too small or too large to cover or affect the ecosystem that it seeks to govern (Epstein et al. 2015; Galaz et al. 2008). For AMR, there is a spatial misfit between the globalizing way that microbes transcend borders and the statist norms and principles that underpin the regime complex for AMR governance (Hoffman, Weldon, and Habibi 2022; Weldon and Hoffman 2021; Wenham, Eccleston-Turner, and Voss 2022). This spatial misfit reflects what Clare Wenham, Mark Eccleston-Turner, and Maike Voss (2022) identify as a contradiction between the globalist need for health governance and the anarchical system of sovereign states in which global health governance necessarily takes place.

Another important spatial misfit in AMR is the uneven distribution of global access to effective antimicrobials, which is caused by failures in the global political-economic system to distribute these lifesaving products equitably and efficiently. Enduring legacies of colonialism, weak healthcare systems, lack of infrastructure, and inabilities to pay all confound this challenge, which essentially means that places where antimicrobials are needed the most face an extremely unjust triple burden marked by high infectious disease, poor access to antimicrobials, and high mortality and morbidity from drug-resistant infections (Murray et al. 2022). Somewhat paradoxically, this lack of access to antimicrobials is a key driver of resistance such that global efforts to mitigate AMR must simultaneously expand access in these locations while reducing use in others.

Finally, there is a related spatial misfit between the sites where the socioecological interaction happens (i.e., where the antibiotics are consumed by individuals around the world) and the sites where governance happens through the regime complex (e.g., in multinational corporation board rooms, UN agency meeting rooms in Geneva and New York, etc.).[1]

2. Temporal Misfits. Temporal misfits occur when institutional dynamics are too fast or too slow compared with their relevant ecological dynamics. They can occur when institutions are ignorant of, ignore, or miscalculate the timespan of an ecological process, or when responses take too short or too long a time to have a positive effect (Epstein et al. 2015; Galaz et al. 2008). Temporal misfits in global AMR governance are caused by the dynamics of the regime complex writ large, the IHR, and the process of innovation for new drugs in the economic system enshrined by the global trade regime. For the regime complex writ large, it is evident that as global AMR mortality rates rise, it is because the global institutions designed to mitigate the threat of AMR cannot match the pace at which microbes evolve, travel, and infect populations.

Another two temporal challenges arise in the event-focused nature of the current IHR.[2] First, the primary focus of the IHR, as outlined in its preamble, is to improve the international response to emergency events. Arising from this aim, articles 12–17 of the IHR outline a set of rules and responsibilities for responding to disease outbreaks, but which are ill-suited to the enduring process of AMR (Kamradt-Scott 2011). Specifically, these articles project a dichotomous understanding of time, implying that the world is either in crisis mode or noncrisis mode. The enduring process of AMR, however, underscores the need for action and mechanisms to address the underlying causes and drivers of resistance to prevent emergencies from happening in the first place (Staupe-Delgado and Rubin 2023).

Second, as noted above, another temporal misfit is the slow response time that it generally takes for the WHO to declare public health emergencies of international concerns (PHEICs). This procedure, which is outlined in articles 6–15 and Annex 2 of the IHR, is used by the WHO to enact emergency global response protocols to emerging disease threats (Hoffman and Silverberg 2018). However, several technical and political barriers often

prevent a timely declaration of a PHEIC, which hinders an effective global response.

The innovation pipeline for new antimicrobial drugs faces several market challenges, highlighting additional socioecological tensions that arise from human economic practices. This lack of innovation is an outcome shaped by principles, norms, rules, and procedures in the trade regime, demonstrating that the traditional system of conferring intellectual property rights to support innovation has largely failed for antimicrobials (Caceres et al. 2022). This system has not been able to provide new antimicrobials at a rate commensurate with increasing human-induced resistance—meaning that existing antimicrobials are becoming less effective faster than new ones are coming out.

More specifically, the antimicrobial market presents numerous barriers that make the traditional intellectual property rights approach ineffective, such as high research and development costs and societal expectations for low-cost and affordable medicines. Furthermore, the usefulness of antimicrobials is often time limited due to inevitable microbial resistance, while the need to limit use and conserve their effectiveness further reduces the antimicrobial market (Kesselheim and Outterson 2011).

In response, it has become increasingly necessary to explore models that delink the cost of research and development from the sales volume of antimicrobials. Strategies like market entry rewards, subscription models ("Netflix models"), or full patent buyouts offer potential solutions to the failure of the market in developing new antimicrobials (Anderson et al. 2023; Singer, Kirchhelle, and Roberts 2020).

As demonstrated by ongoing failures to distribute COVID-19 vaccines, another challenge is the allocation of medical resources via market mechanisms, as new technologies are not distributed equally or on equal time horizons once discovered. Rather, these scarce technologies continue to be distributed along global income, racial, and colonial lines, with high-income countries enjoying the bulk of their benefits (Bajaj, Maki, and Stanford 2022).

In other words, the inability to replenish the depleting pool of antimicrobial effectiveness and optimally distribute new countermeasures represent temporal misfits between the social dynamics of drug development and distribution and the socioecological factors that accelerate microbial evolutionary processes. Moreover, they signal yet another temporal challenge created by the uneven temporal scales that manifest when microbes spread around the world.

3. Threshold Misfits. Threshold misfits happen when institutions cannot prevent, fail to recognize, or cause abrupt shifts in biophysical systems. They can occur when institutions fail to provide adequate response contingencies, initiate action, or provide buffers against mechanisms that lead to irreversible shifts in ecosystems (Folke 2016; Galaz et al. 2008). For AMR, the historical failure of global policy to sufficiently address the issue is itself a threshold problem (Living with Resistance Project 2018). Specifically, the evolution of societies dependent on antimicrobials for improving productivity and as quick fixes means that institutions have hitherto failed to recognize and prevent irreversible shifts in the ecology of microbes, thereby accelerating AMR to the point of a global crisis (Chandler 2019; Kirchhelle et al. 2020; Rogers Van Katwyk, Giubilini, et al. 2020).

Furthermore, AMR is such a complex challenge, meaning several potential threshold problems can arise if policy interventions focus on some aspects of the problem at the expense of others (Weldon, Liddell, et al. 2022). One way these misfits can occur is with the overreliance on popular models such as "the global common-pool resource" model, which draws attention to the conservation of and innovation for the common pool of antimicrobial effectiveness. The risk is that narrowly applied models can obscure important aspects of the issue. For example, the global common-pool resource model, which assumes global non-excludability, suggests that people cannot be prevented from accessing antimicrobials. This assumption, however, is not borne out in our current reality. As noted above, many are indeed excluded from enjoying the benefits of antimicrobial therapies. Consequently, models like "the global common-pool resource challenge" can overlook concerns for access, and interventions drawn from that model may further restrict access or ignore it. Conversely, however, focusing on access without conservation and innovation would accelerate the depletion of antimicrobial effectiveness and increase the likelihood of resistance while squandering precious new antimicrobial stocks. These related threshold effects underscore the interdependencies across the functionally complex challenge of AMR (Hoffman and Outterson 2015).

4. Cascading Misfits. Finally, cascading misfits happen when institutions trigger or are unable to buffer the "effects between or among biophysical and/or social and economic systems" (Galaz et al. 2008, 153). Cascading misfits for AMR draw attention to problematic gaps in global governance around multisectoral and cross-issue planning and action. In particular, the global AMR regime complex contains no crosscutting contingency plans that unite the elemental regimes. This gap means that even if a resistant pathogen from AMR triggered the declaration of PHEIC under the IHR, this human health-specific mechanism has no bearing on how the other elemental regimes in the regime complex operate. Moreover, there is an information gap and related governance gap for mechanisms that can connect the causes and consequences of AMR with those of today's other greatest challenges,

including climate change, biodiversity loss, and zoonotic spillover.

More specifically, biodiversity, climate change, and zoonotic pandemics all have the potential to accelerate AMR either directly or indirectly (Gilchrist et al. 2007; Singer et al. 2016; Strathdee, Davies, and Marcelin 2020; Van Boeckel et al. 2015). AMR, in turn, exacerbates these challenges by diminishing the ability to respond with medical countermeasures while heightening the risk of deadly infection. While the regime complex for AMR includes institutions that also focus on these functionally interdependent problems, they are not equipped with the kind of intersectoral arrangements to address the complex linkages among them.

Part 4: Improving the Ecological Fit of AMR Governance Systems

This analysis illuminates the magnitude of the challenge in making progress toward mitigating and adapting to the risks of AMR. Presently, the institutions governing AMR —embodied by a decentralized regime complex—have primarily evolved with an emphasis on developing the capacity needed to address AMR as a medical problem. However, these problem-solving efforts have largely failed to achieve the interrelated goals of sustaining antimicrobial effectiveness and promoting global health for all. They have also led to the creation of social systems fundamentally misaligned with the ecological characteristics of the problem that they are meant to govern.

The 18 identified misfits reveal deeply rooted structural challenges with the current system of global health governance, as well as the prevailing approach to designing the institutions that constitute it. The persistent inability of existing social systems to adequately address the ecological nature of AMR suggests the need for a paradigm shift in AMR governance, where AMR is approached as a socioecological problem rather than a medical one. This conceptual shift could guide extensive and profound transformations to the many social, political, and economic practices that have the potential to alter microbial ecologies through antimicrobial use. Drawing on our analysis of ecological misfits, this final, more normative section considers such a paradigm shift for global AMR governance. We end by proposing five institutional design principles to navigate the delicate balance between enacting immediate action to mitigate AMR and transitioning to a future of sustainable antimicrobial governance.

A Paradigm Shift for AMR Governance

The inevitability of microbial resistance underscores the inherent unsustainability of current antimicrobial therapies, as well as the need for new ideas to change social practices (Denyer Willis and Chandler 2019; Ventola

2015; Weldon, Rogers Van Katwyk, et al. 2022). It also calls into question the "war on superbugs" analogy often deployed to raise awareness of the challenge (Wallinga, Rayner, and Lang 2015). On one hand, the current rate of antimicrobial innovation needs acceleration, which can be accomplished through mechanisms that address various market failures in the pharmaceutical industry (e.g., via novel market or entirely nonmarket mechanisms). However, a "weapons" approach, fixated on innovation, fails to address the broader context in which antimicrobials are used and distributed. It would mean that the current pace of innovation, which is already inadequate, would need to be radically if not impossibly accelerated to keep pace with the rising demand for new therapies. Instead of engaging in an unwinnable arms race—where microbial evolution typically outstrips our ability to develop and distribute new therapies—shifting our approach to designing social systems that can optimize antimicrobial use, minimize AMR, and maximize the time-limited effectiveness of antimicrobial drugs offers better chances of achieving sustainability. Without such paradigmatic changes, our response to AMR will remain a reactive one, always struggling to outpace microbial evolution rather than sustainably managing it.

Rather than solely focusing on innovating new technologies to solve problems and maintain the status quo of human social systems, a paradigm shift could change the way we approach AMR, leading to new systems that reconfigure human–microbial relations for future sustainability (Jørgensen et al. 2020). With this shift, the object of governance extends beyond merely the social response to infectious disease threats. It also encompasses the coevolution of human societies with and within microbial ecologies—a concept referred to as "coevolutionary governance" (Jørgensen et al. 2020). Coevolutionary governance builds on principles of adaptive comanagement by recognizing, anticipating, and analyzing "interdependent eco-evolutionary dynamics [to] guide human societies toward identified goals" (485). This concept acknowledges that the evolution of human culture is dialectically connected with various forces of microbial evolution, underscoring the need for adaptable institutions capable of sustainably guiding these interactions.

Transitioning to a Future of Antimicrobial Sustainability

Transitioning from the current configuration of human–microbial relations calls for practical changes and transformations to align existing institutional approaches with socioecological understandings of the problem. Guided by a paradigm shift, this transformation would include the development of more sustainable forms of organization, while simultaneously ensuring that the benefits of antimicrobials are accessible to all. Such a transformation will

entail a comprehensive reassessment of existing labor, care, agriculture, and land practices, where antimicrobials are currently employed infrastructurally as expedient solutions to support abundance, profits, and productivity (Denyer Willis and Chandler 2019). This endeavor will, among other things, require substantial investments in hygiene and sanitation, addressing global poverty, and more broadly transforming the conditions under which people live, work, and seek safety (Rogers Van Katwyk et al. 2019). Otherwise, global efforts would be akin to treating the symptoms without addressing the underlying illness.

This transformation, moreover, will involve a tough examination of the ways in which the principle of state sovereignty manifests as an obstacle to unified, global strategies for ecological crises in the Anthropocene (Biermann 2012). In global governance, for example, the principle of sovereignty contradicts microbial ecological realities and the world's resulting shared vulnerability to infectious disease. This vulnerability is facilitated, in part, by the myriad pathways through which humans, animals, and microbes travel around the world and put all countries at risk. Despite these challenges, immediate solutions will have to be pioneered and implemented by states within this very system (Wenham, Eccleston-Turner, and Voss 2022). Therefore, while institutional transformations guided by new conceptions of AMR seem warranted, the current problem of AMR remains a problem both of and for the existing system of sovereign states.

The deep-rooted ideas shaping behaviors that drive AMR suggest that a paradigm shift may be difficult to implement, especially given the ingrained principles and norms of global governance. Certain stakeholders even harbor vested interests in resisting change. For example, pharmaceutical companies continue to oppose regulatory changes that jeopardize their profit margins, while governments resist measures they perceive as encroaching upon their sovereignty. But while initiating and implementing a paradigm shift in AMR governance will be challenging, it is not impossible. For example, the contradictions in today's prevailing principles and norms analyzed in this article indicate ruptures through which new principles and norms may emerge to inform future action.

Balancing Long-Term Transformation with the Urgent Need for Immediate Action

In the interim, adjustments can be made to the existing system to alleviate the dire human suffering caused by the urgent problem of AMR (Hoffman, Bakshi, and Rogers Van Katwyk 2019). However, it is crucial that these adjustments are designed to support rather than detract from larger transformative efforts. Indeed, this approach does not mean forgoing the above-argued shift in approaches to AMR governance. Rather, informed by an understanding of the regime complex's ecological misfits, specific adjustments can simultaneously (1) respond to the problem of AMR within the current configuration of human–microbial relations, (2) mitigate the deeper drivers of AMR in the first place, and (3) transform the existing configuration for long-term sustainability.

Socioecological studies on institutional design, particularly in biodiversity and ecosystems management, provide useful starting points for responding to AMR as an enduring ecological challenge—balancing immediate action with long-term transformation (Folke 2016; Galaz et al. 2008). Five interrelated design principles emerging from decades of empirical investigations on governing socioecological challenges stand out as especially important for improving the fit of AMR governance systems. These principles recognize the inherent complexities and rapidly evolving nature of AMR, and advocate for responsive, informed, and multifaceted strategies. Collectively, these principles represent an alternative normative foundation to the prevailing paradigm informing global AMR action, which we propose could inform future deliberations on designing institutions capable of adapting global AMR governance for coevolution.

Five Principles for Governing AMR as a Socioecological Challenge

1. Acknowledge There Is No Panacea or Silver Bullet for AMR. First, when addressing complex and multifaceted socioecological challenges, including AMR, it is crucial to recognize that there is no one-size-fits-all solution or panacea. Indeed, one of the few generalizable findings from socioecological investigations on institutional design is that universal, simple, and silver-bullet solutions do not exist (Ostrom, Janssen, and Anderies 2007). Socioecological problems manifest differently across different geographies, ecosystems, and cultures. Each region and community may face unique challenges based on specific socioeconomic, environmental, and political conditions (Epstein et al. 2015). This diversity necessitates localized, tailored solutions. Attempting to apply a uniform approach across all these different contexts is likely to result in ineffectiveness or even unintended harmful consequences.

Similarly, the issue of AMR is not monolithic; rather, the challenge varies depending on location, ecosystem, and social context. AMR is an ecologically complex and diverse problem, with different populations facing unique social, economic, and environmental contexts (e.g., some populations overuse antimicrobials while others lack access). Therefore, institutions will need to adapt to fit local circumstances, where each social and microbial ecosystem presents its own set of challenges and considerations (de Campos-Rudinsky 2023). For instance, the strategies suitable for a hospital in a high-income country will be

different from those needed for a farm in a lower-middle-income country. Tailoring local AMR policies for the specific needs of an area, and considering factors like local population density, healthcare access, prevalent pathogens, and labor, care, and land practices can help to address many of the spatial misfits in AMR governance. However, this will require substantial action to overcome the political and economic challenges that currently hinder the optimal global distribution of vital resources, such as effective antimicrobial treatments.

2. Design Agile and Adaptable Institutions with Iterative Approaches and Rapid Cycles of Learning. The second principle revolves around building governance systems that remain adaptable over time. The complexity of ecological challenges, often characterized by high degrees of dynamism, uncertainty, and the potential for abrupt shifts, as well as evolving human preferences, values, and interests, means that what works today may not work tomorrow (Jørgensen et al. 2020). Solutions must therefore be adaptable and capable of evolving along with the changing ecologies that they aim to govern (Ostrom et al. 1999). In this context, durable institutions are not static ones that will stand the test of time, but rather ones that are agile and flexible enough to respond and adapt to inevitable changes.

Agile institutions, designed with iterative approaches to rapid learning, would generate practices more commensurate with the temporal dynamics of microbial evolution and spread. Given many existing uncertainties and a rapidly evolving science and social science evidence base, these integrated processes will inevitably involve trial and error in policy making. In recognizing this challenge, built-in and regular reviews and adjustments can foster institutional cultures of social learning-by-doing, enabling continuous adaptation based on experience and feedback.

The dynamic nature of AMR requires flexible, evolving strategies rather than static ones (Léger et al. 2021). Resistant strains can emerge rapidly, and existing treatments can quickly become ineffective. In response, our governance structures must be adaptable and ready to react to changes swiftly. This principle means that governance structures need to be flexible over time. Developing more fitting institutions for AMR will require normalizing policy experiments, embracing failures, and making revisions. In practice, this principle could be accomplished in various settings, from local to global, by incorporating policy feedback systems where the effectiveness of AMR strategies is evaluated and refined in iterative cycles. The process in the 2015 Paris Agreement, where national commitments to climate action are regularly assessed and ratcheted-up in ambition, provides a useful example (Weldon, Rogers Van Katwyk, et al. 2022). Similar mechanisms for AMR governance could help to address temporal misfits by quickly implementing new guidelines in response to emergent resistant strains, as well as threshold misfits by reassessing and recalibrating interventions when microbial resistance thresholds are crossed.

3. Diversify Practices and Generate a Living and Comprehensive Evidence Base for the Many Facets of AMR. A wide range of diversified practices is essential for promoting location-specific and adaptable policy experiments to address ecological challenges across time and space (Dietz, Ostrom, and Stern 2003). Similar to how biodiversity improves the likelihood of ecosystem resilience, diversity in social systems can improve resilience to political and social shifts and shocks, create and sustain system-wide adaptability and flexibility, and unlock multiple pathways to success (Plummer and Armitage 2007). In tandem with the need for locally adapted policies, agility, and rapid learning, the endeavor to systematically diversify practices can be purposively designed to cogenerate a robust evidence base on what techniques can best support effectiveness in relation to social values (Jørgensen et al. 2020; Léger et al. 2021). This evidence base, derived from a diverse range of practices for the many facets of AMR, could inform adaptation and adjustments, isolating conditions for success where they exist.

The myriad determinants of antimicrobial use—itself a testament to the extent to which antimicrobials are relied upon in various aspects of daily life—mean that diverse practices are needed at varying levels of society. At the biomedical level, diversity is accomplished by exploring alternative therapies to antimicrobials. In agriculture, traditional and alternative practices could be explored to promote yields and sustainability while lessening the reliance on antimicrobials. At the social level, diverse practices could explore means for promoting health and welfare beyond pharmaceutical interventions to more holistic approaches to prevention. At the cultural level, alternative perceptions of food security and more sustainable diets could promote nutrition beyond industrially produced meat and animal products. In the market, a range of public–private partnerships or entirely public models could diversify responses to the economic challenges associated with antimicrobial innovation. And at the governance level, diversity can be accomplished by implementing a range of strategies to regulate and monitor antimicrobial use, foster collaboration across sectors, promote international cooperation, and empower decision making that includes a broad spectrum of stakeholders. By integrating diversity in practices across all levels, it is possible to formulate a comprehensive and effective response to the complex challenge of AMR. Throughout these domains, moreover, a living evidence base can be cogenerated with experiments, informing revisions and adaptations in accordance with new knowledge and evidence as it emerges.

4. Create Links across Locations and Scales. Diversification can help to build resilience and reduce the risk of AMR, but it also requires coordination across different sectors and levels of governance. Evidence from socioecological management of shared resource systems has found that adaptive governance is most effective when smaller efforts are connected to larger networks, especially when challenges are complex and global (Ostrom 1990). Promoting connectivity across various scales—from local to global—ensures that bottom-up initiatives at the community to national levels do not operate in isolation, but rather are woven into a broader, global strategy. It is therefore crucial to create links between different actors, sectors, and scales when managing rapidly evolving and transnational phenomena, such as AMR.

The need for coordination across scales and geographies underscores the importance of bridging organizations—entities that can pioneer the much-needed linkages across diverse sectors, geographies, and scales (Olsson et al. 2007). Bridging organizations perform crucial functions of governance, such as facilitating the sharing of knowledge, resources, accountability, and best practices.

For AMR, cross-scale and cross-sectoral approaches are indispensable given the problem's transboundary and multifaceted nature. Local solutions and grassroots initiatives are vital, but their true potential can only be harnessed when they are integrated into a larger, global framework that recognizes and addresses AMR as a shared, worldwide problem. Bridging organizations can facilitate this integration, connecting localized efforts with global strategies and ensuring that innovations and solutions are supported, visible, and can be adapted to different contexts. For example, a successful approach to AMR in healthcare in one community could be scaled up and incorporated into national and even global health policies, ensuring that lessons learned at one level inform strategies at others. Bridging organizations could enable the scalability of successful local approaches to AMR, fostering the transfer of lessons from the community level to national and global health policies. Equally important is their role in creating connections across sectors—healthcare, agriculture, and environmental management, among others—fostering a multisectoral response to AMR. In strengthening vital linkages across locations and scales, we can cultivate a more holistic and adaptable governance system capable of managing the complexities of AMR.

5. Promote Participation among Stakeholders. Finally, the effectiveness of these measures depends on the involvement of stakeholders (Chaffin, Gosnell, and Cosens 2014). This principle involves mechanisms for participation and incorporating diverse perspectives into decision-making processes. It also necessitates creating rules and policies that are flexible, adaptable, and reflect the needs and circumstances of different stakeholders. Examples

from biodiversity and climate governance underscore that institutions designed to improve ecological fit may inadvertently create social misfits (Moss 2003). This can produce tensions among social values and competing conceptions of objectivity, universality, and desirability across different contexts and over time—conflicts already apparent in the vast regime complex for AMR governance. In addition to questions about improving ecological fit, there are also important questions that remain about how best to sustain social cohesion, uphold democratic principles, and other social values during uncertain and transformative times.

In cultivating participation, the new "AMR Multi-Stakeholder Partnership Platform" hosted by the WHO, FAO, WOAH, and UNEP offers an opportunity to bring together diverse actors across different levels and sectors (WHO 2022), making AMR governance not only more ecologically fitting but also socially acceptable and feasible. In recognizing that the challenge of AMR cannot be tackled by any one sector, organization, or level of governance alone, the platform promises to involve stakeholders from the health, agricultural, environmental, and other sectors, as well as representatives of various levels of governance (from local, to national, to global) and various societal groups (e.g., patients, healthcare professionals, farmers, etc.).

The effectiveness of this global platform for AMR could be gauged by its ability to perform several functions. These include acting as a hub for knowledge exchange and learning, and sharing information, best practices, and lessons learned. The platform could foster policy coordination and harmonization across different sectors and levels of governance, ensuring a more coordinated and effective response to AMR. Additionally, it may also play a role in raising awareness about AMR, advocating for policy changes, enhancing accountability, and mobilizing resources for AMR prevention and control.

Despite ongoing challenges and acknowledged limitations, these lessons from biodiversity and ecosystems governance offer valuable insights for improving AMR governance. Specifically, these strategies provide a road map for research to inform practice; emphasize the need for sustainability, adaptability, and resilience; recognize the importance of democratic principles; and underscore the importance of striking a balance between addressing immediate needs and pursuing long-term goals. While global biodiversity governance has experienced lackluster results in some areas due to insufficient funding, political will, and enforcement, these principles have catalyzed action, providing a basis to evaluate progress. In AMR governance, on the other hand, governance efforts are missing these necessary steps, including metrics, benchmarks, and evidence to inform current and future action. By learning from both successes and shortcomings in these areas, we can work toward more effective and inclusive

Conclusion

When we ask whether an institution is "fit for purpose," we are essentially asking if it can achieve its stated objectives. This raises several important political questions about what and whose purposes and objectives global governance is serving. But the question also directs our attention in a particular way by preempting the idea that institutions *solve* problems. That is, by asking whether institutions can address certain issues, the question assumes that human institutions are self-contained entities that fix problems out in the world, making the site of the intervention external to the institution. What this article posits, however, is that the central question for enduring global health challenges like AMR is not "how do we 'solve' this problem," but rather, "how do we craft social systems that are better aligned with ecological and microbial systems in a shared planetary environment?" Put differently, we should be asking how our institutions can better fit the process of AMR to (1) create systems that enable harmonious coevolution with microbes within planetary systems, (2) minimize the socioecological contradictions that accelerate AMR, and (3) maximize the effectiveness of antimicrobial treatments for infectious disease (Jørgensen et al. 2020). This transition internalizes the issue, bringing the site of intervention from outside somewhere in the world to instead thinking about designing institutions that are contained within and aligned with material planetary realities.

The path to a more fitting relationship with microbes depends on improving our understanding of the intricacies of the human–microbial nexus, where many agree that the human–microbial relationship is overall net positive and symbiotic (Jørgensen et al. 2020). Yet, this article revealed 18 ways that human activity is at odds with microbial processes, accelerating their evolution from symbiotic to pathogenic. It turned attention to the challenges surrounding the principles, norms, rules, and procedures by which AMR is globally governed and drew a series of five principles for designing institutions for AMR, suggesting that it is possible to identify opportunities to transform the prevailing principles, norms, rules, and procedures by which AMR is currently governed. Additionally, by adopting a core International Relations (IR) concept to examine the global social systems emerging around AMR, this article sought to help bridge IR's relative silence about the salience and intensity of today's many pressing ecological challenges, as pointed out by IR scholars (Agathangelou 2021; Burke et al. 2016).

The process of AMR is inevitable and enduring, but its manifestation as a social problem is contingent on the prevailing interplay between human activities and microbial ecologies. As this interplay evolves, the development of new institutions that guide human cultural evolution in tandem with the inherent evolutionary tendencies of microbial life could help to minimize human-induced disease mutations caused by AMR. As we continue to look for ways to mobilize and sustain appropriate global action for AMR, finding political and policy strategies that better fit the problem could help to achieve sustainable antimicrobial use for all. Indeed, the optimal relationship between human societies and microbial ecologies may necessitate forms of social organization that transcend those currently in existence.

Acknowledgments

Notes

1 We thank Clare Wenham for pointing this out to us.
2 It is worth noting that it is still unclear what aspects of the IHR apply to AMR (Kamradt-Scott 2011; Wernli et al. 2011). Yet, in the absence of a global framework for AMR, the IHR represent the closest thing to a global regulation for the issue.
3 Portions of table 2 in this article have been adapted from a prior publication in *The Journal of Law, Medicine & Ethics* (Weldon, Yaseen, and Hoffman 2022).

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