PLANETARY ANTIMICROBIAL RESISTANCE REGIMES AND COLLECTIVE ACTION

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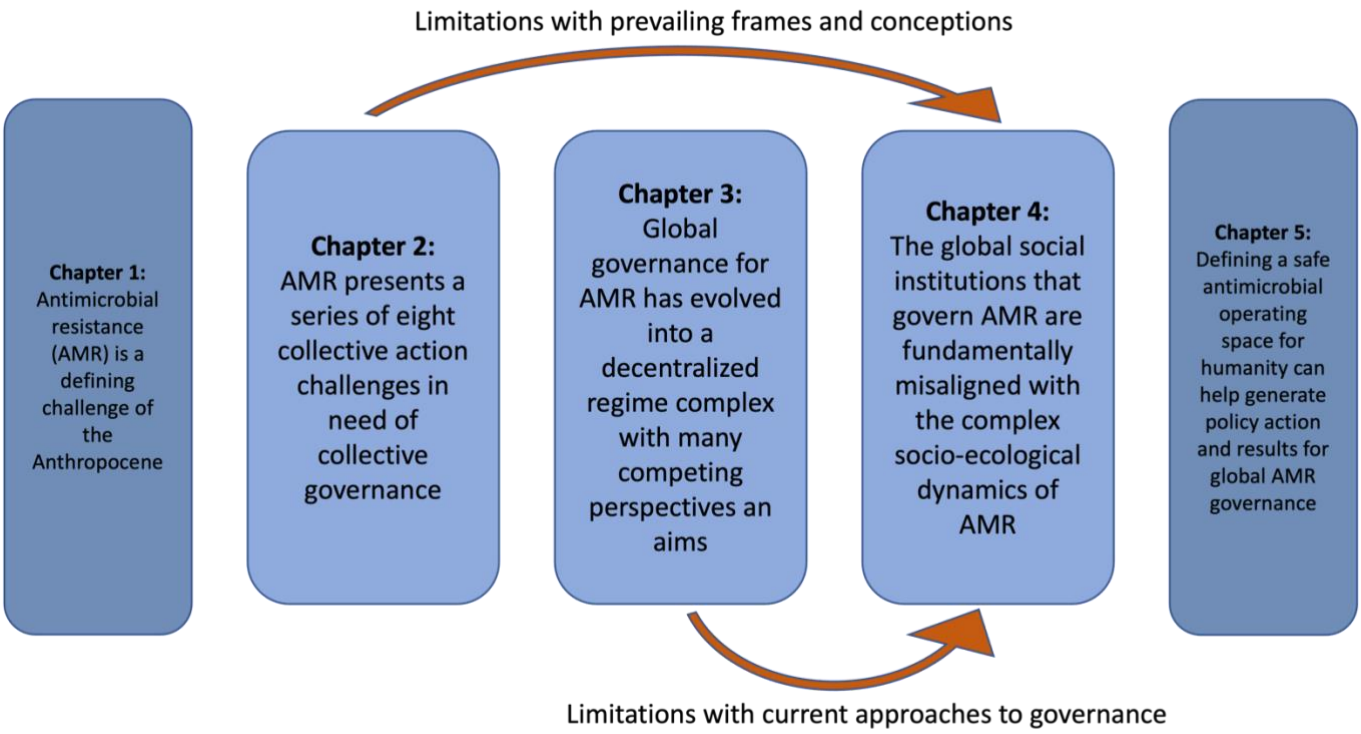
Dissertation Abstract

This dissertation considers how the enduring phenomenon of antimicrobial resistance (AMR) challenges us to reconsider the way we ask questions about and govern global issues. AMR occurs when disease-causing microbes develop resistance to the antimicrobial agents and medicines that are designed to treat, prevent, and stop the spread of deadly infections. AMR, which this dissertation understands as a primarily *social* issue, was associated with 4.95 million deaths in 2019. The introduction to this dissertation presents AMR as a defining problem of the Anthropocene. It proceeds to outline the research inquiries and methodologies adopted, the causes and consequences of AMR, and the main arguments and narrative arc across the dissertation's five chapters. The second chapter explores how the problem of AMR is understood as a series of global collective action problems. It develops a framework to systematically identify the various collective action problems that arise around public and common goods. Applying the framework to AMR, Chapter 2 articulates eight interdependent collective action problems for AMR governance. Chapter 3 then investigates how AMR is governed in today's interconnected world. It identifies and outlines the emerging 'regime complex for AMR governance', which is defined as the array of principles, norms, rules, and procedures that collectively guide human behavior around the challenge. It examines how the complexity of AMR, including its many interlinked collective action problems, has contributed to the rise and evolution of this decentralized global governance structure. Chapter 4 reframes AMR as a socio-ecological problem arising from deep tensions in the relationship between human societies and invisible microbial worlds. It adopts the concept of ecological fit, defined as the alignment between human social systems and biological ecosystems, to diagnose 18 misfits between the social institutions that govern AMR and the ecological nature of the problem. Chapter 4 proposes

three principles for designing global health institutions that better fit the problems they are meant to govern. Finally, Chapter 5 concludes the dissertation by distilling cross-cutting insights and implications for the future of global AMR policy. This final chapter defines a safe antimicrobial operating space for humanity.

Visual Abstract



Dedication

This dissertation is dedicated to all those who have lost their lives and well-being to treatable and formerly treatable infections.

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Chapter 1: Antimicrobial Resistance is a Defining Challenge of the Anthropocene

Introduction

Antimicrobial drugs, such as antibiotics, antivirals, and antifungals, are used to treat and prevent dangerous infections in humans, plants, and animals. They are also essential for enabling lifesaving treatments like surgery, which involve practices that risk exposure to potentially deadly infections. These drugs, however, come with a trade-off: the more we use them, the more likely it is that they stop working (Rogers Van Katwyk, Balasegaram, et al. 2019). This fatal flaw exists because microbes – including disease-causing bacteria, viruses, and fungi – adapt to evade the therapeutic effects of antimicrobial substances. This inevitable process, called "antimicrobial resistance" (AMR), occurs due to a range of factors, including natural evolutionary behaviours exhibited by microbes, as well as selective pressures artificially exerted by human activities. The same antimicrobial agents and drugs are vital across many sectors of human activity, including in healthcare and agriculture, and the way that they are used in these sectors is often inappropriate, which exacerbates the challenge. However, every use, even when prudent and necessary, potentially accelerates the natural process of AMR.

The consequences of AMR are far-reaching, with devastating impacts on human health and the global economy. When antimicrobial drugs stop working, formerly treatable infections become deadly and routine medical procedures – such as cesarian sections, chemotherapies, and joint replacements – become more dangerous as the risk of exposure to untreatable infections increases. It is estimated that 4.95 million deaths were associated with AMR in 2019, including 1.27 million deaths that were directly attributable to this phenomenon (Murray et al. 2022). Left unaddressed, morbidity and mortality associated with AMR are expected to rise rapidly in the coming decades, surpassing the global death toll caused by cancer and costing trillions of dollars

in economic losses (World Bank 2017). Resistant pathogens that no longer respond to treatment can also spread globally through humanity's circuits of movement and cause deadly pandemics (Wilson et al. 2021). If a resistant pathogen spiraled into a pandemic, we would become more reliant on non-pharmaceutical interventions to prevent its spread, such as contact-tracing and mobility restrictions. Given the widespread use of antimicrobial drugs in human health, animal health, and food systems, the high human and economic costs of drug-resistant infections, and the growing pandemic potential of human-induced drug-resistant pathogens, AMR represents a defining challenge for humanity in the Anthropocene.

The first known reports of AMR date back to 1907, with clinical observations noting decreased effectiveness in antimicrobial chemicals after prolonged use (Gradmann 2011). Since then, our understanding of AMR has evolved, revealing that the problem has only become more and more severe. With each new class of antimicrobial drugs discovered since the 1900s, resistance has quickly followed, diminishing the drugs' effectiveness and threatening human health in the process (Kirchhelle and Podolsky 2022). In other words, the problem of AMR has been known for nearly as long as there have been effective antimicrobials, and governments have struggled to craft meaningful policies to curb the emergence and spread of AMR for over a century. Meanwhile, increasing antimicrobial use in the absence of globally adopted strategies to adapt and mitigate against the emergence of AMR has turned the challenge into a global crisis. We now face a serious global predicament where AMR is currently a leading cause of death worldwide, many people still live and die without access to effective antimicrobials, and several antimicrobial drugs teeter on the brink of obsolescence.

After a century of insufficient global action, the antimicrobial era is waning. To help protect and sustain the precious resource of effective antimicrobial drugs, this dissertation

evaluates normative framings and governance arrangements for global AMR policy. Specifically, it investigates the ways AMR is conceptualized as a focus for governance, how it is governed in today's interconnected world, and how new conceptualizations of AMR can unlock new approaches to governing the problem. The dissertation also investigates AMR from a variety of complementary perspectives: as a series of interdependent social challenges; as a set of interlinked global collective action problems; as an intersectoral issue requiring a One Health approach; as an enduring problem in need of a socio-ecological perspective; and, finally, as an exemplar of the ecological challenges that humanity faces in the Anthropocene, where human activity is increasingly disrupting Earth systems – both vast and microscopic. Each chapter of this dissertation approaches the complex and multifaceted challenge of AMR from a unique angle, offering a diverse range of insights. These insights have the potential to guide intellectual reframings and generate effective political strategies, all aimed at achieving sustainable antimicrobial use for the benefit of all.

Through these inquiries, this dissertation also aims to challenge and advance our understandings of ecology in the context of the Anthropocene era. AMR, an emerging challenge arising from the interplay between human action and adaptive microbial behaviours, presents an opportunity to delve into the complexities of both human-human and human-non-human interrelations.

Ecology, as it is commonly understood, refers to dynamic systems of interaction among living organisms and their shared environments. These interactions encompass linear, non-linear, and circular causal chains. However, escalating problems like AMR challenge us to extend our conceptions of ecology beyond simply material environmental relations to also incorporate social and ideational dimensions (Harries-Jones 1995, 7).

Indeed, our existence is shaped by many different and co-constituting ecologies: a material planetary ecology of which we are a part, a social ecology that shapes our worldly interactions, and a normative ecology of ideas and frameworks that guide our perceptions of, and actions towards, the material environment and social world. AMR, emerging as a significant consequence of these shifting material, social, and normative ecologies, offers a valuable perspective. It enables us to reflect on our self-perception, our place in the world, and relationship with the planet, thereby illuminating potential strategies to navigate the myriad challenges of our time.

The remainder of this introductory chapter is structured in four parts. First, it delves into the global challenge of AMR, providing some background on its causes and consequences. In underscoring the urgent threat that AMR poses to humanity, this section considers how the disciplines of political science and international relations can inform effective global responses to this immanent challenge. Second, it discusses the methods and methodological commitments of each chapter, providing an overview of the dissertation's narrative arc. Third, the introduction summarizes the main arguments of the dissertation, which emphasize the need for both short- and long-term strategies to support global collective governance to address AMR – across countries, sectors, and time. Finally, a brief conclusion ends the introduction, leading into the second chapter on collective action problems affecting global AMR governance.

Part 1: The Causes and Consequences of Rising Global AMR

AMR is a complex problem with interlinked challenges for governance (Hoffman et al. 2015). It can occur spontaneously at any time or because of the inappropriate use of an antimicrobial drug. Microbes possess natural adaptive capacities, which can lead to evolutions in their genetic compositions that allow them to withstand threats in their environments (Lopatkin

et al. 2021). When exposed to an antimicrobial drug, microbes may mutate and develop resistance-conferring genes, which allow them to survive and proliferate in the presence of drugs designed to destroy the organism. In some cases, mutated microbes may even possess resistance-conferring traits prior to exposure to a drug, but these traits are not advantageous for the microbe until the drug kills off its non-resistant competitors. In this scenario, the already-mutated microbe with a resistance-conferring trait becomes the dominant microbe in the environment, and what was once considered a "defect" or "weakness" becomes an adaptive capacity allowing the resistant organism to proliferate.

In either case, once a microbe gains drug resistance, it can pass on these special genes vertically to descendant generations (i.e., to their offspring) or horizontally to other microbes (Lacey 1975).[1] Horizontal gene transfer allows for the sharing of resistance-conferring genes, even across strains and species. Moreover, wild reservoirs of free-floating resistance-conferring genes can also cause drug-resistance in pathogens – even if those resistance-conferring genes do not initially develop in pathogenic microbes (von Wintersdorff et al. 2016).

Human intervention accelerates these biological mechanisms at the microbial level, especially the use of modern antibiotics, antivirals, and antifungals (Levy and Marshall 2004). Poor governance and deeply engrained incentives at the societal level also contribute to the problem (Weldon, Liddell, et al. 2022). For example, unregulated antimicrobial pollution and run-off into the environment increase the likelihood that wild resistance will emerge (Singer et al. 2016).

[1] Bacteria possess remarkable evolutionary abilities. Horizontal gene transfer essentially lets bacteria share genetic resources amongst each other, passing on special traits and abilities such as drug-resistance. Horizontal gene transfer can occur via: *transduction*, where resistance conferring genes are inserted into bacterial genomes via viral bacterial phages; *transformation*, where free floating DNA encoding resistance are absorbed by bacteria; and *conjugation*, where bacteria share DNA via plasmids (Drlica and Perlin 2010, 91–98).

More specifically, antimicrobials have become integral components of modern life, essentially functioning as part of the invisible infrastructure that facilitates life as we know it (Chandler 2019). They are often used as quick fixes for labour, care, and hygiene (Denyer Willis and Chandler 2019), and their use is incentivized by social structures that value productivity and abundance (Kirchhelle 2020). However, this reliance on antimicrobials has led to their misuse and the masking of our dependence on their diminishing effectiveness.[2] The widespread demand and availability of antimicrobials, combined with suboptimal prescribing and clinical habits, unenforced regulations in human, animal, and agricultural settings, and the accumulation of antimicrobial pollution in ecosystems, continue to fuel the multifaceted problem of AMR (Weldon, Rogers Van Katwyk, et al. 2022).

Five social challenges affecting AMR

Although AMR is often discussed as a single problem caused by a biological mechanism, it actually presents a series of five interlinked social challenges (Hoffman et al. 2015). These challenges include expanding *access* to antimicrobials, diagnostic technologies, and alternative therapies, while also balancing the need for *conservation* of the limited pool of antimicrobial effectiveness. *Innovation* is also crucial to develop new antimicrobials, diagnostic technologies, and alternative therapies as microbes adapt and evade existing drugs. *Prevention,* meanwhile, can reduce the demand for antimicrobials in the first place by curbing the spread of infections. Finally, global action to address AMR must also redress enduring global health *inequities* within and across populations (Weldon, Liddell, et al. 2022).

i. Access

[2] Like a railing that helps us down a staircase, we don't often think about infrastructure until it fails. Microbial resistance to antimicrobial drugs (i.e., the failure of antimicrobials) renders visible the otherwise unnoticed extent to which we rely upon effective antimicrobial drugs to support and facilitate modern clinical medicine, public health, and ways of life (Chandler 2019).

The first and arguably most pressing challenge in addressing AMR is ensuring that people who need effective antimicrobials can access them (Årdal et al. 2016). Many individuals in lower-income and rural settings still do not have sustainable access to antimicrobials due to weak healthcare systems, unstable supply chains, and poor market incentives (Access to Medicine Foundation 2022). Poor access accelerates AMR by enabling infections to spread. It may also lead to inappropriate use of antimicrobials, such as taking smaller doses over periods of time different than the recommended treatment period or using substandard drugs. Smaller doses and substandard drugs both increase the likelihood of resistance because they are less likely to fully eliminate microbial communities, while also giving microbes the chance to mutate and develop defences.[3] Improving access to antimicrobials in the places that need them most will be crucial to address AMR. This imperative is especially important for low- and middle-income countries (LMICs) that bear a triple burden of poor antimicrobial access, high infectious disease, and high AMR mortality and morbidity (Murray et al. 2022). Several financing strategies exist to improve global access to antimicrobials, but they require global commitments to ensure their implementation (Banerjee, Hollis, and Pogge 2010).

ii. Conservation

Expanding access to effective antimicrobials must also be balanced against the need to conserve antimicrobial effectiveness for current and future generations. However, antimicrobials are often used inappropriately and unsustainably, which accelerates AMR in many parts of the world (Ray et al. 2019). Antimicrobials can be acquired without prescription in some jurisdictions, leading to their misuse when individuals do not fully know if or what antimicrobials are needed (Shafiq et al. 2021). Even in places where prescriptions are required,

[3] In other words, 'what doesn't kill them makes them stronger.'

studies indicate that antimicrobials are widely used without appropriate therapeutic justification (Ray et al. 2019). To address rising drug-resistance, it is crucial to establish better prescribing protocols, increase awareness of AMR among healthcare providers and the public, and tackle the problem of substandard and falsified drugs (Rogers Van Katwyk, Weldon, et al. 2020). However, structural drivers of antimicrobial use are also implicated in the need for conservation efforts. While individual behaviour can be changed, long-term and sustainable solutions must be accompanied by concerted social efforts that alter the structures of incentives and interests that lead to antimicrobial use (Weldon, Rogers Van Katwyk, et al. 2022; Chandler 2019).

A One Health approach (described in detail in Box 3.1) to conservation is also required, as the same antimicrobials that are used in human health are also used in animal health and agricultural settings (Wernli et al. 2020). Greater effort is needed to conserve critically important antimicrobials for human use only, while also establishing regulations to prevent antimicrobial drug run-off into the environment. However, antimicrobials help to improve food production in agriculture and enforcing "human-only" classes without viable alternatives could impact current conceptions of food security (Kirchhelle 2018). Thus, the interdependent challenges of access and conservation intersect across sectors and cannot be addressed in isolation.

iii. Innovation

Innovation – including research and development for new antimicrobial drugs – is crucial to develop new antimicrobials that can replenish the dwindling stock of effective drugs. However, the development of new drugs and technologies is not keeping up with the pace of microbial evolution and spread (Outterson et al. 2016). Market failures, where pharmaceutical firms argue that they are poorly incentivized to discover new drugs, are a significant challenge. For example, in the standard economic model, a firm's profits are dependent on the volume of

goods that they can sell. But, because of inevitable drug-resistance, the potential volume of sales for new antimicrobials is restricted by the time-limited effectiveness of these products (and thus the potential return to investment is diminished). Moreover, new drugs must either sometimes compete against off-patent generics, which restricts potential returns, or be saved in reserve as critically important 'last lines of defence', which presents a necessarily small market.

As a result of these market failures, pharmaceutical firms often cite the high costs of research and development but the low market value of prospective new antimicrobials as the cause of stagnant pipelines (Plackett 2020). This challenge highlights fundamental mismatch between the high social value and the low market value of antimicrobial drugs: pharmaceutical firms perceive a high risk with a low reward for new antimicrobial development, even though new antimicrobials are extremely valuable for societies.

Where the market fails to provide a stable supply of new antimicrobials, alternative research and development models are needed (Singer, Kirchhelle, and Roberts 2020).[4] Specifically, innovative drug financing models, public-private-partnerships, and public research and development can help change the way we approach the challenge of innovation. Such models could mobilize funds by, for example, going beyond traditional sales- and revenue-based approaches (Minssen et al. 2020).

iv. Prevention

Improving global infection prevention is also crucial for global AMR efforts. For example, poor sanitation and hygiene exacerbate AMR by enabling infections to spread, leading to unnecessary and avoidable antimicrobial drug use. Prevention measures can reduce the incidence of infectious disease and lessen the demand for antimicrobials in the first place, such

[4] Perhaps, more accurately, old (and not new) models are needed, as most of the first antimicrobials were discovered and brought to market through government programs (Quinn 2013).

as improving access to clean water, constructing hand washing stations, and enforcing waste-management protocols (Storr et al. 2017). However, great challenges remain for global infection prevention. One key challenge is the lack of standardized AMR surveillance across human, animal, and environmental sectors, which makes it difficult to compare and track the worldwide evolution and spread of infections and AMR rates (Wernli et al. 2017; 2020). To address this challenge, global action must prioritize more accurate and comprehensive surveillance systems that can inform prescribing practices and antimicrobial use.

v. Equity

Equity is a major challenge in global health, and it is especially significant in the context of AMR governance. The social challenges posed by AMR not only expose existing global inequities but also exacerbate them. Equity concerns the distribution of valuable resources and opportunities such as access to antimicrobial therapies, outcomes including morbidity and mortality from AMR, and assets like rapid point of care diagnostics. To ensure a just response, all AMR policies must consider how interventions may reproduce or worsen global health inequities.

For instance, equitably improving prevention requires consideration of the disproportionately high levels of infectious disease that LMICs face (Büyüm et al. 2020). Unfortunately, many LMICs cannot adequately invest in health system capacity due to the legacies of colonialism and current economic structures that do not serve all needs (Ndikumana and Boyce 2011; Viens 2019; Sell and Williams 2020). For innovation, the allocation of global funding raises further questions about who benefits from research and development investments. For example, certain groups can disproportionately benefit when the world, particularly public institutions, invest billions of dollars into innovation, such as pharmaceutical companies in high-

income countries, their investors, and the privileged groups that they tend to hire. Moreover, the COVID-19 pandemic has highlighted the inequitable distribution of new and existing technologies once developed, such as vaccines, diagnostic tests, personal protective equipment, oxygen, and antimicrobials (Phelan 2023). The challenge for equity is that the global system remains self-interested, with states and profit-driven corporations prioritizing their interests, even when their behaviour worsens and prolongs global health crises (Wenham, Eccleston-Turner, and Voss 2022).

Additionally, while no one is immune to resistant pathogens, different sectors of the population face different burdens and risk levels, including uneven distributions of infectious disease prevalence. Race, class, and gender dimensions, as well as intersectional approaches, are significant as women and other marginalized groups are more likely to live in poverty, be frontline and informal workers, and face increased risks of infection exposure during pregnancy, abortion, and childbirth (Schröder et al. 2016; Wenham, Smith, and Morgan 2020). Ultimately, questions about who pays, who gets what, and who is at risk, should drive equity considerations in AMR access, conservation, innovation, and prevention initiatives (Weldon, Liddell, et al. 2022).[5]

AMR undermines global progress[6]

The far-reaching problem of AMR affects nearly all aspects of human life, undermining human health security, human rights, food and environmental security, and economic

[5] I wish to thank Elias Mossialos who, through his lectures on Financing Healthcare Systems, drew my attention to these three fundamental questions for health policy: "who pays, who gets, and who is at risk?".

[6] AMR undermines progress when progress is defined as forward movement toward desired and morally agreeable ends. But AMR also provides a unique way to challenge enlightenment philosophies and conceptions of progress, modernity, universality, and linearity. These questions are for future research and are not taken up in this dissertation.

development. If left unaddressed, AMR has the potential to undermine development efforts and stymie global progress, best exemplified by the way it threatens the Sustainable Development Goals (SDGs) (Esiovwa et al. 2022). For instance, SDG 3 seeks to improve human health, but without effective antimicrobials, common and formerly treatable infections can be fatal. Routine medical treatments also become much riskier.

In addition, AMR impacts other underlying determinants of health, including nutrition, which is captured by SDG 2 on ending hunger. Rising AMR already disrupts fragile food supply chains, particularly in places where populations rely upon antimicrobial usage in animal agriculture to ensure food security. AMR also threatens the economic security of healthcare systems, with the costs of AMR jeopardizing the ability to provide care (World Bank 2017).

The impacts of AMR are disproportionately borne along the lines of race, gender, and income, which undermines SDGs 1, 5, and 10 on ending poverty and reducing income and gender inequality. The inequities of AMR are already evident in the uneven burden of infection, mortality, and morbidity in lower-income settings (Murray et al. 2022). These injustices need to be rectified urgently. Moreover, the harms of AMR stand to reproduce colonial relations between high-income countries, where the bulk of antimicrobial investment occurs (Simpkin et al. 2017), and LMICs that continue to bear the greatest infectious disease burden (Institute for Health Metrics and Evaluation 2020). Despite these differential risks, microbes do not discriminate, and AMR is a transnational threat from which no person, community, or country is immune.

The transnational and multifaceted problem of AMR cannot be solved through biomedical interventions alone. Addressing the underlying social causes of AMR is essential, such as poor sanitation and hygiene, inappropriate use of antimicrobials, and inadequate infection prevention measures. And to do so, we need coordinated responses that involve not

only healthcare professionals and researchers but also policymakers, civil society organizations, and the public. Political strategies are needed to mobilize the necessary resources, build the necessary alliances, and overcome the various institutional barriers and challenges that hinder global AMR efforts.

Political science, and international relations in particular, can play a key role in guiding the global response to address AMR by analyzing the political, economic, and social relations that contribute to the emergence and persistence of AMR. International relations for AMR can help navigate the complex and dynamic system of global health governance, where actors and interests often conflict and diverge, and where power and politics *always* shape health outcomes across the globe. It can also identify and inform effective policy solutions that can be implemented at local, national, and global levels. A more critical international relations perspective, moreover, can help scrutinize global human-non-human relations, including human-microbial and ecological interactions.

More specifically, international relations theories, such as constructivism, offer conceptual and methodological tools to investigate how AMR has gained traction on the international stage, including the role of discourses, norms, and power. Other theories, such as realism and liberalism, offer perspectives on how interests-based power dynamics and institutionalized cooperation mechanisms affect AMR governance outcomes, respectively. Meanwhile, a historical materialist approach can illuminate the dialectical and historical interactions between social relations of production and microbial ecologies, revealing how specific social, ecological, and institutional arrangements have become possible with the advent of effective antimicrobial technologies. Overall, political science and international relations

approaches can support meaningful actions that are evidence-informed and feasible, maximizing the likelihood of achieving lasting and meaningful impact on this critical issue.

Part 2: Methodology

Five broad questions informing the dissertation

This dissertation is organized around five overarching questions that guide the investigation of AMR:

1. Why is AMR a defining social challenge?
2. How is AMR conceptualized as a problem for global governance?
3. How is global AMR currently governed?
4. How can new perspectives and frameworks enhance AMR governance?
5. What would an improved policy approach, grounded in these new perspectives, look like?

These investigations underscore the political dimensions of the challenge, engaging with the operation of power through governance, decision-making procedures, and resource distribution at global and local levels. They probe the mechanisms by which challenges like AMR are understood, prioritized, and governed, which involves navigating the power-laden dynamics of a diverse range of institutions and actors with varying interests, norms, rules, and agendas. Additionally, these inquiries consider how new frameworks and policies may reconfigure existing governance structures. In doing so, they imagine a future that potentially transforms human social and human-microbial relations – tasks that are inherently political in nature.

This dissertation proceeds in five chapters, each inspired by and responding to one of the central inquiries. Overall, each chapter provides a unique perspective so that the dissertation collectively answers the five questions. In recognizing the complexity of the issue, the

dissertation also engages with five different frameworks for understanding AMR, each of which overlays the five central inquiries introduced above. Below is a more specific breakdown that outlines the central inquiry and framework adopted by each chapter, which is also summarized in Table 1.1.

Chapter breakdown and narrative arc

The introduction of this dissertation discusses AMR as a biological process and as a series of five interdependent social challenges for governance. In acknowledging the complexity and the need for diverse interpretation for AMR, it provides multiple definitions, perspectives, causes, and consequences of the challenge. In working with different epistemologies and ontologies, it further discusses the need for multiple interpretations of AMR to provide a nuanced understanding of its social and material drivers.

Chapter 2 explores the complex problem of AMR as a focus for global governance. It systematically analyzes the different governance challenges posed by AMR by reviewing the literature on AMR governance and collective action. Specifically, Chapter 2 provides a generic framework to systematically identify the various collective action problems that arise around public and common goods. The chapter applies the framework to AMR, explaining why and how the challenge requires global collective action across eight unique but interdependent situations where individual interests conflict with collective interests, including stag hunts, volunteer dilemmas, and weakest link problems (defined in Table 2.2). Chapter 2 concludes by discussing the limits of collective action theory and highlighting the need for alternative conceptualizations for AMR, which are explored in the third and fourth chapters.

Chapter 3 investigates how AMR is governed as an intersectoral problem in today's interconnected world. The chapter investigates the past 75 years where governments have

struggled to craft effective and sustainable global strategies for AMR. It observes that because of these struggles, global efforts for AMR are currently forming a decentralized array of multiple institutions with overlapping and sometimes conflicting principles, norms, rules, and procedures. This emerging 'regime complex for AMR governance' is adopted as an analytical framework to systematically chart the various actors and institutions implicated in AMR governance (Weldon, Yaseen, and Hoffman 2022). The chapter examines how the problem's complexity, including its many collective action problems, has contributed to the rise of this decentralized global governance structure. Additionally, the chapter traces how the emergence of One Health ideas provided international organizations with a normative justification for integration and convergence on AMR. It ends by arguing that while promising in the short-term, One Health ideas have limits that require complementary perspectives to inform longer-term solutions.

Chapter 4 considers one such perspective by reframing AMR as a socio-ecological problem arising from deep tensions in the relationship between human societies and invisible microbial worlds. This chapter adopts a socio-ecological perspective and the concept of ecological fit to identify 18 misfits between the global social institutions that govern AMR (i.e., the regime complex explored in Chapter 3) and the ecological nature of the problem. The chapter considers whether strategies applied in global biodiversity governance can help guide strategies for more durable and effective global health institutions that better fit the problems they are trying to manage.

Chapter 5 concludes the dissertation with a focused policy analysis. It identifies cross-cutting insights and implications for the future of global AMR governance. This chapter builds upon and synthesizes the concepts introduced throughout the dissertation, such as collective action, One Health, regime complexes, and socio-ecological understandings for AMR. It draws

on recent scholarship, such as the Stockholm Resilience Centre's planetary boundaries framework (2009) and Kate Rawoth's doughnut model of sustainable development (2017), to define a safe antimicrobial operating space for humanity in the Anthropocene. Using this model, the conclusion provides a means to identify collective solutions for the five social challenges brought forward in this introduction.

Table 1.1: Summary of Key Research Contributions

	Central Inquiry	**Framework for understanding AMR**	**Specific Research Questions**	**Key Findings**	**Theoretical Contributions**	**Methodological Contributions**	**Empirical Contribution**
Chapter 1: Antimicrobial Resistance is a Defining Challenge of the Anthropocene	Why is AMR an urgent social challenge?	AMR is a biological process that presents a series of five interdependent social challenges that threaten human health and development.	Why are multiple perspectives needed to understand and address AMR? How can political science and international relations contribute to the global response?	AMR requires global collective action, intersectoral cooperation, and socio-ecological perspectives. Political science and international relations can contribute to interdisciplinary and holistic approaches.	An argument for epistemic pluralism when considering knowledge and action for complex global challenges.	A discussion of the methods leveraged across this dissertation.	An overview of the dissertation, summarizing a range of short term and long-term strategies to support collective, intersectoral, and enduring action for AMR.
Chapter 2: Analyzing AMR as a Series of Collective Action Problems	How is the global problem of AMR conceptualized as a problem for governance?	AMR is a series of interdependent global collective action problems.	Why is AMR considered a series of global collective action problems? What collective action problems does it present, how do we know, and what is the distribution of interests around each one?	AMR presents at least eight interlinked collective action problems. Collective action theory has major limitations that prevent it from providing a sufficient basis to govern AMR.	A framework to understand the various ways that cooperation problems manifest around complex challenges generally and for AMR specifically.	A replicable method to demystify complex challenges and decipher concrete and tangible collective action problems for governance.	A list of eight collective action problems for AMR governance.
Chapter 3: The Evolving Regime Complex for	How is the global response to AMR	AMR is an intersectoral problem requiring a One	Prior research has demonstrated that AMR is currently governed via a	The rise of One Health ideas caused a paradigm shift	An analysis that extends regime complex theory by looking at the	A synthesis of historical institutionalist and constructivist	A narrative historical account of how the idea of One Health led

Antimicrobial Resistance Governance: The role of norms, paradigms, and international organizations	currently governed?	Health approach.	regime complex, but why has a regime complex for AMR governance emerged? What role did AMR's various collective action problems play in the formation of this decentralized governance structure?	that contributed to the integration of international work plans on AMR. The integration of AMR- relevant international organizations contributed to the evolution of the regime complex for AMR governance.	role of ideas and the agency of international organizations during regime complex evolution.	interpretations on the role of changing ideas in institutional settings. A generic framework to understand the emergence and effect of new ideas on regime complex governance.	various international organizations to integrate their work on AMR, contributing to the evolution of the regime complex for AMR governance.
Chapter 4: **"**Fit for Purpose?" Assessing the Ecological Fit of the Social Institutions that Globally Govern AMR	How can a new understanding promote better governance?	AMR is an enduring problem in need of a socio-ecological approach.	Why are prevailing understandings and approaches to governing AMR limited? How can a socio-ecological perspective unlock new approaches to govern AMR globally?	The problem of global AMR is not governed as a socio-ecological problem, which has produced 18 misfits between the ecological dynamics of the problem and its corresponding governance institutions.	An application of historical materialist methods of dialectical analysis to understand the socio-ecological problem of AMR.	An operationalization of the concept of ecological fit for application to the global governance of AMR.	A list of 18 misfits in the current way that AMR is governed.
Chapter 5: Toward a Safe Antimicrobial Operating Space for Humanity	What would an improved policy approach, grounded in these new perspectives, look like?	AMR is a planetary problem.	How can we envision and achieve sustainable antimicrobial use for all in the Anthropocene?	Flexible, adaptable, and resilient institutions for AMR can leverage polycentricity and break down silos for more holistic governance.	A new model to understand AMR that defines the safe antimicrobial operating space for humanity.	A synthesis of the methodologies employed throughout the dissertation.	An application of eight design principles to the new doughnut model for AMR. A synthesis of the empirical findings uncovered throughout the dissertation.

On epistemologies, ontologies, and theoretical commitments

In writing this introduction, I am reminded of the wise words of Levi Strauss, who said, "*History* is therefore never history, but *history for*"; Robert Cox, who said, "Theory is always *for* someone and *for* some purposes"; and Hidemi Suganami, who reminds us, 'There is no history as it happened, only history as it is told'.[7] Along similar lines, I acknowledge that there is no such thing as apolitical political science research and that specific theoretical commitments inform my critical problem-solving perspective.

Specifically, this dissertation draws on various epistemologies to present multiple different angles that come together to provide a clear picture of the complex challenge of AMR, including positivism, constructivism, and historical materialism (Table 1.2). I begin with the notion that the practice of knowing – knowledge, its acquisition, and application – are constantly challenged by the complexity of the problems that we face today, such as climate change, biodiversity loss, and AMR. Indeed, these problems, arising in the Anthropocene, challenge not only our concepts but also the way we construct and devise concepts to access truth and understand reality (i.e., our epistemologies and ontologies). As a result, they problematize ways of knowing, being, and acting in the modern conjuncture. For example, 'certainty' for these problems is a concept belied by the limits of our possible comprehension in the face of their multilayered, non-linear, and dynamic systems of causality. Our ability to perceive such complexity is limited by our embeddedness within the very 'ecologies' we are trying to understand, where our perceptions are always mediated through our worldviews and are influenced by prior conceptualizations of 'matters of fact' like cause and effect, and, indeed, reality and truth themselves.

[7] Or, in his original Latin phrasing: "*res gestae* equals *historia rerum gestarum"*.

On one hand, problems like AMR are material and feel very real, resulting from seemingly inarguable facts of the universe. We can see microbes evolve, observing material transformations in their biology that make them immune to our medicines; people get sick and die when pathogens, including resistant ones, proliferate in their bodies. The positivist (or empiricist) paradigm that structures conventional scientific inquiry helps to isolate and explain these natural occurrences. Applied to AMR, this worldview is crucial to comprehend the biological mechanisms of resistance and its epidemiological spread. With its focus on discerning knowledge through the observation of quantifiable phenomenon, this episteme can access such 'facts of microbial nature'. Furthermore, with its emphasis on repeatability, generalizability, and explanation through cause-and-effect reasoning, this empirical scientific paradigm is crucial for uncovering new antimicrobial drugs and treating illness, especially as it underpins modern biomedical perspectives. This paradigm, moreover, is also helpful for discerning patterns, anticipating trends, and designing interventions informed by empirical facts.

However, despite the power of analysis provided by positivist epistemologies in these regards, a purely positivist approach is unlikely to be sufficient in addressing the multifaceted and *socially driven* problem of AMR. For instance, it is difficult to pinpoint accurately with laboratory sciences the critical social, cultural, economic, and political dimensions that significantly influence the development and spread of resistance. Where positivist sciences often rely on methods that isolate causality through decontextualization, these social aspects can only be understood through contextualization within specific social environments. And while it is possible to incorporate scientific principles into social inquiry when investigating these dimensions (e.g., as in the IR schools of neo-realism and liberalism), the difficulty in achieving randomized control trials, which are the gold standard for causal inference, makes these social

investigations less legitimate within evidential hierarchies, which represent positivist conceptions of validity.[8] But the limitations of purely positivist worldviews are even more problematic when we recognize that human antimicrobial use is not only a function of bacterial pathology, but also a complex social practice influenced by patient and consumer demands, cultural perceptions of illness and wellness, economic incentives, and regulatory frameworks. Indeed, these intricate, messy, and socially constructed phenomena are not well suited to the ideals of empirical investigation and mechanistic intervention.

Therefore, there is a need to incorporate alternative epistemologies. The constructivist approach, for example, recognizes that our knowledge of material reality is not merely 'discovered', but is also socially constructed. Reality is always mediated through ideas, which form our perceptions of the material and social world. For AMR, this means recognizing that the 'truth' about AMR, and possible solutions, are not solely biological, but are also inherently social. This worldview requires looking at how the problem of AMR is rendered intelligible through the ways that it gets framed in relation to prior ideas and perceptions. These problem framings, moreover, operate to legitimize certain social solutions and responses to AMR. For example, when we say that AMR is a social problem, this framing operates to presuppose social, and not solely biomedical solutions.

In applying historical materialism, moreover, we can understand that knowledge and truth are not only socially constructed but also historically specific. Perceptions of reality and truth are products of social relations and the result of individuals and collectives trying to interpret and make sense of their material conditions. In other words, the way the world is understood – truth, reality, and the appropriate methods for uncovering and understanding such

[8] Here, there emerges a challenge where positivist theories tend to project a claim on a monopoly of valid knowledge.

contested concepts – is a product of social and material interactions unique to a given historical period.

Table 1.2: Different Ways of Approaching Research for the Phenomenon of AMR

	Positivism	**Constructivism**	**Historical Materialism**
Truth is…	Objective and absolute	Subjective and socially constructed by individuals and collectives	Socially constructed and historically contingent
Reality is…	Real and natural	Socially constructed based on how we understand and interpret material reality	Socially and materially constructed, a product of the interaction between humans and their environments
Ideas…	Reflect reality	Mediate reality	Are the product of social and historical processes, shaped by existing material conditions and social relations
Methodology is…	Empirical	Both empirical and reflexive	Historical and dialectical for material and social conditions
Example of AMR research question:	What are current resistance rates of *X* microbe to *Y* drug in *Z* locations?	How does the way we perceive and communicate AMR affect how people act?	How have modern antibiotics transformed human material and social conditions?
Example findings:	In Canada, "The rate of methicillin-resistant Staphylococcus aureus infection reported by sentinel hospitals continued to increase, from 2.80 per 10,000 patient-days in 2012 to 3.17 in 2017" (Health Canada 2018).	"[L]ocal interpretation of pathogenicity, … may help to account for the high frequency of resort to antibiotics in treating common RTI and UTI symptoms that we observed in our study clinics" (Lambert et al. 2019).	"Archival work with stored soil and clinical samples produces a record described here as 'the biology of history': the physical registration of human history in bacterial life" (Landecker 2016).

Integrating these diverse epistemologies presents a challenge. They offer different understandings, not only of 'what' AMR is, but also 'how' it should be understood, studied, and addressed. The challenge is extended further when considering how these various ways of knowing can best inform action. If knowing is uncertain, intersubjective, contingent, and multilayered, then acting based on knowledge becomes significantly challenging and inherently contestable. If our actions are informed by what we know, but knowing is always partial, constructed, and often incomplete, then action can never really be certain to produce expected results.

This uncertainty, indeed, these theoretical challenges overall, mandate epistemological and methodological humility, flexibility, and pluralism. Thus, the epistemology employed throughout this dissertation is purposively eclectic, recognizing that we need to continually scrutinize knowledge, recognize its limitations, and be willing to adapt actions based on new insights. In embracing an interdisciplinary approach, this dissertation acknowledges that 'knowing' is always evolving, and, therefore, 'acting' must be flexible enough to accommodate these shifts. Scientific knowledge, while powerful, is but one way of knowing. It needs to be balanced with other forms of knowledge – social, experiential, and local – to craft holistic and adaptable political responses to complex issues like AMR.

Beyond these theoretical commitments, my worldview is notably influenced by the 1978 Alma Ata declaration, which emphasizes that "economic and social development, based on a New International Economic Order, is of basic importance to the fullest attainment of health for all and to the reduction of the gap between the health status of the developing and developed countries" (WHO 1978). This serves as my starting point for an economic vision and understanding of promoting health for all, and I am committed to researching and writing about

the various uneven distributions of wealth, resources, and opportunities that hinder this more equitable future. However, I recognize that my privilege as an educated, able-bodied man living in the settler-colonial state known as Canada shapes my perspective. This means that I primarily write this dissertation as an ally for those who do not enjoy the same privileges as I do – or, perhaps more accurately, whose exploitation enables my own privileges. Despite the various forms of privilege that I possess, my experiences as a first-generation university student and a mixed-race child of an immigrant from the Global South have led me to develop a deep concern for global issues.

Considering these commitments, this dissertation adopts a critical perspective by recognizing that our societies and social relations are inherited from the past, historically contingent, and continually changing. However, the dissertation is also problem-solving in that it is concerned with improving health outcomes globally. My critical problem-solving perspective recognizes that the urgent problems we face in the Anthropocene require immediate action within the system that currently exists. I posit, however, that efforts to address these existential problems in the historical present 'as it is' do not necessary detract from, but can in fact support transformative efforts to achieve a healthier world for all – a potential future that 'ought to be'.

Part 3: The Argument of the Dissertation, Summarized

To summarize the arguments put forward in this dissertation, AMR poses a series of interdependent social challenges that demand coordinated and collaborative global efforts. Tackling the social drivers of resistance, such as improving access, conservation, innovation, prevention, and equity, requires multiple perspectives to address different aspects of the problem. A wide range of approaches, investigations, and strategies are needed to support collective action across countries, sectors, and time (Hoffman et al. 2015).

The transnational nature of AMR means that global cooperation is necessary. Meanwhile, the intersectoral drivers of use and microbial spread demand a coordinated One Health response across human, animal, agriculture, and environmental sectors (Robinson et al. 2016). Finally, since the co-evolution of humans and microbes is an inevitable and long-lasting process, cooperation over time is required to maximize the time-limited effectiveness of antimicrobial drugs and achieve sustainable antimicrobial use for all (Jørgensen et al. 2020).

AMR requires global collective solutions

Resistance to antimicrobials can arise anywhere they are used, and resistant microbes can easily spread across the world. As seen during the COVID-19 pandemic, emerging pathogens and their variants have significant power to repeatedly evade vaccination and disrupt social life. With the continued global movement of goods, people, animals, and microbes, no single country can wholly mitigate the transnational threat of AMR on its own. Global cooperation across countries is essential to prevent the loss of effective antimicrobials (Hoffman and Behdinan 2016). While some countries have developed national policies to promote the appropriate use of antimicrobials (Rogers Van Katwyk, Grimshaw, et al. 2019), these policies are underutilized and less likely to be effective without unified global commitments to tackle AMR (Rogers Van Katwyk, Giubilini, et al. 2020).

The multifaceted challenge of mitigating AMR underscores the need for strong, coordinated, and global mechanisms to manage its risk and protect the effectiveness of antimicrobials as a precious and shared resource. Equitably addressing the related pillars of access, conservation, innovation, and prevention requires collective action to strengthen global defences against AMR and build durable institutions to mitigate and adapt to its multisectoral impacts. In an interconnected world, the global response to AMR will only be as strong as the

weakest response in any given setting. It only takes one initial microbial event to set forth a potential pandemic. Measures to address AMR are unlikely to achieve sustainable impact unless all countries commit to and undertake bold action to prevent and respond to AMR.

Achieving this level of collective action across all countries will require global political mobilization to optimize the distribution of resources, such as medical countermeasures, and implement new systems and strategies to prioritize antimicrobial access in places that need them the most. However, despite the need for collective action to address this global threat, many actors pursue their own interests. Few have incentives to restrict their use of antimicrobials through conservation or invest in research and development for new antimicrobial drugs to replenish the depleting pool. Even though all countries collectively stand to gain from sustained access to effective antimicrobials, there remain economic and political incentives to act selfishly at the expense of the collective benefit (Baekkeskov et al. 2020). As a result of these collective action problems, the continued supply of effective antimicrobials remains precarious, their distribution remains inequitable, and they continue to be overused, misused, and abused, which accelerates the development of resistance.

Addressing AMR as a series of interdependent collective action problems requires a more granular understanding of the specific collective action problems that AMR presents. Understanding the distribution of interests across these collective action problems can also clarify the purpose of global efforts. Addressing these collective action problems will require political strategies to overcome conflicts between individual-level interests and collective interests. These strategies must support desired behaviours, curb undesired behaviours, and align individual and collective interests for AMR solutions.

AMR requires a One Health approach

To effectively address AMR, it is essential to coordinate efforts through a One Health approach (Léger et al. 2021). A One Health approach recognizes that the use of antimicrobials affects many sectors, including human health, animal health, plant health, agriculture, and the environment. Specifically, many societies rely on antimicrobials as critical infrastructure to treat and prevent infectious diseases in humans, animals, and plants, improve crop and agricultural yields, and enable life-saving medical procedures (Chandler 2019). However, the same antimicrobials are used across settings, and improper waste practices accelerate AMR in natural environments. For instance, in many parts of the world, wastewater from hospitals and farms is often not properly treated, leading to antimicrobial pollution in the environment (Singer et al. 2016). Microbes can easily transfer across species. As the COVID-19 pandemic demonstrated, they can also travel quickly around the world. As such, solutions and strategies must be commensurate with these intersections and address the dynamic causes of AMR both globally and across spheres of human activity.

While addressing AMR as a One Health problem is crucial, it is not without challenges. One of the major challenges is the need for cross-sectoral governance initiatives that overcome divergent mandates, practices, funding, and accountability mechanisms at both national and global levels. For example, challenges remain for coordination across international organizations like the World Health Organization, Food and Agriculture Organization, World Organization for Animal Health, and United Nations Environment Programme (Spencer et al. 2019; Lee and Brumme 2013). These challenges are reflected across national ministries of health, agriculture, trade, and the environment (dos S. Ribeiro, van de Burgwal, and Regeer 2019).

AMR requires a socio-ecological approach

AMR transcends conventional boundaries among countries, sectors, and even species and time. Human antimicrobial use and adaptive microbial behaviours have a dialectical relationship that underscores the socio-ecological nature of the problem (Wallinga, Rayner, and Lang 2015). Humans use antimicrobials to facilitate modern ways of life, which puts selective pressures on microbes that lead them to evolve and develop resistance. Resistance, in turn, undermines human social systems that depend on antimicrobials as ecology-transforming tools. The rate of AMR is a feature of the way human behaviours accelerate microbial evolutionary traits. Thus, AMR is a long-enduring problem that requires transformative approaches, not quick fixes and silver bullets (Denyer Willis and Chandler 2019).

Moreover, AMR is a planetary challenge that must be analyzed from a planetary perspective (Living with Resistance project 2018). This perspective invites us to see AMR as a function of how humans exist on the planet, defined by physical and ecological limits. This framing brings AMR governance onto the same plane as other planetary challenges such as atmospheric, biodiversity, and climate governance. By adopting a planetary and socio-ecological perspective, we can situate AMR as a One Health challenge within a complex mix of Earth systems, including the biosphere and Earth's microbiological ecosystems (Léger et al. 2021).

Addressing AMR as a socio-ecological problem will require durable institutions that guide human cultural adaptation alongside natural and human-induced microbial evolution. Global health institutions, including the decentralized regime complex for AMR governance, must be aligned with the planetary dynamics of complex microbial ecologies. This includes addressing the several conflicting tensions between human antimicrobial use and microbial evolution. By adopting a long-term outlook for AMR mitigation, guided by a commitment to

sustain a safe antimicrobial operating space, we can work towards lessening the demand for, use of, and reliance on antimicrobials, making sustainable solutions more likely and achievable.

Conclusion

Over the course of history, we have experienced the power of microbes to disrupt daily life, even in the largest, richest, and most prepared industrial economies and societies. Now, swift global collective action is needed to prevent the evolution and spread of resistant microbes across countries, sectors, and time. Indeed, antimicrobial drugs have been crucial for achieving monumental global health gains over the past century. However, the global rise of AMR threatens to undo these gains. For over a century, the world has struggled to craft effective and sustainable global strategies for AMR. The COVID-19 pandemic has further complicated global health efforts (Tomczyk et al. 2021). Nevertheless, a renewed interest in improving global health governance in the wake of COVID-19 presents a unique opportunity to generate global action on AMR. We must seize the opportunity, preserve our ability to treat infectious diseases, and take measures to protect antimicrobials for human health. Global solutions will require strategies to maximize the time-limited effectiveness of antimicrobial products, continually develop new antimicrobial drugs through research and development, optimize their equitable distribution, and minimize the emergence of drug-resistant infections over time. In the long-term, we must also craft durable institutions that can navigate the evolving relationship between humans and microbes, mitigate and adapt to the future risks of AMR, and sustain effective antimicrobial use for all.

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Chapter 2: Analyzing Antimicrobial Resistance as a Series of Collective Action Problems

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Chapter Abstract

Antimicrobial resistance (AMR) causes over 1.27 million deaths annually, making it one of today's most urgent health threats. Given its urgency, there are often calls for large-scale global initiatives to address AMR. However, collective action theory has yet to be applied to the problem in a systematic and coherent manner. Fuller engagement with collective action theory is necessary to avoid the risks of: incorrectly characterizing the kinds of challenges that AMR presents; simplifying the problem by reducing it to a single type of collective action problem while ignoring others; and overstating the ability of collective action theory to formulate effective solutions. This chapter develops an analytical framework for collective action problems concerning public goods (i.e., goods that are non-excludable and non-rivalrous) and common goods (i.e., goods that are non-excludable and rivalrous). When analyzed with this framework, we find that the governance of AMR poses eight distinct collective action problems. This more granular framing of AMR provides, in our view, a better basis to develop policy solutions to address different aspects of AMR as a governance problem. We conclude with proposals for future research.

Introduction

Collective action problems occur when a cooperative solution is prevented by the strategies dictated by the self-interest of actors considered individually. Given the difficulties associated with overcoming collective action problems, there are entire fields of study devoted to understanding how they arise and evolve, and how to manage them. Often, this includes the use of familiar models like the 'tragedy of the commons' and 'stag hunts' (defined later in table 2.3) (Kollock 1998), with suggested solutions that rely on market or imposed governance mechanisms (Ostrom 1990).

Characterizing a given governance problem as a collective action problem – or as a specific type of collective action problem – can provide a useful diagnostic and thereby guide policy responses. However, getting the diagnosis wrong may misguide policy responses. The challenge, then, is to fine-tune the analytical tools by means of which the diagnostic or characterization is performed. Some researchers have noted, indeed, that the imprecise use of concepts from collective action theory has the potential to generate conceptual confusion when a mischaracterization becomes widely – and uncritically – accepted (Moon, Røttingen, and Frenk 2017; Smith and MacKellar 2007).

The governance of antimicrobial resistance (AMR) is one such area. AMR is a complex, multifaceted global challenge that poses an urgent threat to human health and wellbeing (Murray et al. 2022; Laxminarayan et al. 2013). It is caused by a natural evolutionary process that is artificially accelerated by human behaviours. Through this process, microbes, including disease-causing bacteria, evolve to evade the antimicrobial substances we use to kill them or stop their spread, such as antibiotics (Murray et al. 2022). To simplify the complex challenge and help identify policy responses, AMR has sometimes been characterized as 'tragedy of the commons',

where every use of an antimicrobial drug potentially diminishes the future effectiveness of these substances (Padiyara, Inoue, and Sprenger 2018). In other words, what is rational at an individual level (e.g., promoting health or productivity with antimicrobial use) generates a sub-optimal outcome at the collective level (i.e., depletion of the global common pool of antimicrobial effectiveness).

While this connection is well-made, collective action theory has yet to be applied systematically to elucidate AMR's other complex and interlinked facets. And despite calls for large-scale global initiatives to address AMR, collective action theory has yet to be applied to the problem coherently. Although AMR, is often presented as a collective action problem, such characterization is rarely fleshed out (Hoffman et al. 2015). In some cases, AMR is simply treated as a tragedy of the commons, which is but one type of collective action problem (Roope et al. 2019). In other cases, AMR is mischaracterized as a global public good rather than a global common good (Eggleston, Zhang, and Zeckhauser 2010; Patel et al. 2023)[9].

Additionally, AMR researchers have not yet problematized the fundamental assumptions of collective action theory when applying it to the challenge, despite four major limitations affecting the theory. For example, collective action theory seeks a level of generalizability that risks obscuring the nuances required to address AMR's many interlinked and complex facets. An additional three limitations arise from the theory's core assumptions about rationality, static systems, and Pareto optimality, which are discussed in section four.[10]

[9] In contrast with common-pool resources, global public goods are non-rivalrous – a distinction discussed in section 2 and applied to AMR in section 3.

[10] The concept of Pareto optimality is further discussed in Part 4. A situation is said to be Pareto Optimal when a distribution of goods is such that no one can be made better off without making someone else worse off. If a situation is Pareto-deficient, then the distribution of goods is not maximized, meaning some can be made better off without making others worse off.

This lack of systematic engagement with collective action theory is not unique to AMR (Jagers et al. 2020), but it is particularly pressing in this context due to the massive risks posed by drug-resistant infections. Fuller engagement with collective action theory in the analysis of AMR is necessary to avoid three main risks: 1. incorrectly characterizing the kinds of collective action problems that AMR presents; 2. oversimplifying AMR as a governance problem by reducing all its facets to a single type of collective action problem while ignoring others; and 3. overstating the ability of collective action theory to formulate effective solutions. Such risks are not merely theoretical. Each of them could translate into misguided – and thereby ineffective or even counter-productive – policy responses. More generally, the massive effort required to mobilize the international community to provide a collective response to AMR can only succeed if there is sufficient clarity of purpose, which in turn requires a diagnostic of the problem that is as accurate as possible.

Leveraging and clarifying the rich tradition of social science research on collective action theory is crucial to avoid these risks, as different problems require distinct solutions. The endeavour to craft effective policy options for global problems, moreover, requires a nuanced yet precise understanding of the many social challenges that they present. Adopting AMR as a case study where these issues persist, therefore, has a twofold benefit: not only can a deeper understanding of collective action theory support future global AMR policy formation, but it can also demonstrate how collective action theory can be applied to other global challenges more precisely, such as climate change and biodiversity loss.

To reach this higher level of precision, this chapter proceeds in four parts. First, it reviews how previous research has applied only narrow forms of collective action theory to the problem of AMR. Second, the chapter develops a general framework to identify and catalogue

collective action problems. Third, the chapter applies the framework to prior research on AMR governance challenges. In doing so, it demonstrates that AMR presents at least eight interlinked collective action problems, including a tragedy of the commons and multiple stag hunts, volunteer's dilemmas, and weakest link problems (defined later in table 2.3). These collective action problems arise around both common-pool resources and public goods for AMR governance (defined in table 2.2). The fourth section discusses the limitations of applying collective action theory to AMR, contrasting the former's assumptions about rationality, static models, and Pareto optimality with other ideas about social practices, dynamic models, and distributive justice respectively. Finally, the chapter concludes with some ideas for future research to address the collective action problems that AMR presents, arising from the findings and limitations noted above.

Part 1: Previous Applications of Collective Action Theory to AMR

Interdisciplinary research on AMR is flourishing. Within this burgeoning space, many scholars note that AMR presents a wide range of interlinked challenges that demand an even greater array of solutions (Hoffman and Outterson 2015; Rogers Van Katwyk, Giubilini, et al. 2020; Rogers Van Katwyk, Weldon, et al. 2020; Wernli et al. 2017). At minimum, prior research has identified at least five major governance challenges affecting AMR, as outlined in Chapter 1. These are 1. improving *access* to antimicrobials, diagnostic technologies, and alternative therapies; 2. enhancing *conservation* to preserve the effectiveness of existing antimicrobials for current and future generations (also known as antimicrobial stewardship); 3. spurring *innovation* for new antimicrobial agents, diagnostic technologies, and alternative therapies; and 4. bolstering global infection *prevention* measures. These governance challenges compound existing health inequities within and across populations (e.g., between high-income and low-income countries,

or between rural and urban populations), which must be recognized and addressed by any policy intervention. Thus, a fifth challenge, 5. the challenge of achieving *equity in policy responses*, represents a transversal issue that cuts across the first four (for a longer treatment of these five governance areas, see Weldon et al. [2022]).

Many AMR scholars have made a connection between collective action theory and these five social challenges affecting AMR (Padiyara, Inoue, and Sprenger 2018; Hoffman and Outterson 2015). Indeed, most acknowledge that some level of global cooperation and collective action is necessary to effectively address these interdependent dimensions of the problem. Beyond these acknowledgements, however, none have sought to systematically elucidate the many and various kinds of collective action problems that AMR presents. Instead, most AMR research applies collective action theory in one of three narrow ways.

First, some studies and reports outline and explain AMR governance challenges with indirect references to collective action theory (Wernli et al. 2017; Harbarth, Albrich, and Brun-Buisson 2002; Léger et al. 2021; Holmes et al. 2016; Weldon and Hoffman 2021; WHO 2015; IACG 2019; Wallinga, Rayner, and Lang 2015; Laxminarayan et al. 2020; Outterson 2005; Outterson et al. 2016). For example, the World Health Organization's Global Action Plan on AMR does not explicitly use the term "collective action problem". However, it nevertheless outlines various economic and political incentives that result in suboptimal investments in pharmaceuticals, while calling for "national and international multisectoral action and collaboration." (WHO 2015). In another example, Laxminarayan et al. (2020) discuss limited progress on global AMR commitments, noting that commitments are not translating into policy action (Laxminarayan et al. 2020). In the face of this inadequate action, the researchers note that global cooperation and coordination are necessary to address the different facets of AMR.

Finally, Eggleston et al. (2010) and Patel et al. (2023) refer to antimicrobials as ‘global public goods’, without fully defining a global public good or considering its relevance to collective action theory more broadly. Without explicitly linking AMR to collective action theory, these works use the vocabulary of collective action to describe the characteristics of certain problems. Thus, the theory becomes the sub-text, making it difficult to understand fully if or how it was applied to support certain conclusions.

In a similar vein, others make use of terminology from collective action theory to assert points without formal theoretical justification. They suggest that AMR represents a collective action problem in need of global cooperation without defining what a collective action problem is (Hoffman et al. 2015; Årdal et al. 2016; Baekkeskov et al. 2020; O’Neill 2016; OECD 2018; Outterson and Hoffman 2015; Minssen and Nordberg 2020; Padiyara, Inoue, and Sprenger 2018; Laxminarayan et al. 2013). For example, Outterson and Hoffman (2015) argue that conserving antimicrobial effectiveness represents a global collective action problem that will require financial support for some countries. Ardal et al. (2016) similarly argue that addressing AMR will require global collective action, particularly in the areas of access, responsible use, and innovation.

These references to collective action theory serve a purpose—they point to the potential relevance of the discourse and motivate the idea that global cooperation is needed. However, without fully clarifying what a collective action problem is and how these problems arise in AMR, the same works can cause confusion. Specifically, there is a tendency to conflate distinct concepts like coordination, cooperation, collaboration, and collective action (defined later in table 2.1). Furthermore, there is little explanation of the factors causing the collective action problems, their consequences, or theory-led solutions.

Finally, some works are over-specific in their reference to collective action theory. They argue that AMR requires collective action to address a "global common pool resource challenge" and avoid a potential "global tragedy of the commons" (Roope et al. 2019; Rogers Van Katwyk, Giubilini, et al. 2020; Harring and Krockow 2021; World Bank 2017; Moon, Røttingen, and Frenk 2017; Anomaly 2010; Baquero and Campos 2003; Dyar et al. 2016; Foster and Grundmann 2006; Porco et al. 2012; O'Brien et al. 2014; Andresen and Hoffman 2015; Woolhouse et al. 2015; Rushton 2015). For example, Roope et al. (2021), the World Bank (2018), and Rogers Van Katwyk et al. (2021) all define antimicrobial effectiveness as a common-pool resource. They proceed to argue that without effective collective action, the common pool of antimicrobial effectiveness will continue to be diminished. Roope et al. (2021) suggest that conceptualizing antimicrobial effectiveness as a common pool resource could enable a closer application of economic theories and methods to the problem of AMR. Meanwhile, Rogers Van Katwyk et al. (2021) argue that global attempts to manage the common pool resource of antimicrobial effectiveness can learn important lessons from climate governance.

While accurate, these works focus on the tragedy of the commons without fully defining other collective action problems. Thus, they risk reducing the multifaceted challenge of AMR to only the *conservation* of the common pool resource of antimicrobial effectiveness. Ultimately, these analyses overemphasize one narrow aspect of the problem at the expense of a more holistic and complete understanding. Doing so restricts the range of insights that can be developed and increases the likelihood of reinforcing existing path dependencies. A fuller range of AMR collective action problems can be identified, but this first requires a method to clarify, identify, and catalogue the different types of collective action problems that can arise during global cooperation problems.

Part 2: A Method to Analyze Collective Action Problems

Definitions for collective action

Beginning with a concrete definition of the concept, we develop a generic framework to identify and catalogue collective action problems. We then apply the framework to translate the governance challenges affecting AMR into a list of eight collective action problems (table 2.4).

We draw on Jager et al.'s (2020) recent work to define a collective action problem as:

> A scenario where some actors' short-term self-interests are inconsistent with longer-term collective interests. The inconsistency between individual and collective interests requires some actors to act against their short-term self-interest for the collective benefit to be achieved (Jagers et al. 2020).

The advantage of this definition is that it differentiates collective action problems from both the narrower concept of social dilemmas and the broader concept of cooperation problems. It further opens an opportunity to acknowledge that some collective action problems require coordination (i.e., aligning objectives and activities), while others require collaboration (i.e., substantive work toward a collective objective) (table 2.1; figure 2.1). We accept and endorse Jager et al.'s (2020) definition after considering how two seminal definitions of collective action problems can cause confusion by potentially conflating collective action problems with social dilemmas. After distinguishing collective action problems from social dilemmas and cooperation problems, we move on to consider another conceptual layer, namely, the difference between coordination and collaboration problems.

Table 2.1 Different Types of Cooperation Problems

Concept	**Definition**
Cooperation Problem	A problem that requires actors to work together toward a collective objective.

Collective Action Problem	A specific cooperation problem where some actors have short-term self-interests that conflict with longer-term collective interests.
Social Dilemma	A specific cooperation challenge where each actor has short-term interests that conflict with longer-term collective interests, regardless of what others do.
Coordination Problem	A specific cooperation problem that requires actors to align their objectives and activities. Depending on the distribution of costs associated with coordination, these problems can manifest as collective action problems.
Collaboration Problem	A specific cooperation problem that requires actors to work together on a joint activity. Collaboration problems are often collective action problems, as they usually require some actors to eschew their short-term interest in favour of the collective interest.

i. Social dilemmas, collective action problems, and cooperation problems

Many attribute the modern interest in collective action problems to Mancur Olson, who asserted that "rational, self-interested individuals will not act to achieve the common or group interest" (Olson 1965, 2). Elinor Ostrom, a prominent scholar of collective action problems, similarly suggested that if "each individual selects strategies based on a calculus that maximizes short-term material benefits to self, individuals will take actions that generate lower joint outcomes than could have been achieved" (Ostrom 2009, 1:186).[11] The problem with these seminal definitions, though, is that they can conflate collective action problems with social dilemmas.

A social dilemma is said to occur when:

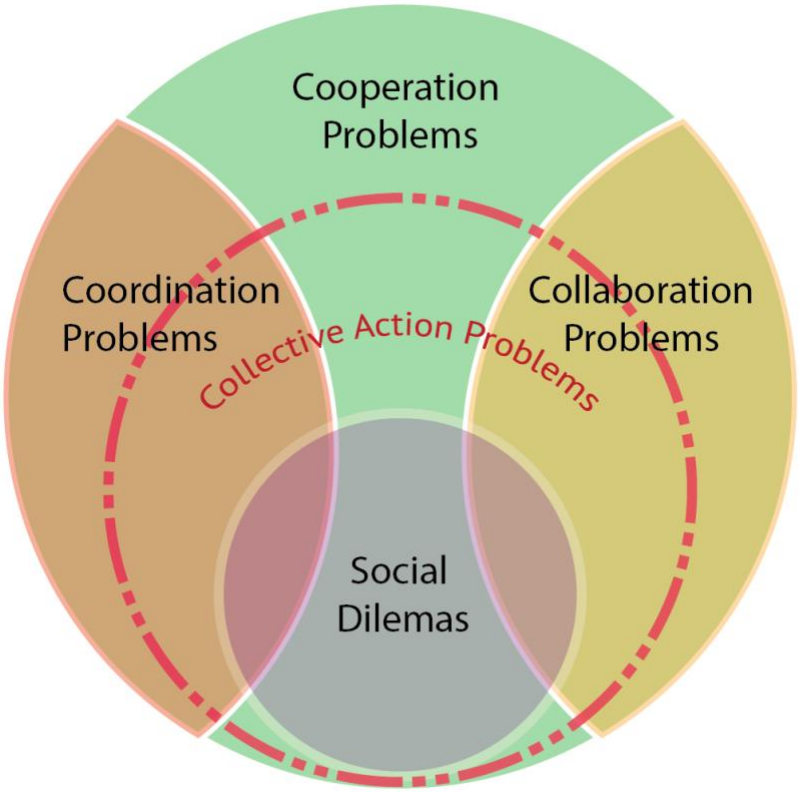
[11] Cooperation has been the subject of much social inquiry throughout history, and some classical and early modern thinkers even present formulations of collective action problems. For example, Aristotle, Cicero, Ibn Khaldun, Hobbes, Locke, Hume, and Rousseau all present scenarios that we would now call collective action problems (Skyrms 2004).

> "The payoff for **each** individual actor to act in self-interest (called *defecting*) is higher than the payoff for acting in the interest of the collective (called *cooperating*), **regardless of what others do**. And **all individual** actors receive a lower payoff if all defect than if all cooperate (R M Dawes 1980, 170)(R M Dawes 1980, 170)" (emphasis added)

The confusion arises because collective action problems are often defined without any specification about the number of actors who may have self-interests in conflict with the collective interest. Many researchers, including Olson and Ostrom, describe collective action problems as social dilemmas in that *all* actors have interests that conflict with the collective. However, collective action problems can arise where any combination of the three bolded conditions are not met for a true social dilemma. First, a situation may arise where only some actors have short-term interests that conflict with the collective interest.[12] Second, it is possible to conceive that certain actor interests will be shaped by what others do. For example, defecting away from a group of cooperators may make defection more costly than beneficial. Alternatively, defection by some can create a negative feedback loop incentivizing others to defect as well, which would then make cooperation more costly than beneficial. Finally, there can be a scenario where some actors benefit more from total defection than from total cooperation if cooperation imposes significant costs on them (an example here may be limiting carbon emissions). Essentially, this means that all social dilemmas are collective action problems, but not all collective action problems are social dilemmas (Jagers et al. 2020). In other words, social dilemmas are a subset of collective action problems.

[12] The term "some" is used in our definition to denote a subset of the N-number of actors involved and leaves open the possibility that "all" actors have interests in conflict since "all" is still one potential subset of the total N-number. Consider the difference between "some", which is used in the definition, and the statement "some, but not all", which is not used.

Figure 2.1: Cooperation Problems



The relationship between collective action problems and cooperation problems is easier to see. Specifically, collective action problems are an especially challenging type of cooperation problem. Where collective action problems are not carefully defined, however, there is a tendency to conflate terms, such as collective action and cooperation, and to use them interchangeably. This confusion arises because the term ‘collective action problem’ gives no clue to the extra element in its definition, which is the inconsistency between individual and collective rationality (Kollock 1998).

The defining challenge for collective action problems is that some actors will have to eschew their short-term self-interests in favour of longer-term collective interests. Otherwise, the collective is unlikely to find it easy or desirable to cooperate. The concept of ‘collective action

problems' loses its precision if one thinks that *all* cooperation problems are collective action problems. Rather, it is helpful to note that not all cooperation problems are collective action problems, since it is possible to have a situation where cooperation may be logistically challenging (perhaps due to numbers, funding, distance, etc.), but mutuality is present (Olson 1965; Barrett 2007). To see this, imagine a sports team where all members share a common objective of winning, but must find strategies by which to cooperate and achieve that objective together. This cooperation problem is not a collective action problem since all actor interests are aligned with the collective long-term interest.

ii. The distinction between coordination and collaboration within cooperation problems

Having explained the relationships between cooperation problems, collective action problems, and social dilemmas, it is helpful now to consider another conceptual plane that arises *within* cooperation problems. Stein (1983) differentiates between two types of cooperation problems where the conditions for cooperation are fundamentally different. These are coordination problems and collaboration problems (table 2.1; figure 2.1) (Stein 1982).

Coordination problems emerge when actors do not have a dominant strategy or a single preferred outcome, but all have a common interest in avoiding a mutually bad outcome. These problems are called 'problems of common aversion' that require coordination. Coordination is a mutually agreed-upon or imposed course of action that is not necessarily immediately the most preferred, but which prevents a mutually undesirable outcome. Coordination problems, therefore, typically require different strategies to address and can often be mitigated through information sharing and standard setting.

Coordination problems are cooperation problems, but they are not necessarily collective action problems. *However*, they can result in collective action problems. Specifically, a

collective action problem may arise in situations that require coordination when the costs of coordinating for some are higher than the immediate payoffs, such that their immediate self-interest is to not coordinate. For example, during international coordination problems, questions may arise about whose standards get universalized and which N-number of countries bear the cost to change their practices. In these situations, some, but not all, countries may face significant costs for coordinating.

In Stein's typology, collaboration problems are a type of collective action problem. Collaboration problems emerge "when independent decision making leads to equilibrium outcomes that are Pareto-deficient[13] in which all actors prefer another given outcome to the equilibrium outcome" (Stein 1982, 304).(Stein 1982, 304). These conditions mean that actors must jointly work together on an activity to achieve the mutually desired outcome and avoid the mutually undesired collective outcome. Unlike coordination, which simply denotes aligning, harmonization, or standard-setting, collaboration problems specifically require countries to work together, especially in productive ways (e.g., creating new rules, norms, and practices). This is a subtle, yet important difference if only to parse out coordination problems as potentially lower-hanging fruit for policy intervention, as coordination tends to be easier to achieve. Collaboration problems, on the other hand, are usually more difficult because the process of jointly producing or achieving something often requires that some actors eschew their short-term interests in favour of the long-term optimal collective outcome.

A framework of collective action problems

Building on our definitions, we develop a framework to analyze the collective action problems that arise around the use and provision of public goods and common-pool resources

[13] See footnote 1 in this chapter for a definition.

(figure 2.2) (Moon, Røttingen, and Frenk 2017; Kollock 1998). This framework enables us to distinguish between: (i) the type of good around which the collective action problem emerges (table 2.2.), (ii) the key question about use or provision at the heart of the collective action problem, (iii) the interests that actors have around that question, (iv) the collective action problem that those interests produce, and (v) whether the collective action problem requires coordination or collaboration.

iii. Different types of goods

The framework examines the distribution of interests that cause collective action problems around common-pool resources and public goods (table 2.2). In this conceptualization, common-pool resources and public goods are not themselves collective action problems, but goods around which collective action problems emerge. The main difference between public goods and common-pool resources is that collective action problems for public goods only arise around questions about how the public good is provided (e.g., who covers the cost of provision). Public goods are not depleted by use (e.g., information is a public good). For common pool resources, on the other hand, collective action problems emerge around both questions of how it gets provided *and* how it gets used (e.g., who gets what share of the resource) (figure 2.2). A summary of public goods and common goods can assist in understanding how collective action problems arise around these goods.

iv. Public goods

Public goods are non-excludable and non-rivalrous (table 2.2), meaning that actors cannot be prevented from using the good (non-excludable) and one actor's use of the resource does not detract from the abilities of others to also use the resource (non-rivalrous). Since a precondition for public goods is that one's use does not deplete the resource, 'who uses' a public

good is less of a concern. Instead, the focus for public goods is on ‘who provides’ them (Figure 2.2).

Table 2.2: Types of Goods

	Rivalrous	**Non-Rivalrous**
Excludable	Private goods (excludable and rivalrous)	Club -goods (excludable and non-rivalrous)
Non-Excludable	Common-pool resources (non-excludable and rivalrous)	Public goods (non-excludable and non-rivalrous)

As mentioned above, public goods are not themselves collective action problems. Instead, they are goods which require collective work to provide and maintain, such as laws, streetlights, and information. The provision of a public good becomes a problem of collective action when the action of some actors following their self-interests does not result in the provision of a necessary public good (Dougherty 2003).

The incentives that actors face when considering whether to cooperate for providing a public good can resemble different collective action problems, depending on the nature of the good. For example, if the provision of the public good only requires one or a small number of actors to volunteer, but volunteering imposes an individualized cost only on those who act, this situation is defined as “a volunteer’s dilemma”. In a volunteer’s dilemma, actors may be incentivised to wait as long as reasonably possible before volunteering with the hope that some other actor will pay the cost of providing the public good before they do. The volunteer’s

dilemma, as well as another three collective action problems for provision (i.e., ‘the public goods game’, ‘the weakest link problem’, and ‘the stag hunt’) are defined in table 2.3.

Sometimes, a public good gets provided by a single best effort, where an actor’s self-interest results in a behaviour that ends up providing the public good (Barrett 2007). For example, if a nation is threatened by an asteroid, a multi-billionaire or single country’s space program might provide a spacecraft to knock the asteroid off course. This example may still be conceptualized as a collective action problem, however, as the solution does not change the underlying scenario where the public good is only provided when one or a few actors choose to volunteer. Rather, it demonstrates that it is sometimes in a single or small group of actors’ best interests to act in a way that provides a public good.

v. Common-pool resources

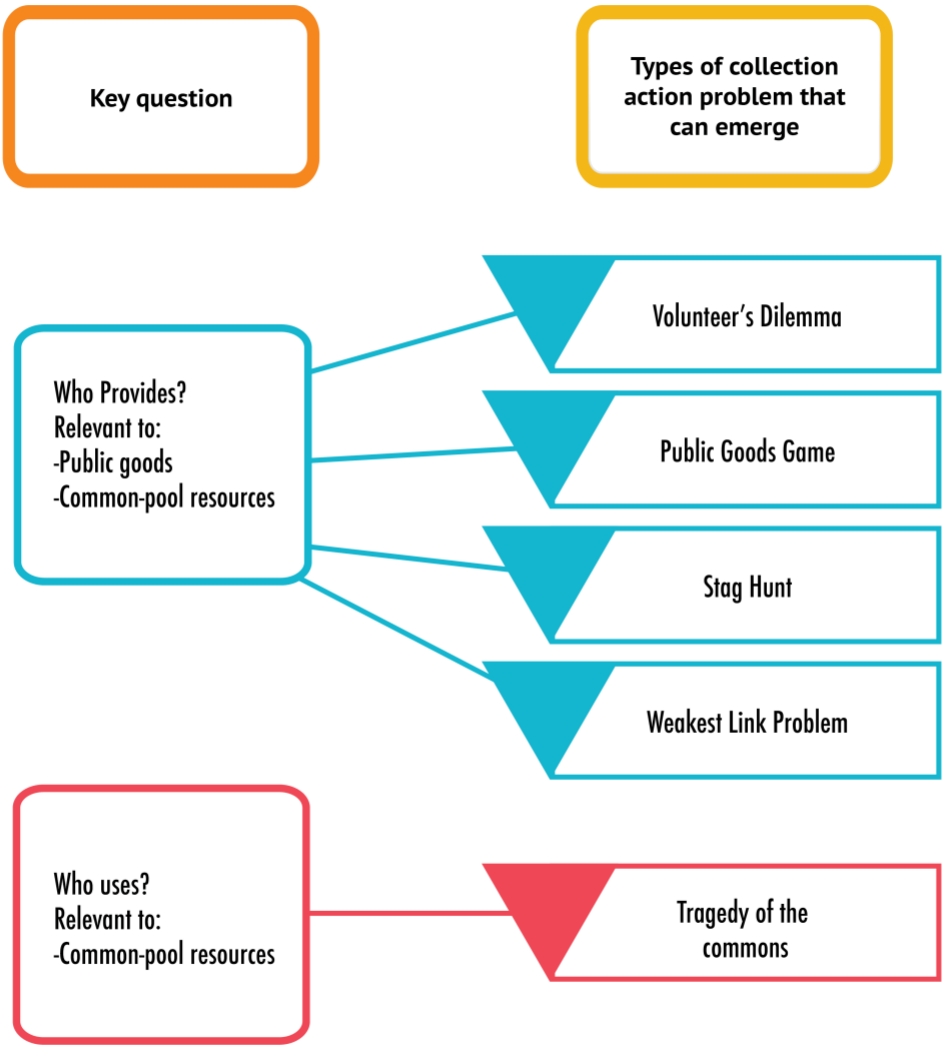
Common pool resources are non-excludable and rivalrous (table 2.2), meaning there are concerns for both ‘who provides’ and ‘who uses’ the resource (figure 2.2). Like public goods, variations of the same provision problems can all manifest around questions about the provision of common-pool resources (i.e., volunteer’s dilemmas, public goods games, weakest link problems, and stag hunts). But with an added level of concern for ‘who uses’ the common resource, additional collective action problems can arise. (Ostrom 1990). A typical example of a common pool resource is a pond or fishery that many people use, but which no one owns. The risk with common pool resources is that without sufficient measures to restrict use or replenish stock, overuse by any or all actors can deplete the overall supply. Specifically, this result in a collective action problem called ‘the tragedy of the commons’, which occurs when actors following their self-interests results in the overuse and depletion of the resource, obstructing the

collective interest of sustaining the resource's long-term viability for everyone's benefit (table 2.3) (Robyn M. Dawes 1975).

Table 2.3: Different Types of Collective Action Problems

Type of collective action problem	**Challenges for achieving the collective objective**
The Volunteer's Dilemma	The provision of the good or resource only requires one or a small number of actors to volunteer, but volunteering imposes a cost only on those who choose to act.
The Stag Hunt	The highly prized good or resource (i.e., the stag) is only provided if all actors cooperate fully. However, actors may choose to defect and receive a lower, but guaranteed, payoff (i.e., a hare).
The Public Goods Game	The good or resource is only provided insofar as individuals make contributions to the public pool, which is then augmented by some factor (a multiplier) and equally distributed to all regardless of how many or how much was contributed.
The Weakest Link Problem	The good or resource is only provided when all actors contribute above a minimum threshold, but some actors lack the means or motivation to contribute.
The Tragedy of the Commons	All actors have an incentive to over-use the resource, but if some (or all) choose to over-use, then the outcome is worse than if all (or an X number) had chosen to cooperate.

Figure 2.2: Collective Action Problems Around the Provision and Use of Shared Resources



vi. Interests and outcomes

In these various collective action problems, actors have interests that lead them to be indifferent, defect, or act against the common interest. Broadly, the interests can arise due to self-interested cost-benefit calculations, or alternatively, actors may miscalculate long-term costs and

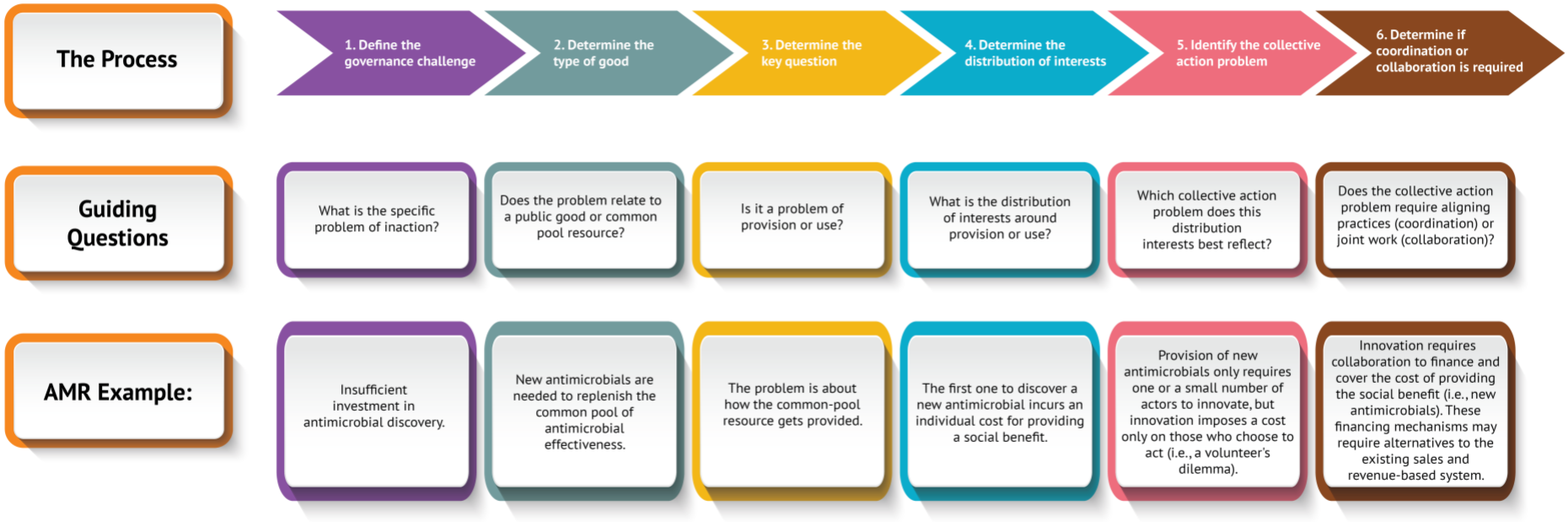
benefits at the time of decision.[14] The interests that actors face within collective action problems can be further distinguished from the outcomes that follow from self-interested behaviour. These potential outcomes include free riding and externalities (Hoffman et al. 2015). In most collective action problems, free riding appears when actors do not contribute but still benefit from the action of others. Meanwhile, negative externalities occur when the costs of using a resource are not immediately borne out by the user but are instead borne out by others in the collective (Kaier and Frank 2010). Recalling our earlier analogy of a depleting fishery, these externalities can be hidden for some time, and only come to a head when the resource is critically low. Positive externalities, on the other hand, occur when the benefits of using a resource are acquired beyond the resource's immediate users. Some examples of positive externalities include herd immunity from vaccination, or alternatively, infection prevention from good sanitation and hygiene practices.

A process to catalogue collective action problems

To evaluate which governance challenges constitute collective action problems, we begin by drawing on the five major governance challenges affecting AMR, elaborated more fully in our prior research (e.g., see Weldon et al. 2023). We then determine whether that governance challenge relates to a public good or a common-pool resource and ask whether it is a problem with the provision or use of that good. Next, we identify the distribution of interests around questions of provision or use. This allows us to assess which collective action problem the distribution of interests most closely resembles. Finally, we ask whether the problem requires coordination or collaboration (Figure 2.3) (Kollock 1998).

[14] Miscalculations are sometimes called "internalities" in behavioural economics.

Figure 2.3: A Process to Identify and Index Collective Action Problems



Part 3: AMR is a Series of Eight Interlinked Collective Action Problems

In applying our framework to AMR, there first emerged a few paradoxical considerations that may explain why some researchers have previously and inappropriately described antimicrobials as global public goods. The confusion arises because antimicrobial products *per se* are private goods for individual consumption (rivalrous and excludable), but the *antimicrobial effectiveness* of these products is a shared and finite common-pool resource (rivalrous and non-excludable) (Weldon et al. 2022). Simultaneously, effective antimicrobial products are essential to support good health and well-being for all, which can be conceptualized as a non-rivalrous and non-excludable global public good if achieved.[15]

Global AMR governance depends on the appropriate management of both common and public goods. With the clarity provided by our framework, we discuss the collective action problems that arise around the use and provision of these common pool resources and public goods for AMR governance. We consider three collective action problems for the common-pool resource of antimicrobial effectiveness, suggesting that if sufficiently managed, this common-pool resource can provide the same benefits as a global public good. Finally, we draw attention to two examples of collective action problems for the provision of other important global public goods, which must also be addressed to adequately mitigate the threat posed by AMR.

Ultimately, we found eight collective action problems for AMR around both common-pool resources and public goods (table 2.4). In addition to the much-discussed tragedy of the

[15] These paradoxical nuances highlight a potential limitation of collective action theory, where the ambition to create generalizable conclusions can obscure the complex social challenges that AMR presents.

antimicrobial commons, AMR also presents volunteer's dilemmas, weakest-link problems, and stag hunts.[16]

[16] Unfortunately, collective action theory's assumptions about optimized systems (i.e., 'Pareto Optimality') leave little room to consider the governance challenge of *equity* – a limitation further taken up in the proceeding section.

Table 2.4: Eight Collective Action Problems Affecting AMR Governance

The relevant AMR governance area	The governance problem	The type of good or resource	Key question: provision or use?	The interests that actors have	The collective action problem	Is coordination or collaboration required?
Conservation	Suboptimal *conservation* and subsequent overuse of antimicrobial effectiveness	The common-pool resource of antimicrobial effectiveness	Use	Negative externalities: the costs associated with use (of antimicrobials) are carried by the collective and not the user. Defection (from conservation efforts) results in a higher immediate payoff than cooperating. Free ride off others who conserve their use.	1. Tragedy of the commons	Collaboration
Innovation	Suboptimal investments in *innovation* for new antimicrobials to provide and replenish the common-pool resource	The common-pool resource of antimicrobial effectiveness	Provision	Wait for someone else to pay the costs associated with developing new antimicrobials. Free ride on the efforts of others.	2. Volunteer's dilemma	Collaboration

Access	Suboptimal provision of universal *access* to effective antimicrobials	The common-pool resource of antimicrobial effectiveness	Provision	Achieving access to antimicrobials for all requires establishing minimum thresholds for access everywhere, but some countries may not currently have the means to do so.	3. Weakest link problem	Collaboration
Prevention	Underinvestment in the provision of public AMR surveillance systems to support *prevention*	The public good of public and standardized surveillance for infectious disease and resistance spread	Provision	All countries have an interest in achieving global AMR surveillance, and global surveillance is only achieved if all contribute. But some are unable to contribute because of poor funding. There are unrealized positive externalities and wealthy states do not accurately assess the benefits of investing in surveillance capacities of lower-income countries.	4. Weakest Link Problem	Collaboration

Prevention	Suboptimal provision of coordinated AMR surveillance systems methods to support *prevention*	The public good of public and standardized surveillance for infectious disease and resistance spread	Provision	Defection offers a lower but certain payoff of local, but unstandardized surveillance whereas cooperation offers a higher payoff but imposes a cost to switch methods.	5. Stag Hunt	Coordination
Access	Suboptimal provision of universal *access* to diagnostic technologies and alternative therapies	The public good of diagnostic technologies and alternative therapies	Provision	Achieving access to diagnostic technologies could enable more accurate and precise antimicrobial prescribing, and access to alternative therapies could lessen the demand for antimicrobials. But achieving access for all requires establishing minimum thresholds for access everywhere. Some countries may currently lack the means to do so.	6. Weakest Link Problem	Collaboration
Innovation	Suboptimal investments in *innovation* to	The public good of health innovation	Provision	Wait for someone else to pay the costs associated with	7. Volunteer's dilemma	Collaboration

	provide surveillance, diagnostic technologies, and alternative therapies			developing these new technologies. Free ride on the efforts of others.		
Prevention	Suboptimal investments to provide global infection *prevention*	The public good of global infection prevention (global security from the threat of infectious disease)	Provision	All countries have an interest in improving infection prevention and global infection prevention is only achieved if all contribute because pathogens cross national borders. But some are unable to contribute because of a lack of funding. There are unrealized positive externalities and wealthy states do not accurately assess the benefits of investing in infection prevention in lower-income countries.	8. Weakest Link Problem	Collaboration

Conservation of, innovation for, and access to antimicrobial effectiveness

As previously noted, antimicrobial effectiveness resembles a non-excludable but rivalrous common-pool resource. Importantly, the common-pool resource of antimicrobial effectiveness is not itself a collective action problem. Rather, in applying the insights from collective action theory discussed above, there are three collective action problems that emerge around this resource: one related to how it gets used and two related to how it gets provided.

First, as well described in the literature, the *conservation* of antimicrobial effectiveness represents a tragedy of the commons scenario. In this scenario, actors (e.g., patients, farmers, and countries) face a choice to either cooperate and restrict their use of currently effective antimicrobials, or defect and use currently effective antimicrobials without restriction (Roope et al. 2019). Patients who are concerned about their health, farmers who are concerned about their yields and income, and countries that are concerned about their economy's productivity and competitiveness, may all be compelled by their individual rationality to defect and use as they please. But, if enough actors decide to defect and use antimicrobials without considering the collective interest of sustaining antimicrobial effectiveness, then the resource will diminish (O'Brien et al. 2014). Overcoming this collective action problem will require global collaboration to establish, implement, and enforce guidelines on antimicrobial use to ensure that the resource is sustained.

Second, there is a volunteer's dilemma around *innovation* for new antimicrobials to provide and replenish the common pool of antimicrobial effectiveness. While the tragedy of the commons is well-described for questions about use, the provision of the resource through innovation is often discussed only in terms of market failures. The current lack of innovation for new antimicrobials is indeed fuelled by many market failures (Outterson et al. 2016), but how

these market failures get addressed (e.g., through prizes or other push-pull incentives) become questions of collective action when reframed to ask who pays and who is responsible for enacting the required solutions. The collective action challenge for innovation arises because only one or a few countries or pharmaceutical firms need to pioneer the initiatives required to foster the innovation of new drugs. However, these initiatives impose a cost only on those who volunteer. Actors, therefore, are incentivised to wait as long as possible with the hope that someone else will pay to pioneer these socially beneficial initiatives. The governance challenge of overcoming this failure of the market to sustain innovation for new antimicrobials, therefore, may be better represented as a problem of coordination and collaboration for funding to overcome a volunteer's dilemma.

Third, there is a weakest link problem for providing *access* to the common pool resource of antimicrobial effectiveness. In a strict sense, common-pool resources must be available to everyone to be considered non-excludable. However, many around the world still do not have access to effective antimicrobials (Murray et al. 2022). Intellectual property law, for example, operates to transform non-excludable resources into excludable resources to incentivize innovation (Outterson 2005). Other existing global challenges, such as inabilities to pay for medicines, poor infrastructure to ensure their reliable supply and delivery, and prohibitive market entry laws, all restrict access to this precious resource (Årdal et al. 2016; Access to Medicine Foundation 2022). The persistent access gap means that antimicrobial effectiveness is, in our current reality, excludable.

This excludability means that the common-pool resource of antimicrobial effectiveness has not yet been sufficiently provided to all.[17] Establishing access to antimicrobials everywhere

[17] Another way to frame this argument is to consider "who is included in the global antimicrobial commons".

will require all countries to exceed a minimum threshold of access to effective antimicrobials for their populations (Årdal et al. 2016). Since not all countries have the means to do so, overcoming this weakest link problem will require wealthier countries to eschew their own self-interest and invest in the human and animal health care systems of other countries. Simultaneously, pharmaceutical firms may need to forgo some economic profits to ensure that this objective is met.

As the tragedy of the commons for *conservation*, the volunteer's dilemma for *innovation,* and the weakest link challenge for *access* all arise around the common pool of antimicrobial effectiveness, these three challenges are interdependent. For instance, imprudent access undermines conservation and squanders innovation; conservation constricts access and hinders innovation by shrinking already small markets; and innovation without conservation is wasteful, and without universal access is unjust (Hoffman and Outterson 2015).

But if all three collective action problems are sufficiently addressed, then the common-pool resource will essentially provide the same benefits as a global public good. For this to happen, everyone must have access to the resource so that it is truly non-excludable. Simultaneously, access must be sufficiently prudent, and innovation must be sufficiently steady such that the resource's rate of depletion does not exceed the rate of its supply. By reducing the rate at which the resource gets use, prevention measures improve the efficiency and ease of achieving sustainability (i.e., lower use = less resistance = longer-lasting drugs = less need for innovation to replace ineffective medicines). If these conditions are met, then antimicrobial use could become not very rivalrous, and the common resource could, in theory, operate like a public good.

The provision of public goods for AMR governance

Other AMR governance challenges are better classified as collective action problems related to the provision of public goods, not common-pool resources. Two examples that illustrate this point are infection prevention (Moon, Røttingen, and Frenk 2017) and global AMR surveillance (Chen, Evans, and Cash 1999). Global infection prevention and AMR surveillance have the potential to be global public goods if achieved, since they are both theoretically non-rivalrous and non-excludable. However, neither have been sufficiently provided due to ongoing collective action problems.

First, providing global infection prevention represents a weakest link challenge because to achieve it, all countries must have the minimum capacity to maintain infection prevention and control. A resistant pathogen can emerge anytime an antimicrobial is used, and microbes travel quickly in today's globalized world. This globally shared vulnerability means that the collective protection provided by global infection prevention requires collaboration to ensure that all countries can effectively prepare and respond to new outbreaks. Collective action theory suggests that overcoming this collective action problem to provide this global public good will require some countries to eschew their immediate interests (e.g., by investing more money in health-related infrastructure and capacity in other countries). Indeed, there are unrealized positive externalities for providing this global public good, where countries could acquire benefits from investing in better infection prevention and control measures beyond their borders.

Second, global AMR surveillance represents another potential global public good where information about resistance development, prevalence, and spread could provide non-excludable and non-rivalrous benefits to all by promoting more precise local and global responses. However, this potential global public good has not yet been provided sufficiently due to underinvestment and the privatization of data collection systems. Similar to prevention,

achieving global AMR surveillance represents a weakest link problem that will require every country to establish and maintain minimum capacities to track resistance. Achieving this goal, moreover, may require countries to act against their immediate interest and invest in the health care capacities of other countries.

The understanding that information from surveillance can be a global public good helps to situate the role of the World Health Organization and its efforts to provide global AMR surveillance through its Global Antimicrobial Resistance and Use Surveillance (GLASS) program. GLASS could transform global AMR surveillance into a public good if it is successfully brought what is now mostly private surveillance data on AMR into the global public domain.

The global public good of AMR surveillance data would be maximally effective and efficient if the global community achieved standardized metrics and reporting procedures under a harmonized grammar of data coding to enable global tracking and comparison. In working toward this common objective, however, global efforts for surveillance may encounter another collective action problem – a stag hunt around coordination. More specifically, key questions could arise about whose standards get universalized and who bears the cost of transitioning their data collection methods. If every country needs to adopt the same action for surveillance, but only some incur a cost to change their methods, then those countries may find compelling short-term benefits for defecting to their own traditional methods along the way.

Part 4: The Limits of Collective Action Theory and Directions for Future Research

Thus far, the chapter has explained how collective action theory can be more systemically applied to AMR governance research and elucidated eight distinct collective action problems that AMR presents. However, collective action theory has important limitations arising from three

core assumptions, which are not necessarily borne out in our normal, imperfect, and dynamic world**.** These assumptions are about rational choice, static systems, and Pareto efficiency. To further nuance the application of collective action theory to AMR, this section discusses these limitations and assumptions, contrasting them with ideas about social practices, dynamic systems, and distributive justice respectively.

Rationality

Most applications of collective action theory, including in AMR research, adopt a rational choice approach. Within this approach, it is thought that people, institutions, and countries behave as rational actors who make strategic calculations and choose from a menu of possible options the course of action that maximizes their utility goals. However, there is an abundance of both theoretical and empirical research that demonstrates that this assumption is rarely ever met in practice (Hertwig et al. 2004). In brief, actors often act sub-optimally or make mistakes because of informational constraints and ignore or forgo action that they know is in their best interest (Kahneman 1994).

Fundamentally, rational choice approaches try to explain human behaviour. Their outlook is that actors have interests, and they act to maximize those interests. Yet, another approach is to look at social practices. Where rational choice approaches suggest that actors calculate the costs and benefits associated with a range of options and then proceed with self-seeking behaviour, a social practices perspective suggests that human behaviour is guided by settled practices and acculturation to certain norms. Decisions are shaped by how people experience the world around them, not constant cost-benefit calculations based on an ever-present knowledge of what is desired and a constant strategic outlook to get it. Instead, social practice approaches suggest that decisions on how to act are mostly shaped by culture, norms, and ideologies. As DeMarrais and

Earle put it, “rational actor models are intuitively sensible starting points, but actors’ self-interest is modulated by levels of trust, past experience, perceived benefits, local circumstances, culture, and ideology.”

Whether one emphasizes the relative importance of interests or the social structures that modulate them will significantly affect the way the problem and needed solutions are understood. When investigating the problem of antimicrobial overuse, for example, a rational choice perspective might suggest that the problem is driven by calculative, self-seeking actors that do not face the true cost of their actions. These negative externalities skew their internal decision matrix toward consumption, even when it is not necessary. From this understanding, mechanisms that internalize the cost of the negative externality, such as taxes equal to the externality’s unpaid cost (i.e., “Pigouvian taxes"), are proposed solutions (Giubilini 2019; Hollis and Ahmed 2013). These solutions, it is presumed, are supported by the idea that if rationalistic actors faced the true cost of their consumption, then that new cost would alter their decision matrix and lead them to change their behaviour around antimicrobial use accordingly. However, when viewed from a social practices perspective, the incentives that actors face are less of a concern than the social structures that shape those incentives, and, as such, those structures, not actor action, become the target for policy intervention (Chandler 2019; Denyer Willis and Chandler 2019).

Static systems

Another set of challenges arises due to the static nature of most collective action models and interpretations. As they are often applied in AMR settings, collective action models suggest that actors have pre-defined and static interests. Furthermore, the rules of the game are also typically held constant in these models, meaning that the parameters of the model are also

assumed to be static. In this way, the models deployed in collective action theory are essentially like single snapshots in time, leaving collective action theory with no solid way to handle scenarios where the rules of the game change over time (Scoones et al. 2007). This assumption is especially controversial with increasing calls to adopt ecological and evolutionary perspectives to govern AMR as an enduring biological reality.

The question for collective action research is how to model dynamic systems that start out with one set of parameters, but then change to another set of parameters partway through after some event or threshold gets crossed (Scoones 1999). It would be akin to playing a game of chess that unexpectedly changes into a game of checkers and then into a game of backgammon without any indication or warning. Normally, with complex dynamic systems like AMR and climate change, the inclination is to simplify with models and heuristics to help understand the problem more intuitively, which then helps to strategize solutions. But such abstractions risk oversimplification, and collective action models, which are like snapshots in time, have limits. One outstanding challenge with dynamic complex problems like AMR is how to handle uncertainty around thresholds, tipping points, and new data that can change our understanding of the features of the problem in real-time (Scoones 1999; Ritchey 2011). Where collective action theory seeks to atomize discrete problems and simplify through abstraction, an alternative approach could involve a more holistic and system-wide perspective, which – while perhaps being less intuitively appealing – may be better adept at integrating complex and entangled dynamics.

Pareto optimality

Finally, collective action models often adopt a view of efficiency informed by Pareto optimality. Pareto optimality is defined as a distribution of outcomes where no one can be made

better off without making someone else worse off. Put differently, a system is said to be Pareto efficient if all possible goods are distributed to the maximum extent possible. Yet, crucially, Pareto optimality says nothing about the equity or fairness of that distribution. For example, a system that contains 10 goods and 2 actors is said to be equally Pareto efficient if one person has all 10 goods, leaving 0 for the other, as it is if both actors have 5 goods each. As such, when dealing with models that are informed by Pareto optimality, there needs to be an extra effort to move from an understanding of 'optimized' to an understanding of equitable distribution.

One helpful field on this matter is distributive justice (Nozick 1973). Research on distributive justice is not concerned with maximized distributions and optimized resources in the same way as economics; rather, it is concerned with the fair distribution of those resources. (Varian 1975). Questions about distributive justice nuance the discussion on responding to the incentive and payoff structures that collective action problems present and provide a way to think about the equity issues that cut across AMR governance challenges.

A distributive justice lens for AMR instructs us to look at fairness across three dimensions: 1) international (Caney 2001), 2) intergenerational (Barry 2017) and 3) inter-species (Morreale 2021). International distributive justice is about fairness across countries considering histories of exploitation and legacies of colonialism. For example, countries or people who have been historically denied antibiotics may have a claim to use them extensively in this generation, even if implications for the future are unclear. Meanwhile, intergenerational distributive justice is about balancing the need for effective drugs now (access in the present) with the needs of future generations (investing in new drugs and transformative social and economic practices in the long term). Finally, inter-species distributive justice is concerned with fairness across the various lifeforms implicated by AMR. The plethora of competing human-animal-environmental

priorities of AMR requires some sense of justice that weighs human needs against the needs of animals, plants, and the environment. Ultimately, across these three dimensions, distributive justice tells us that a scenario can arise where some interests should be prioritized ahead of others to achieve fairness.

Conclusion

Continuing to apply collective action theory to today's many urgent complex challenges remains an important and promising line of inquiry for better understanding them and their needed solutions. Specifically, a deeper engagement with collective action literature can nuance and sharpen our understanding of these challenges, including AMR. The framework we developed enabled us to categorize collective action problems based on the type of good around which they occur. By applying our framework to AMR, we found several collective action problems beyond those that arise around the common pool of antimicrobial effectiveness. Indeed, we deciphered a short-list of many other AMR collective action problems. In addition to a tragedy of the commons around antimicrobial use, AMR also presents a series of other collective action problems like volunteers' dilemmas, stag hunts, and weakest link problems - each with its own unique incentive structures and challenges. Future research on collective action could apply similar methods of reasoning to other complex problems.

Wherever collective action is used to inform policy, policymakers must consider the outstanding limitations of collective action theory. These limits require additional frameworks for research and practice when designing equitable governance institutions for dynamic and evolving threats like AMR. Despite these limitations, we contend that policymaking will be able to reach better-formulated solutions with a better understanding of the kinds of collective action challenges that AMR presents. Specifically, by enumerating a series of specific collective action

problems, future research could investigate other areas of global governance where these specific collective action problems occur and assess whether strategies or techniques mobilized to solve analogous collective action problems in those other settings can be translated into lessons to better govern AMR. With this concrete elaboration of the many types of collective problems for AMR, future research and policy should look for collective solutions that can transform these problems of collective inaction into collective solutions.

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Chapter 3: The Evolving Regime Complex for Antimicrobial Resistance Governance: The Role of Norms, Paradigms, and International Organizations

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This chapter builds on prior research published in *The Journal of Law, Medicine, and Ethics,* 2022, 50(S2), which was co-authored with Safaa Yaseen and Steven J. Hoffman. This chapter represents the original work of the author, including further insights, revisions, and expanded discussions that advance our understanding of the subject matter.

Chapter Abstract

Antimicrobial resistance (AMR) is a complex, intersectoral, and long-enduring problem, with no single global institution set to comprehensively govern it. Instead, global efforts for AMR are forming a decentralized array of multiple institutions with overlapping and sometimes conflicting principles, norms, rules, and procedures. This emerging "regime complex for AMR governance" is not surprising: the inherent complexity of contemporary global politics has produced regime complexes for many other problems, including climate change, biodiversity, and refugee governance. However, the rise of a regime complex for AMR governance raises several empirical and theoretical puzzles, and its future success remains uncertain. This chapter analyzes the regime complex for AMR and uses this case study to test the current state of regime complex theory, including its explanations for how and why regime complexes emerge. It finds that in addition to existing explanations on the role of structural, functional, and interest diversity, international organizations (IOs) can also contribute to the formation of regime complexes when new ideas compel them to forge strategic alliances across their existing areas of work. In the case of AMR, the emergence of One Health ideas provided IOs with a normative justification for integration and convergence on AMR, which contributed to the rise of the regime complex. Leveraging insights from regime complex theory, the chapter identifies strategies that can improve the prospects of global AMR governance. Whether the recent social mobilization around "One Health" will translate into actionable measures by states is yet to be seen.

Introduction

The threat of antimicrobial resistance (AMR) has been known for nearly as long as effective antimicrobial drugs and substances have been available (Podolsky 2018; Kirchhelle and Podolsky 2022). However, most global reports still indicate that not enough is being done to limit the emergence of drug-resistant microbes or curb the rising mortality and morbidity that they cause (Murray et al. 2022). Even after the development of a Global Action Plan in 2015 (WHO 2015), the adoption of a high-level UN General Assembly resolution in 2016 (United Nations 2016), and the completion of an Inter-Agency Coordination Group on AMR in 2019 (IACG 2019), governments still struggle to craft and fund comprehensive, coherent, and effective global governance mechanisms to mitigate and adapt to the risks of AMR (Weldon and Hoffman 2021).

The challenge for achieving these mechanisms is that AMR is a complex, intersectoral, and long-enduring problem, with no single global institution set to comprehensively govern it. Instead, global efforts for AMR are forming a decentralized array of multiple institutions with overlapping and sometimes conflicting principles, norms, rules, and procedures (Orsini, Morin, and Young 2013; Weldon, Yaseen, and Hoffman 2022). This 'regime complex for AMR governance' has emerged after decades of evolving attempts to govern the problem globally. But to date, these attempts have only produced piecemeal and discrete initiatives often bound by path-dependent institutional mandates in both international and domestic settings (Rogers Van Katwyk, Giubilini, et al. 2020). These numerous initiatives by industry, civil society, international organizations (IOs), and academic networks now form the regime complex's diffuse frontiers of activity (Figure 1) (Weldon, Yaseen, and Hoffman 2022; Wernli et al. 2022). Motivated by a variety of divergent interests across states and sectors of human activity, these

initiatives have evolved with overlapping and sometimes competing aims and scopes across human health, animal health, and agricultural sectors (Held et al. 2019; Kirchhelle 2020; 2018b; Podolsky 2018). Adding an additional layer of complexity to this emerging governance structure, these ongoing initiatives are and have been underpinned by an ever-evolving science around the problem of AMR and its needed solutions (Wallinga, Rayner, and Lang 2015; Wernli et al. 2017). For example, while recent advances have led to a greater appreciation for the problem's intersectoral nature, many uncertainties still exist regarding the extent to which reducing antimicrobial use in agriculture affects resistance rates in humans (Weese et al. 2022).

The formation of this regime complex is not surprising. Various forces have converged to produce regime complexes for many other problems, including climate change (Keohane and Victor 2011), biodiversity (Morin et al. 2017), and refugee governance (Betts 2013). However, the rise of a regime complex for AMR governance raises both empirical and theoretical puzzles. For instance, the growing influence of One Health principles (defined in box 3.1 and elaborated on later when discussing normative convergence in the regime complex) and the establishment of a Quadripartite Collaboration among the World Health Organization (WHO), Food and Agriculture Organization (FAO), World Organizations for Animal Health (WOAH), and United Nations Environment Programme (UNEP) signify a shifting composition of the regime complex for AMR governance. More specifically, One Health ideas have been used by the Quadripartite Collaboration to normatively justify integration and convergence on AMR. These developments raise questions about how IOs can leverage norms, act like entrepreneurs, and recast institutional configurations within regime complexes. Emanating from the increasingly adopted norm of One Health, a new 'logic of appropriateness' (March and Olsen 2011) for intersectoral action and planning has significantly shaped the regime complex's current form and its future prospects.

Yet, despite these evolutions, the future effectiveness and durability of this governance structure for AMR remain uncertain.

This chapter analyzes the regime complex for AMR governance and uses this case study to test specific claims of regime complex theory, including its explanations for how and why regime complexes emerge. In doing so, it reveals both similarities and differences in the rise of the regime complex for AMR governance when compared to the formation of other regime complexes. Most of the regime complex for AMR governance can be explained by core tenets of regime complex theory, including the AMR regime complex's decentralized array of loosely coupled, sometimes conflicting, but usually reinforcing characteristics (Keohane and Victor 2011). However, some unique features of the regime complex for AMR governance require a greater appreciation for the political agency of international organizations (IOs) and the importance of ideas than contemporary theory offers. In particular, the evolution of a Quadripartite Collaboration requires a better understanding of how ideas can influence IO policy and how IO policies can subsequently shape the evolution of regime complexes.

To achieve this understanding, the chapter applies a historical institutionalist lens to the history of global AMR governance efforts, informed by constructivist insights on the role of ideas. In doing so, it emphasizes the dynamic interaction of actors, institutions, and ideas within the context of structural and functional complexity. By adopting this approach, the chapter extends regime complex theory by considering the conditions under which IOs, guided by new ideas, are likely to drive and shape the evolution of regime complexes. It demonstrates that IOs can reshape regime complexes when new ideas compel them to forge strategic alliances across their existing areas of work.

Box 3.1: One Health

Essentially, a One Health approach takes a wide view to see how global problems cut across human, animal, and environmental sectors of activity. In doing so, it creates additional opportunities for addressing the dynamic causes of health challenges, which more siloed perspectives could otherwise miss. The development and spread of drug-resistant microbes is influenced by practices across different sectors, and resistant microbes spread easily across humans, animals, and the environment. It is often argued, therefore, that the many intersectoral drivers and consequences of AMR make One Health ideas especially pertinent for understanding and managing this issue.

Recently, a One Health High-level Panel defined One Health as

> *"an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals and ecosystems. It recognizes the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and inter-dependent. The approach mobilizes multiple sectors, disciplines and communities at varying levels of society to work together to foster well-being and tackle threats to health and ecosystems, while addressing the collective need for clean water, energy and air, safe and nutritious food, taking action on climate changes and contributing to sustainable development."* (FAO et al. 2021)

Part 1: Existing Regime Complex Theory: Structural, Functional, and Interest-Based Drivers of Complexity

Regime complexes are arrays of international regimes that have overlapping and conflicting principles, norms, rules, and procedures (Orsini, Morin, and Young 2013). Essentially, they are collections of interacting international institutions and actors. Theories of regime complex formation seek to explain why these international institutions and actors form decentralized and loosely coupled governance structures rather than centralized and hierarchical ones (Keohane and Victor 2011; Alter and Raustiala 2018). In this growing area of research, various scholars have employed different approaches to explain the emergence of regime complexes, reflecting the diverse ways to analyze institutions more generally (Gomez Mera 2020).

Theorists of regime complex formation emphasize the importance of various explanatory factors. For instance, some scholars have pointed to structural factors, including the proliferating number and scope of international rules and increasing actor density, as key drivers of regime complex evolution (Alter and Raustiala 2018; Alter and Meunier 2009). Others have emphasized functional factors, such as the need to address interlinked and interdependent challenges under conditions of uncertainty (Johnson and Urpelainen 2012). Others yet have highlighted interest-based factors, such as the pursuit of diverse initiatives guided by a variety of incentives in the context of global power imbalances (Benvenisti and Downs 2007).

In addition, institutional and normative factors have been identified as significant contributors to regime complex dynamics. Institutional factors refer to the role of IOs and other forms of institutionalized cooperation, which can facilitate or impede the coordination of actors and initiatives (Helfer 2009). Normative factors, meanwhile, relate to the shared beliefs, values, and expectations of actors involved in the regime complex, which can shape their behavior, decision-making procedures, and outcomes (Park 2021; Margulis 2013).

Many scholars draw on more than one of these factors to show how variables, such as increasing rule density (structural), uncertainty (functional), and linkages across problems and institutions (functional and institutional), can create incentives for actors (interest-based) to seek a diverse range of initiatives instead of a centralized regime (Keohane and Victor 2011).

While these generic explanatory factors are still relevant, the rise of the regime complex for AMR governance requires additional elaboration on the unique roles of IOs and ideas. Before Part 2 draws on historical institutionalism and constructivism to expand on these two areas, this first part of the chapter discusses the relevance of existing regime complex theory. Indeed, existing theory provides useful and pertinent explanations of the role of structural complexity,

functional complexity, and interest diversity in the rise of the regime complex for AMR governance.

Structural diversity

The regime complex for AMR governance, like all other regime complexes, emerged within a specific and historically contingent global political context, characterized by structural factors that tend to produce regime complexes (Lee and Brumme 2013; Spicer et al. 2020; Alter and Raustiala 2018). These factors include the proliferation of international rules, actors, and institutions, as well as the persistence of functionally interdependent global issues. Indeed, many scholars have emphasized these structural factors to explain the rise of other regime complexes. For example, Raustiala and Victor (2004) attribute the rise of the regime complex for plant genetic resources to the increasing depth and scope of international rules (Raustiala and Victor 2004). Meanwhile, Raustiala and Alter (2018) suggest that most regime complexes emerge due to structural and functional factors (2018). While noting that the process of regime complex formation can involve deliberate action, they argue that the broader political context of global governance makes the emergence of regime complexes almost inevitable.

Without centralized leadership and coordination under international anarchy, states and non-state actors independently devise strategies to safeguard their own health and security interests. Within this global political context, a growing number of actors and rules have emerged to address AMR along path-dependent trajectories (Wernli et al. 2022). First, the number of international actors engaged in AMR governance has increased in recent years. These include public-private partnerships, such as the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) and the Global Antibiotic Research and Development Partnership (GARDP), which aim to address funding and leadership gaps for antibiotic drug

development. They also include various global civil society groups like Action on Antibiotic Resistance (ReACT) and the Antibiotic Resistance Coalition (ARC), which seek to raise awareness and promote action on the issue (Figure 3.1).

Furthermore, many already established global institutions have recently started to prioritize AMR governance. For example, in launching the Global Health Security Agenda (GHSA) in 2015, a group of 44 states sought to expand action on AMR beyond the United Nations (UN) system (GHSA 2015). That year, these states committed to address the threat of AMR and protect the effectiveness of medical countermeasures such as antimicrobials. The G7 also promised to improve funding for antimicrobial access, conservation, and innovation in their 2016 Ise-Shima Vision for Global Health (G7 2016). Later in 2017, the G20 identified AMR as a key area of focus in their efforts to promote economic and human development (Figure 3.1) (G20 2017).

In addition to a growing number of actors, the number of rules applicable to AMR in international legal realms has also recently increased (Table 3.1, Column 4). Existing trade, environmental, and health agreements are increasingly recognized as contributing directly or indirectly to AMR governance (Rogers Van Katwyk, Weldon, et al. 2020; Morin and Blouin 2019). As a result, several international agreements have emerged as key features of the AMR regime complex, governing the surveillance of AMR, as well as the development, production, distribution, use, and disposal of antimicrobial products (WHO, FAO, and WOAH 2020).

The 2005 revision of the International Health Regulations (IHR), for example, has many provisions that are relevant to AMR governance (Wernli et al. 2011; Rogers Van Katwyk, Weldon, et al. 2020). Specifically, IHR Articles 5, 6 and 8 stipulate that states must maintain the core capacities needed to monitor and report public health outbreaks (WHO 2005b). Further to

these articles, WHO confirmed in 2014 that "the capacity to perform antimicrobial susceptibility testing, which can inform surveillance of AMR, also falls within the scope of the IHR" (World Health Organization 2014, XIX) (Table 3.1). Indeed, the IHR were used by the government of the United Kingdom in 2018 to determine the international threat of a multi-drug resistant gonorrhea detected in the country. Although it was not declared a public health emergency of international concern (PHEIC), the international community was promptly notified of the incident and information was shared between the UK and the country where the infection was acquired via the mechanisms set out in the IHR.

Beyond existing health agreements, trade agreements, such as the Agreements on the Trade-Related Aspects of Intellectual Property (TRIPs), the Agreement on the Application of Sanitary and Phytosanitary Measures (SPS), and the Agreement on the Technical Barriers to Trade (TBT), all help to structure the global system of drug development and distribution (Rogers Van Katwyk, Weldon, et al. 2020). [18] However, this system, which is based in market logics of rationality, has previously clashed with other objectives in the regime complex. For example, various market failures plague the innovation pipeline for new medical countermeasures like antimicrobial drugs.

Examples of these market failures include the low market value of antimicrobial products, which do not reflect their high use values, such as promoting human health and agricultural productivity. The low market value of antimicrobial products signals to pharmaceuticals firms that new drugs are unworthy investments. Consequently, these firms

[18] Given the human health threat posed by drug-resistant infections, the SPS and TBT enable countries to set and enforce trade rules that prevent antimicrobial products or products made with antimicrobials from entering their domestic markets. More recently, a review committee of TBT determined that the increasing threat that AMR poses to cross-border trade will require stronger guidelines for applying the SPS and TBT to regulate the movement of antimicrobial products across political boundaries.

underinvest in antimicrobial research and development, leading to the under provision of new and socially valuable medicines (Outterson et al. 2016). [19] This under provision, in turn, inhibits other social objectives, such as universal access to medicine as a human right (Motari et al. 2021; Mercurio 2017).

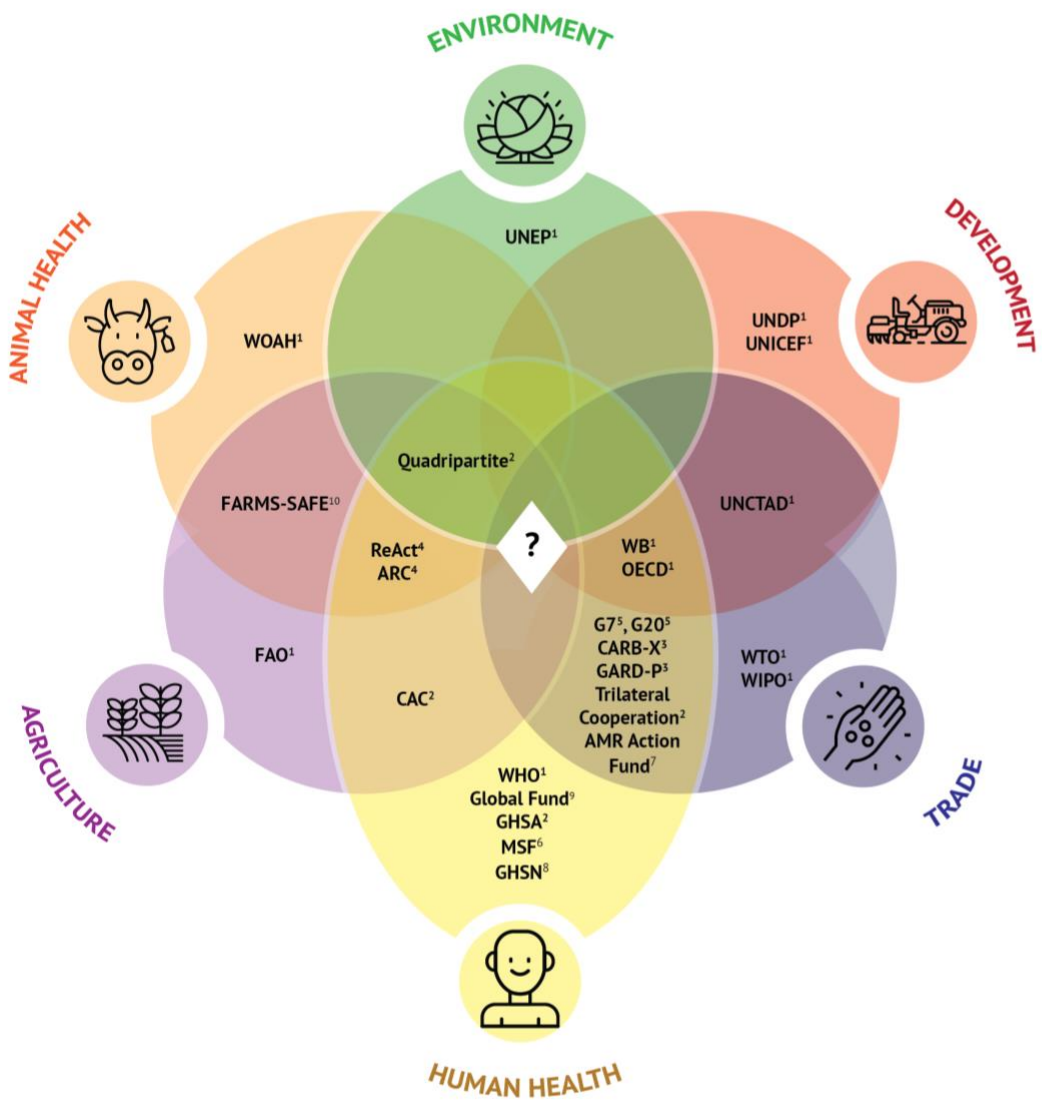
To address these challenges, non-market mechanisms such as public-private-partnerships and fully public options are gaining recognition, including CARB-X and GARD-P. Specifically, these mechanisms can implement push and pull incentives for new antimicrobial drugs. Studies by Outterson et al. (2016), Simpkin et al. (2017), and Singer, Kirchhelle, and Roberts (2020) all highlight the importance and potential of these non-market approaches.

Third, these new actors and rules governing AMR have emerged along path-dependent trajectories and within a densely populated global political arena. As Raustiala and Alter (2018) argue, the prevailing condition of international anarchy, under which all regime complexes emerge, means that new and old rules, institutions, and actors coexist in a non-hierarchical manner. This condition, moreover, results in a complex legal landscape where global problems are governed by a suite of formal and informal agreements. So, while the adoption of a Global Action Plan on AMR in 2015 and a UN resolution in 2016 marked important milestones in the global governance of AMR, they did not automatically displace existing agreements. Older rules and norms and continue to shape AMR governance. The international legal landscape for AMR now contains many agreements, all with varying degrees of relevancy, comprehensiveness,

[19] The contradiction between the high use value and low exchange value of antimicrobials is but one market failure affecting antibiotic research and development. Pharmaceutical production, especially for drugs like antibiotics, resembles a natural monopoly with high fixed costs (initial investments for research and development), but low and declining marginal costs of production (each additional unit of production usually costs only "pennies per pill"). Other industries that resemble natural monopolies include telecommunications, software, and what we know now as 'public utilities' like tap water and electrical grids. Industries of this nature tend to confer significant first-mover advantages and monopoly pricing power, resulting in market failures from sub-optimal market competition.

bindingness, and enforceability (Ruckert et al. 2020; Rogers Van Katwyk, Weldon, et al. 2020; WHO, FAO, and WOAH 2020) (Table 3.1; Column 4).

Figure 3.1: Key Global AMR Actors Mapped Across Sectors



Key Actors for AMR Governance

- ARC: Antimicrobial Resistance Coalition
- CAC: Codex Alimentarius Commission
- CARB-X: The Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator
- FAO: Food and Agriculture Organization
- ARC: Antimicrobial Resistance Coalition
- GARD-P: The Global Antibiotic Research & Development Partnership
- GHSA: Global Health Security Agenda
- GHSN: Global Health Security Network
- Global Fund: The Global Fund to fight AIDS, Tuberculosis, and Malaria
- MSF: Médecins Sans Frontières
- OECD: Organization for Economic Cooperation and Development
- Trilateral Cooperation: Trilateral Cooperation on Public Health, Intellectual Property and Trade
- Quadripartite: Quadripartite Collaboration of the World Health Organization, Food and Agriculture Organization, World Organization for Animal Health, and United Nations Environment Programme
- ReACT: Action for Antimcrobial Resistance
- UNCTAD: United Nations Conference on Trade and Development
- UNDP: United Nations Development Programme
- UNEP: United Nations Environment Programme
- UNICEF: United Nations Children's Fund
- WB: World Bank
- WHO: World Health Organization
- WOAH: World Organization for Animal Health
- WTO: World Trade Organization
- WIPO: World Intellectual Property Organization

Types of actors for AMR governance

1. Intergovernmental organization
2. International coalition or task force
3. Public-private-partnership
4. Global civil society
5. Intergovernmental forum
6. Independent, self-governed, non-profit organization
7. Public-private-partnership
8. Academic/research network
9. International financing institution
10. Research centre

Table 3.1: The Anatomy of the Regime Complex for AMR Governance

Elemental Regimes in Regime Complex for AMR governance	Principles	Norms	Rules	Procedures
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);	• Multilateral decision making at WHA; • IHR Annex 2 on the reporting and declaration of a Public Health Emergency of International Concern (PHEIC).

			• Reserve new and critically important antimicrobials for human use only.	
Humanitarian Biomedicine	• Access to essential medicines including effective antimicrobials is a human right; • Human suffering can be alleviated with bio medication intervention; • Human suffering demands 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); • Health for all; • Human right to health; • 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; • Médecine Sans Frontiers (MSF); • International Committee of the Red Cross (ICRC).
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; • Sanitary and phytosanitary measures (SPS) of the World Trade Organization (WTO);	• Multilateral decision making at WOAH.

			• Terrestrial Animal Health Code; • Aquatic Animal Health Code; • Manual of Diagnostic Tests for Aquatic Animals; • Manual of Diagnostic Tests and Vaccines for Terrestrial Animals.	
Agriculture	• Food security and food justice demand that all people have physical and economic access to safe and nutrition food; • Antimicrobials are an important tool that can promote food security.	• Food systems should be sustainable, productive, and efficient; • Promotion of human, animal, 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 FAO.
Trade	• Intellectual Property rights promote progress and innovation, including	• Free trade and global capital flows;	• The Agreement on Trade-Related Aspects of Intellectual Property	• Ministerial Meetings;

	for novel antimicrobials and therapies; • Free and unrestricted trade contributes to health; • Non-discrimination in trade.	• State sovereignty and enshrined right to protect human health; • Measures to reach other policy objectives should minimize impact on trade; • Private property rights.	Rights (TRIPS) of the WTO; • The Agreement on the Application of Sanitary and Phytosanitary Measures (SPS); • The Agreement on Technical Barriers to Trade (TBT)	• WTO Dispute resolution mechanisms; • Voluntary and compulsory licensing.
Development	• Access to medicine including effective antibiotics is a human right; • Development depends upon access to certain health rights; • Development improves health and health security.	• Health for all is crucial for generating and improving labor markets; • Sustainable development and SDGs; • State sovereignty over natural resources.	• Convention on Biological Diversity (CBD) and its Nagoya Protocol on Access and Benefit Sharing; • United Nations Conference for Trade and Development BioTrade Initiative;	• CBD Conference of the Parties; • United Nations Development Programme.
Environment	• Environmental health is essential for human health; • Common but differentiated responsibilities;	• Sustainable Development; • Precautionary principles to potential degradation; • Benefits from biodiversity and	• 1000s of Multilateral Agreements (MEAs); • Some MEAs are focused on specific species, e.g., the 1946 Convention on Whaling and the 1979 Bonn Convention on the	• Multilateral decision making through the UNEP.

• AMR in environment poses risks to environmental and human health.	environmental conservation should be shared; • Universal access to basic and common biological and plant genetic resources; • State Sovereignty.	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 UNEP.

Principles = beliefs of fact, causation, and rectitude

Norms = standards of behaviour defined in terms of rights and obligations

Rules = specific prescriptions or proscriptions for action

Procedures = prevailing practices for making and implementing collective choice

As a result of these persistent structural factors, there are significant leadership and governance gaps, redundancies, and overlaps (Rochford et al. 2018). New actors, such as those mentioned earlier, are emerging to fill these gaps (Figure 3.1). However, the structural complexity of contemporary politics means that these new actors are influenced by, and must subsequently navigate, the complex web of existing actors and institutional arrangements. The high costs associated with dismantling older institutions further leads to accretion and increasing density (Gómez-Mera, Morin, and Van de Graaf 2020).

Given the increasing structural complexity of global politics, it is difficult to create comprehensive arrangements that can unite the growing number of actors and rules for AMR, especially as AMR is a complex problem with diverse understandings and needed solutions.

Problem diversity

Indeed, the complexity of AMR has also contributed to the emergence of this regime complex. As the functionalist argument goes, states craft international institutions to enhance cooperation around shared challenges by, among other things, lower their transaction costs. When problems are complex, however, they can become difficult to manage through a single institution (Gomez Mera 2020; Keohane and Victor 2011). Scholars have previously demonstrated that a problem's functional complexity contributes to the formation of a regime complex around it. For example, in their analysis of the regime complex for climate governance, Keohane and Victor (2011) demonstrate how the inherent complexity of climate change makes a single institutional response to its many facets unfeasible, especially when a variety of actors have divergent interests for each facet of the problem.

Similar obstacles can be observed in AMR governance. To help simplify the complex problem, Chapter 1 identified five critical challenges affecting AMR governance, which are mutually interdependent (Weldon, Liddell, et al. 2022). These are:

1. improving *access* to antimicrobials, diagnostic technologies, and alternative therapies,
2. enhancing *conservation* to preserve the effectiveness of existing and future antimicrobials,
3. spurring *innovation* for new antimicrobials, diagnostic technologies, and alternative therapies,
4. bolstering global infection *prevention* measures to reduce the need for antimicrobials, and
5. achieving *equity* within and through policy interventions across the first four challenges (Weldon, Liddell, et al. 2022).

These five governance areas, moreover, present several cooperation problems that require an array of collective solutions, as described in Chapter 2. Any attempt to address AMR comprehensively must generate political strategies to overcome global collaboration and coordination problems, including a volunteer's dilemma for innovating new antimicrobials, a tragedy of the commons around their use and conservation, and a weakest link challenge for providing universal global access to antimicrobials, diagnostic technologies, and alternative therapies everywhere.

In other words, AMR is a multifaceted problem with distinct but interlinked challenges, each with its own unique incentives for actors to cooperate or not. Many of these facets, moreover, fall under various institutional remits across sectors and scales of activity. As with climate change, the complexity of AMR and its many possible interpretations has also created an opportunity for multiple competing interests for different actors, such as states, patients, and

farmers (Kirchhelle 2018a; Weese et al. 2022; Held et al. 2019). In turn, the varied distributions of interests, power, and needs around AMR governance have led to selective engagement with some aspects of the problem, producing diffuse and diverse initiatives rather than comprehensive ones (Spencer et al. 2019).

Interest diversity

Thus, the emergence of a regime complex for AMR governance can also be attributed to the lack of sufficiently similar interests among key states and actors to establish a comprehensive regime. At first, it may seem counterintuitive for states to prefer fragmented and decentralized governance arrangements when comprehensive ones promise greater efficiency. However, it is important to recall that regime complexes are never entirely the result of deliberate action. Rather, their formation involves structural forces, which constrain deliberate action over time (Gomez Mera 2020; Alter and Raustiala 2018). Within the current structure of contemporary politics, moreover, some states may face incentives that lead them to prefer complexity, and their deliberate actions can contribute to the formation of decentralized regime complexes. For example, states may prefer institutions with limited scopes when the potential gains from comprehensive arrangements are marginal or uncertain and the costs of transforming their behaviour is high (Rabitz 2018). Alternatively, some states may prefer fragmentation because the lack of centralized mechanisms augments their power (e.g., in the absence of centralized accountability mechanisms) (Benvenisti and Downs 2007).

For AMR, the existence of divergent interests has led groups of states and non-state actors to pursue separate initiatives. These discrete efforts, as discussed below, has led to the creation of the diffuse system that now constitutes the regime complex. This phenomenon is facilitated, in part, by the functional complexity of AMR – where the issues' far-reaching nature

can be interpreted differently depending on time and place. Consequently, divergent interests have emerged, contributing to the selective pursuit of specific initiatives within the complex (Held et al. 2019; Spencer et al. 2019).

More specifically, competing interests in the context of a limited supply of effective antimicrobials, and unequal distributions of access, needs, and power, have prevented a centralized regime. Antimicrobials have been crucial for supporting health, agriculture, and labour productivity over the past century (Chandler 2019; Kirchhelle 2018a). Given their profound impacts and benefits, antimicrobials are among humanity's greatest discoveries. But these benefits are not and have not been equally enjoyed by all. Instead, since antimicrobial medicines were first produced on an industrial scale during World War II, they have proven to be a great advantage only for those who have access to them (Ramanan Laxminarayan et al. 2016; Swann 1983). With concerns for curbing antimicrobial use to conserve effectiveness for current and future generations now mounting, debates about the ethical distribution of burdens and benefits for AMR are reminiscent of 'the green debates' about sustainable development.

High-income countries (HICs) have historically benefitted the most from antimicrobials, while many middle-income countries (MICs) and low-income countries (LICs) have yet to benefit to the same extent (Årdal et al. 2016). The most recent reports documenting antimicrobial consumption highlight a shift in global consumption patterns, with consumption rates accelerating fastest in MICs (Van Boeckel et al. 2015). But with HICs now prioritizing the need for restricting use to conserve antimicrobial effectiveness and promoting policies focused on education (Kirchhelle et al. 2020; Overton et al. 2021), it can easily appear as though they are 'kicking away the antimicrobial ladder' while reproducing colonial-era paternalism.

For example, an ongoing challenge in global health is that HICs can easily convene and fund global policy summits that are not necessarily representative of all voices, set priorities for global programs and initiatives at these summits, invest in research and development according to their own needs, and pioneer global regulations that reflect their interests and concerns (Büyüm et al. 2020; Phelan 2023; Karunakara 2021; Fukuda-Parr, Buss, and Ely Yamin 2021). For AMR, HICs tend to prioritize conservation efforts in domestic settings by restricting overuse and inappropriate use. These efforts translate into an emphasis on conservation in global discourses, even though conservation is not necessarily the top priority in other settings (Overton et al. 2021).

Many MICs, for instance, have different interests and needs. Some MICs have recently pushed back against conservation-focused efforts, emphasizing the importance of continued access to antimicrobials and the intellectual property rights associated with antimicrobial innovation and discovery (Pokharel, Raut, and Adhikari 2019). Other MICs, including India, have prioritized investments in drug development, while also crafting policies to subsidize the growing cost of antimicrobials to improve affordability and access. In the context of shifting power relations, yet other MICs have emphasized the importance of antimicrobials for protecting and fostering their nascent industries. Brazil, for example, has highlighted the important role that antimicrobials play in promoting its evolving animal agriculture industry, while suggesting that it would not participate in global efforts that threaten this sector (Held et al. 2019).

The situation that low-income countries (LICs) face is far more serious (R. Laxminarayan and Heymann 2012). Many LICs face a paradoxical triple burden of high infectious disease, poor access to antimicrobials, and high burdens of AMR-related mortality and morbidity (Murray et al. 2022). Compounding these challenges, LICs are often the most limited in their ability to

influence international negotiations and political outcomes. For example, resource constraints often prevent LICs from sending lawyers and delegations to multiple and simultaneous legal negotiations (Dentico and Naik 2022; Hoffman 2012). In this context, LICs identify priorities such as strengthening health infrastructure for access to antimicrobials, diagnostic technologies, and primary care, as well as improving sanitation and hygiene practices to prevent infectious disease prevalence (Raut and Adhikari 2016; Berman et al. 2022). Measures to improve market entry and supply chains for antimicrobials access have also been identified as key concerns for many LICs (Access to Medicine Foundation 2022). This is not to say that LICs do not recognize the importance of antimicrobial stewardship. Rather, they emphasize the immediate and numerous lives that can be saved with better access to effective drugs and infection prevention measures. These aims are not only crucial for mitigating global resistance but also for protecting the health and well-being of millions of people around the world (Ranjalkar and Chandy 2019; Berman et al. 2022).

Overlaying these interests across states, divergent interests across sectors have also prevented the emergence of a unified governance structure. For example, in human health settings, antimicrobials are essential for treating infections and enabling live-saving treatments like chemotherapy and surgery (Rogers Van Katwyk et al. 2019). The crucial role that they play in supporting human health has generated identifiable interests within that sector. Primarily, these interests revolve around access, conservation, and innovation for antimicrobials to protect human health. These interests manifest in rules that restrict new and critically important antimicrobials for human use only (WHO 2017). But reserving human-only classes of antimicrobials can conflict with important interests within animal health and agricultural sectors, where antimicrobials are used to improve yields and productivity to feed more people with less

energy, space, and costs (Weese et al. 2022; Kirchhelle 2018a). Thus, curbing antimicrobial use in agricultural settings in favour of human health interests can potentially undermine food security, which also has human health implications (Chien 2013). Agricultural settings in lower- and middle-income countries, moreover, often face resource constraints that make it difficult to replace antimicrobials with other measures – meaning that their food systems are at a higher risk of insecurity without antimicrobial access (Weese et al. 2022).

The distribution of interests across states and sectors has made it difficult to achieve a unified regime for AMR, especially since AMR is such a complex problem. This distribution of interests has led smaller groups of states and non-state actors to selectively engage with some aspects of the challenge and pursue discrete initiatives to suit their needs (Spencer et al. 2019). Moreover, the simultaneous and interdependent challenges posed by AMR, including expanding access while conserving effectiveness, highlight difficult trade-offs that can create conflicting interests across states and sectors (Hoffman et al. 2015). The human health sector in HICs, for example, have different interests and needs than small and medium-scale farmers in MICs, even though both depend upon the same pillar of sustained antimicrobial effectiveness.

Part 2: Advancing the Role of IOs and Ideas in Regime Complex Theory

As much of contemporary regime complex theory suggests, the anarchical structure of contemporary global politics, the functional complexity of the problem, and the absence of common state interests for a comprehensive regime all help to explain the emergence of the regime complex for AMR governance. But these three forces also converged to create an opportunity for IOs, including the WHO, FAO, WOAH, and UNEP, to shape the regime complex in a way that is unpredicted by existing explanations.

More specifically, existing theory suggests that the existence of multiple and often competing interests and ideas among states contributes to the emergence of regime complexes. What the regime complex for AMR governance reveals, however, is that a process of social convergence around a single idea prompted various IOs to form linkages across their areas of work, thereby contributing to meaningful changes in the regime complex. Building on existing regime complex theory, this section provides a framework to elaborate on how the norm of "One Health" influenced the regime-shaping work of WHO, FAO, WOAH, and UNEP.

The Agency of IOs

First, while many scholars generally accept that regime complex formation can result from deliberate action – although they differ on the relative importance of such agency versus the structure of global politics (e.g., see Keohane and Victor 2011 and Alter and Raustiala 2018) – scholars often reserve the concept of agency for states and their elite representatives with the power to influence international negotiations. For instance, Alter and Meunier (2009) argue that institutional interactions within regime complexes are largely driven by states and their representatives.

In contrast with this narrower conception of agency, some researchers have recently demonstrated that IOs can play important political roles within regime complexes (Gomez Mera 2020). Indeed, as Margulis (2021) notes, there is substantial evidence demonstrating that IOs have the capacity to operate as independent political actors, which regime complex theory has largely ignored.

In addressing this lacuna, many recent studies have shown how IOs often exercise agency to pursue their interests and political objectives within regime complexes. For example, Gómez-Mera (2020) demonstrates how representatives of "the International Labor Organization (ILO)

and the United Nations Office for the High Commissioner for Human Rights (OHCHR) used regime shifting and forum-linking strategies to promote norms and reframe issues" (Gomez Mera 2020, 20). Margulis (2021) further shows how the World Food Programme (WFP), OHCHR, and FAO sought to influence decision-making at the WTO, "to ensure that international trade rules did not undermine world food security and efforts to combat hunger" (Margulis 2021, 873). Others show how IOs can contribute to regime complexity when they establish and promote linkages with subsidiary organizations (Johnson 2014; Jinnah 2011; Gómez-Mera 2016). Finally, Morse and Keohane (2014) and Held (2019) demonstrate international organizations can contribute to regime complex formation when they seek to expand their influence beyond their traditional areas of work. For example, the World Bank started expanding its scope into matters of global health throughout the 1990s (Einhorn 2001; Held et al. 2019; Morse and Keohane 2014). Thus, IOs are not just structural components of regime complexes (e.g., arenas and forums for state interaction), rather, they operate in many ways as political actors, capable of exercising agency and influencing outcomes in global politics.

The role of ideas

Second, existing regime complex theory contains limited scholarship on the influence of new and emerging ideas during the evolution of regime complexes. Instead, normative factors, such as the role of ideas, are often established as contextual variables, and are frequently investigated only insofar as they affect the actions of states. For example, Keohane and Victor (2011) and Morin and Orsini (2016) all show how uncertainty can lead to divergent ideas and interests among states, resulting in competing perceptions of the issue at hand and potential solutions (Morin and Orsini 2013; Orsini, Morin, and Young 2013; Keohane and Victor 2011). As previously noted, such competition contributed to the rise of a regime complex for AMR

governance. However, existing regime complex theory fails to provide a framework for investigating how new ideas shape IO action, and, in the case of AMR governance, how a new idea transformed the regime complex.

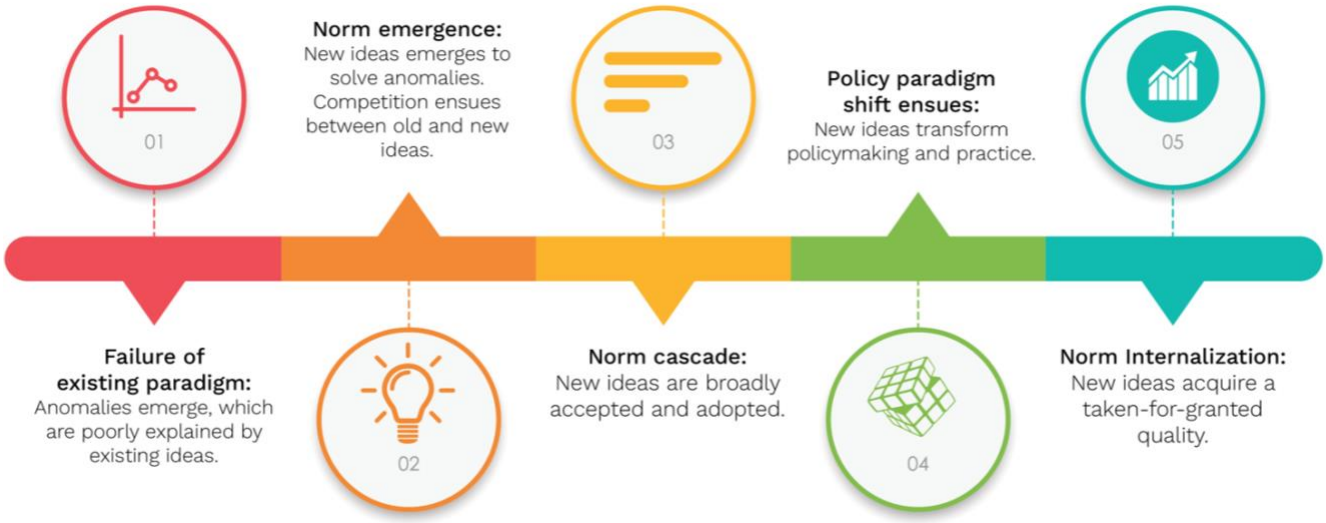
Where regime complex theory is silent, scholarship and concepts from other investigations on the role of ideas are instructive. Much has been written on the effect that new and emerging ideas have on and within international relations. For example, in their seminal investigation on the life cycles of norms, Finnemore and Sikkink (1998) demonstrate that norms evolve following a generic life cycle defined by three stages. These are norm emergence, norm cascade, and norm internalization. Norms emerge when norm entrepreneurs pioneer new ideas that offer alternative conceptions of appropriate behaviour and successfully persuade state leaders and international bureaucrats to embrace them. After norms emerge through the efforts of norm entrepreneurs, they cascade throughout states, IOs, and other institutions through a process of dynamic imitation. Various motivations can compel actors to adopt the new norm, including pressure to conform, acceptance (agreement), strategic alignment, and other reputational concerns. Finally, there comes a point where norms become internalized and acquire a 'taken-for-granted' quality. They become so embedded as the dominant frame that they effectively structure perceptions of the world, the problems within it, and possible policy solutions to inform practice (Finnemore and Sikkink 1998, 895–96).

When ideas change within institutional settings (i.e., when new norms emerge, cascade, and become internalized), this transformation can have profound impacts on subsequent behaviours and outcomes. Peter Hall's 1993 seminal work on policy paradigms, for example, explains how new ideas can displace older ideas and, through this process, revolutionize an organization's approach to action (Hall 1993). To make this case, Hall introduces the concept of

a policy paradigm, which is defined as "a framework of ideas and standards that specifies not only the goals of policy and the kind of instruments that can be used to attain them, but also the very nature of the problems they are meant to be addressing" (Hall 1993, 279)

Hall argues that policy paradigms, which are collections of ideas that structure beliefs about problems and needed solutions, will transform in much the same way as scientific paradigms during scientific revolutions (as argued by Thomas Kuhn in 1962). In particular, the emergence of repeated policy failures and the accumulation of anomalies will eventually precipitate a shift in the deep-seated ideas that structure the overall paradigm. A shift of this nature often coincides with the emergence of new ideas that sufficiently explain prior failures, while offering reasonably believable alternatives. When new ideas displace old ideas, it causes a wholescale change that, like a *gestalt shift*, can transform the institution's entire policy approach. In other words, the adoption of new ideas, if sufficiently different than older ones, can not only change the calibration of instruments, techniques used, or overall objectives, but also the very understanding of the problem and approaches needed to address it (Hall 1993, 283–84).

Figure 3.2: Norm Lifecycles and Paradigms Shifts



A synthesis of Finnemore, Sikkink, and Hall's analyses of the role of ideas provides a general timeline for understanding how new ideas can emerge, displace old ideas, revolutionize institutional approaches to policy, and transform subsequent action (Figure 3.2).

Part 3: The Evolution of One Health Ideas in Global AMR Governance

This generic framework can illuminate how a history of evolving attempts to govern AMR globally shaped the current regime complex. In brief, early efforts by the WHO, FAO, and WOAH to govern AMR from 1945 to the 1980s were defined by siloed and sector-specific initiatives (Overton et al. 2021). These siloed approaches were informed by an incomplete understanding of AMR and pursued within the narrow institutional mandates of each organization. The insufficiencies of these narrow approaches to adequately address AMR became increasingly apparent as several anomalies emerged, which were unexplainable by the old paradigm informing action (Landecker 2016). One Health ideas entered international policy discourses during the 1980s and 1990s, at a time when siloed initiatives were not translating into effective outcomes for AMR governance (Gibbs 2014). In this context, One Health, which emphasizes the interconnections among human, animal, and environmental health, provided a sufficiently believable explanation for past policy failures, as well as an alternative framework for future initiatives. Specifically, it suggested that a more holistic paradigm was needed to fully address AMR. One Health eventually gained enough legitimacy and traction to become the dominant frame guiding the policies of the FAO, WHO, and WOAH in 2008. The transition to One Health ideas eventually led to a policy paradigm shift within these IOs. It precipitated a new policy approach for the WHO, WOAH, FAO, and, later, the UNEP, which aims to transcend the narrow sectoral scopes of each organization in favour of a collaborative, intersectoral partnership

(Wernli et al. 2017). It transformed the way that these IOs operate, pushing them toward greater levels of integration, as evidenced by the fundamentally different policy outputs generated by the organizations in recent time (described further below). Guided by One Health ideas since the early 2000s, these IOs have sought out and forged synergistic linkages across their areas of work, thereby contributing to the rise of the regime complex for AMR governance.

The evolution of the regime complex demonstrates that despite the recent paradigm shift, past policy actions, based on antiquated understandings of the problem, still constrain the regime complex's ability to respond to AMR in light of improved understandings of the problem. To see the relationship between knowledge and path-dependency, consider how policy actions are informed by the available science at the time. Then, as new knowledge emerges, as it has with AMR over the past several decades, resulting new policies must be applied in the context of existing older policies informed by previous, often less complete understandings of the challenge (Landecker 2016). For example, past interpretations of, and proposed solutions to AMR have fallen within a history of individualizing responsibility for health and wellbeing (Denyer Willis and Chandler 2019). Based on these hyper-individualistic worldviews, AMR has at times been projected as a problem of individual overconsumption with proposed solutions offering individual behavior-changing mechanisms and improved education. In contrast, the One Health turn has led to a greater recognition of the social structures and deeply embedded incentives that drive antimicrobial consumption across sectors and countries (Tompson, Manderson, and Chandler 2021; Weldon, Rogers Van Katwyk, et al. 2022). This evolving understanding of the problem has created contradictions in policy action, as attempts to implement new policies based on a more holistic understanding of the problem occurs in a context of existing policies informed by older, more narrow perspectives. In other words, the persistence of individual-focused policy

responses in the context of shifting perspectives about the causes of AMR is creating a contradiction between newer, wholistically focused policy discourses and older, less complete, and individualizing ones (Chandler 2019).

The historical progression of global AMR governance efforts across the following five distinct eras elucidates how international organizations have effectively utilized norms to guide their actions, profoundly influencing the landscape of governance efforts. As these norms evolved, IOs entrepreneurially used them to recast institutional configurations, reshaping the governance terrain in the process. However, the persistence of overlapping paradigms and the path dependency inherent over time have generated unique challenges that are relevant today. These challenges serve as a testament to the intricate and dynamic nature of the governance landscape for AMR.

Early efforts: siloed approaches (1945 – 1960s)

Previous and now antiquated understandings of AMR informed the creation of past policy initiatives, and those initiatives lacked intersectoral collaboration. Under a condition of uncertainty in this early era, three dominant ideas structured the paradigm that informed policy action. First, AMR was perceived as a problem of overconsumption predominantly occurring in the Global North, where the bulk of global antimicrobial consumption was taking place (Overton et al. 2021). Second, AMR was seen primarily as a problem for the future, not one in need of immediate or escalating concern (Levy and Marshall 2004). And, finally, AMR was perceived to be manageable through narrow intra-sectoral action. For example, a joint report of the WHO and FAO in 1963 titled, “The Public Health Aspects of the use of Antibiotics in Food and Feedstuff,” concluded that the economic gains from antimicrobial use in food production outweighed the

human health risks posed by AMR (WHO Expert Committee on Public Health Aspects of the Use of Antibiotics in Food and Feedstuffs 1963).

In this early period, a now outdated understanding of the problem supported the policy paradigm informing IO action. The available knowledge at the time did not indicate a need for early cross-sectoral collaboration, but rather justified the opposite. Guided by this early paradigm, efforts to govern AMR globally were generally restricted to the narrowly defined scope of each individual IO. This narrowness meant that IOs, such as the FAO and WHO, pioneered their own AMR policies in accordance with their original institutional mandates. For example, the WHO started strengthening AMR surveillance as early as 1961. These early initiatives, however, were limited to the human sector only (WHO Expert Committee on Antibiotics 1961).

In other words, the paradigm at the time supported siloed initiatives, which further entrenched the path-dependent sectoral divides across these IOs. The colonial distribution of power weighing interests at the time further facilitated actions that favoured HIC interests at the expense of a more global outlook (Overton et al. 2021).

The emergence of anomalies: the continued rise of global resistance (1960-1980s)

During this era of siloed approaches, the problem of AMR continued to rise, resulting in anomalies that were not well explained by the existing paradigm informing policy action. Specifically, the continued rise of resistance in both developing and developed countries, as well as emerging scientific evidence of horizontal resistance transfer and cross-species spread of resistant microbes, began to undermine the logic of the old paradigm.

First, evidence that the problem of AMR was a growing problem everywhere was mounting. AMR was increasingly recognized as more than just a future problem for the global

north due to overconsumption. During the 1970s, the emergence of ampicillin resistant *Haemophilus influenzae* and *Neisseria gonorrhoeae* in industrial counties indicated that AMR was an escalating problem in need of immediate responses (Levy and Marshall 2004). Furthermore, the rise of multi-drug-resistant Tuberculosis (MDR TB) in developing countries during the 1980s challenged the notion that AMR was primarily a concern for industrialized countries (Overton et al. 2021). Finally, advances in the scientific evidence base demonstrated that resistance could transfer between microbes not only vertically to descendent generations, but also horizontally across microbial strains and species via mobile genetic elements now known as plasmids (Lacey 1975; Watanabe 1963). Additionally, other scientific discoveries during this period found that resistant microbes could spread from animals to humans (Podolsky 2018).

These phenomena were unanticipated and poorly explained by the prevailing policy paradigm at the time. Indeed, the emergence of these anomalies undermined assumptions about the very nature of the problem and its needed solutions. But without a strong normative justification that provided a sufficient explanation or alternative, the type of work and where it occurred did not change in this era. Although some reports on AMR published by the WHO, FAO, and WOAH throughout 1960-1980s mention the need to address antimicrobial usage in animals as well as humans, they rarely address issues related to cross-sectoral governance, planning, or partnerships (Overton et al. 2021). Moreover, given the continued uneven distribution of power in global health governance, early recognition of rising MDR TB rates did not change the focus of most global report and actions (Overton et al. 2021, 5). Instead, they continued to be predominantly occupied with AMR in industrial countries.

Despite emerging inconsistencies in the paradigm informing action, understandings of problem did not fundamentally change during this era. Among HICs, meanwhile, divergent

interests and understandings of the problem resulted in different regulatory approaches – underscoring the way that interests, problem framing, and path dependency can weave across countries, sectors, and time. For example, the United States (US) and European Union (EU) have adopted different approaches to governing antimicrobial use in agriculture (Kirchhelle 2020; 2018a). The 1969 publication of the Swann report prompted Great Britain and other European countries to take a precautionary approach and ban the use of therapeutically important antimicrobials in animal agriculture (Kirchhelle 2018c). Lacking a comprehensive approach, however, these efforts resulted in the overuse of other non-essential antimicrobials (Podolsky 2018). Meanwhile, in the US, economic interests within the country's agricultural industry precluded the adoption of Swann-like measures by the US Food and Drug Administration (FDA). Driven by consumer concerns and cost-benefit assessments, the FDA would later direct its efforts toward emphasizing rational use and monitoring antimicrobial residue in food rather than banning the use of specific antimicrobials (Kirchhelle 2019).[20]

These varying approaches to AMR governance contributed to the structural complexity that now characterizes the regime complex for AMR governance. Meanwhile, at the global level, the absence intersectoral efforts further entrenched the path-dependent sectoral divides across IOs. Indeed, the policies that emerged during this time did not evolve to be fundamentally different from the preceding era, but rather progressed only through minor adjustments and recalibrations.

Norm entrepreneurship: One Health explains past failures and anomalies (1980-2000s)

[20] These divergent approaches to AMR reflect longstanding differences between American and European understandings of health promotion in society, with the USA adopting a risk assessment model and the EU following precautionary principles (Chernomas and Hudson 2013).

The idea of One Health began to emerge in international policy debates during the 1980s (Lee and Brumme 2013; Gibbs 2014). Essentially, One Health principles emphasize the interdependence of human, animal, and environmental health. It suggests that the intrinsic relationship of these domains requires coordinated governance institutions across them. This idea would later induce a radical change in the approach of IOs, producing a fundamental shift in policy when compared with the preceding eras.

It should be noted, however, that the idea of One Health is not new. There is evidence of similar ideas in the 19th-century work of Rudolph Virchow, who studied the cross-species dynamics of microbes (Cardiff, Ward, and Barthold 2008). William Osler, another 19th-century pathologist, argued for a similar concept arising from his comparative investigation of human and animal pathologies (which Osler referred to as 'One Medicine') (Cardiff, Ward, and Barthold 2008). Even before these studies, many Indigenous and traditional non-western understandings of wholistic wellbeing have long emphasized the interdependence of human, animal, and environmental health (Chalmers and Dell 2015; Hillier et al. 2021). Thus, the emergence of One Health can best be seen as a renewed interest in an old concept (Schwabe 1984).

In this renewal, the publication of scientific and educational resources helped to "mainstream" the concept of One Health, especially in veterinary circles. For example, the third edition of Calvin Schwabe's book, *Veterinary Medicine and Human Health*, is seen to be a pivotal moment (Lee and Brumme 2013; Zinsstag et al. 2011). The book articulated a well-received argument that the connection between human and animal health required a unified approach to address infectious disease (Chien 2013).

The emergence of One Health ideas during this time coincided with another movement led by civil society to recognize the global nature of AMR. Most notably, the efforts of Stuart Levy helped to increase awareness of AMR as a global problem in need of an array of global solutions (Podolsky 2018). Where Levy's efforts focused on transforming perceptions of AMR from the local to global level, proponents of One Health, such as Schwabe, advocated for an analogous shift from narrowly divided and sectoral efforts to collaborative and intersectoral ones.

The idea of One Health, in particular, suggested that past policy failures and emerging anomalies could be explained by a lack of coordination among institutions narrowly focused on one aspect of an inherently multisectoral issue. In contrast with more narrow conceptions, One Health principles emphasize the links among human, animal, and environmental health, providing a more holistic perspective of the causes and consequences of AMR. Guided by these ideas, progressively more reports called for intersectoral action in the 1990s and early 2000s. Some started to make explicit recommendations for governance mechanisms to address the proliferation of actors and rules for AMR, while bridging the gaps created by distinct, sector-specific organizations (WHO Division of Emerging and other Communicable Diseases Surveillance and Control 1997; WHO Division of Emerging and other Communicable Diseases Surveillance and Control and International Federation of Pharmaceutical Manufacturers Associations 1998).

Norm cascade: a One-Health paradigm shift (2000-2015)

While One Health ideas began to emerge in the 1980s and 90s, it was not until the early 2000s that increasing recognition of its value eventually precipitated a norm cascade within key

IOs (Chien 2013; Overton et al. 2021).[21] The norm cascade can be traced through several moments, especially the cross-sectoral initiatives that emerged among the WHO, FAO, and WOAH during this timeframe.

Indeed, these three organizations started to work more closely together during the 2000s and advocated for stronger intersectoral collaboration on AMR. First, a report from a joint meeting of the WHO, FOA, and WOAH in 2000 outlined a set of "Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food" (WHO, FAO, and WOAH 2000). Later in 2001, the WHO outlined a strategy for containing antimicrobial resistance, which affirmed its vision for a more integrated approach to global AMR governance (WHO Anti-Infective Drug Resistance Surveillance and Containment Team 2001). Specifically, the 2001 strategy called for greater recognition of the human health impacts of non-human antimicrobial use as indicated in the report published in 2000. Later in 2003 and 2004, on the recommendation of the Executive Committee of the Codex Alimentarius Commission, the FAO, WHO, and WOAH convened a set of two joint expert workshops on non-human antimicrobial usage and antimicrobial resistance. The reports from these workshops further emphasize the significant human health impacts of non-human antimicrobial usage and the growing need for cross sectoral governance mechanisms – in direct contrast with past approaches based on earlier conceptions of the problem (WHO, FAO, and WOAH 2003; 2004).

Concurring with these reports was a growing recognition of the value of One Health in civil society (Gibbs 2014). For example, on September 29th, 2004, the Wildlife Conservation Society hosted symposium of human and animal health experts in New York. Emerging from

[21] Through qualitative interviews with international officials within the WHO, FAO, and WOAH, both Chien (2013) and Spencer et al. (2019) find that acceptance (agreement) and strategic alignment (for budgetary purposes) were the perceived 'micro-level' mechanisms for adopting the norm.

this symposium, participants published a set of 12 principles for implementing One Health ("the Manhattan Principles"). The Manhattan Principles helped to develop One Health ideas into a specific framework for policy action, calling for international and interdisciplinary approaches to prevent disease.

Then, during a series of expert working groups on antimicrobial usage in aquaculture in 2006 (WHO, FAO, and WOAH 2006), a series of expert meetings on critically important antimicrobials in 2005 and 2007 (WHO 2005a; FAO, WOAH, and WHO 2008), and a series of international ministerial conferences on Avian Influenza in 2007 and 2008 (Press Information Bureau of the Government of India 2007; WOAH 2008), the term One Health began to appear as a concrete call to action. Specifically, the idea of One Health was used an explicit justification for greater integration across IOs and to produce intersectoral strategies and governance mechanisms.

For example, during an international ministerial conference on Avian and Pandemic Influenza in 2007, cross-sectoral partnerships, guided by One Health principles, were recommended for pandemic preparedness and response (Press Information Bureau of the Government of India 2007). In 2008, a combined publication of the FAO, OIE, WHO, UNSIC, UNICEF, and World Bank further argued that mitigating the risk posed by AMR required a "wide-ranging collaboration across sectors and disciplines… [including] inter-agency and cross-sectoral collaboration and partnership" (WHO et al. 2008, 6). Of particular importance, One Health ideas were used to support calls for greater integration of the WHO, FAO, and WOAH's AMR initiatives (WHO et al. 2008). Finally, these One Health-informed calls to action were reaffirmed at an International Ministerial Conference on Avian and Pandemic Influenza in Sharm el-Sheikh, Egypt in 2008 (WOAH 2008).

The momentum grew in 2010 as One Health ideas continued to inform IO action. A concept note, published that year, formally established a "tripartite collaboration" among the WHO, FAO, and WOAH (FAO, WOAH, and WHO 2010). The concept note argued that "managing and responding to risks related to zoonoses and some high impact diseases is complex and requires multi-sectoral and multi-institutional cooperation" (FAO, WOAH, and WHO 2010, 2). In recognizing this imperative, the Tripartite collaboration emphasized "the critical need for collaboration between the three organizations" (FAO, WOAH, and WHO 2010, 6). The report further outlined the Tripartite's commitment to work "more closely together to align activities related to the animal-human-ecosystems interfaces in order to support member countries" (FAO, WOAH, and WHO 2010, 6).

After the publication of this note, the newly formed tripartite collaboration began developing a framework to address health risks at the human-animal-environmental interface, seeking to craft "strong partnerships among players who may have different perspectives on some issues and different levels of resources" (FAO, WOAH, and WHO 2010, 3) From here onward, One Health was used as a justification to strengthen the Tripartite's cross-sectoral collaboration on key issues such as AMR. In contrast with earlier ideas that justified divided efforts and little collaboration, the idea of One Health suggested that the lack of coordination and collaboration across sectors was a primary cause of past policy failures. Thus, guided by One Health principles, the Tripartite began creating strategic linkages across their areas of work, aiming to achieve an integrated approach to AMR.

With a One Health paradigm shift underway, the Tripartite organized a high-level technical meeting to build and generate political momentum for One Health action in 2011 (WHO, FAO, and WOAH 2012). The meeting emphasized three preeminent One Health

challenges, including AMR. At the meeting, participants discussed and identified opportunities to generate political will, actively engage states and ministers, and advance the implementation of One Health principles.

Finally, in 2015, the Tripartite produced a new policy instrument that was fundamentally different that older ones, namely, Global Action Plan on AMR (WHO 2015). This new policy instrument embodied One Health ideas and is further evidence of a paradigm shift in the understanding of AMR and its needed solutions (Chien 2013). Specifically, the Global Action Plan opens with the sentiment that "underscores the need for an effective "One Health" approach involving coordination among numerous international sectors and actors" (WHO 2015, VII).

The endorsement of the GAP by WHA Resolution (67.25) is another crucial piece of evidence demonstrating the cascade of One Health ideas, as well as a fundamental shift in the paradigm informing global policy action on AMR (WHA 2014). Further to the GAP's calls for a "whole of society engagement including a one-health approach" (WHO 2015, 5), the WHA resolution explicitly affirms the "need for a coherent, comprehensive, and integrated approach at global, regional, and national levels, in a "One Health" approach and beyond, involving different actors and sectors such as human and veterinary medicine, agriculture, environment and consumers" (WHA 2014, 56).

The adoption of One Health principles transformed the ideas that structure IO approaches to AMR, including how the problem is conceived and, thus, how it should be addressed. The One Health turn ultimately contributed to the current collaboration among IOs, which is a key feature of the regime complex for AMR governance. As noted by Wernli et al., the adoption of One Health principles during this time provided "a converging frame to promote collaboration between [WOAH], FAO and WHO" (2017, 6). Following the implication of One Health ideas,

IOs began to favor overlaps and create programs of work to transcend their sectoral divides. They forged linkages across technical areas of work guided by new scientific justifications, leading to greater levels of integration.

Internalization? (2015 - present)

Since 2015, One Health has continued to inform global policy approaches for AMR governance (Léger et al. 2021; Wernli et al. 2020). More recently, AMR has even been heralded as 'the quintessential One Health problem' (Robinson et al. 2016; Velazquez-Meza et al. 2022). That it seems so simple to state that the intersectoral issue of AMR requires intersectoral governance mechanisms, suggests the concept resonates on some intuitive level among scientists and policymakers. This appeal to intuition may signal a certain level of internalization. However, persistent frustrations with the lack of intersectoral cooperation in global health, especially at the level of states, suggests otherwise (Spencer et al. 2019).

Regardless, there have been many important advances that suggest that the concept of One Health continues to operate as a guiding framework for global AMR policy. For example, the UNEP formally joined the WHO, WOAH, and FAO in 2022, and the Tripartite Collaboration evolved into the Quadripartite Collaboration, leading to the further integration of One Health-relevant international organizations (UNEP, WHO, FAO, and WOAH 2022). Furthermore, other actors prioritizing AMR governance, including the G7, G20, GHSA, and civil society organizations, have also adopted One Health as a guiding frame for action in this most recent period.

Ultimately, throughout these five distinct eras, the pioneering work of IOs and non-state actors in formulating and promoting new policies, especially under the One Health framework, have had a unique impact on the regime complex for AMR governance. Through their dynamic

contributions to problem awareness and framing, policy development and proliferation, and norm entrepreneurship and dissemination, these actors actively shaped the evolution of the regime complex for AMR governance. Their roles as catalysts for dialogue, conduits for information, advocates for policy and paradigm change, and, increasingly, as independent drivers of policy implementation and governance are instrumental in understanding why the regime complex for AMR governance has taken its current form.

Part 4: Toward a 'One Health Regime Complex?'

The widescale adoption of One Health among IOs and other non-state actors prioritizing AMR indicates that One Health ideas continue to influence and shape the regime complex for AMR governance. But the recent One Health paradigm shift, and the subsequent emergence of a Quadripartite Collaboration in 2023, has not resulted in a unified regime. AMR is still governed by a relatively decentralized regime complex composed of several divergent principles, rules, norms, and procedures (Spencer et al. 2019; Weldon, Yaseen, and Hoffman 2022).

Indeed, while the new idea (normative) provided a new understanding of the problem (functional) and lead to integration among key IOs (institutional), the underlying generic forces of regime complex formation are unrelenting (Lee and Brumme 2013). Despite the recent One Health turn across IO approaches to AMR governance, the structural and functional complexity affecting AMR, combined with persistently different interests across states and sectors, limits the implementation of intersectoral measures (Spencer et al. 2019).

Path dependent constraints affecting IOs.

For example, three additional path-dependent constraints now affect the Quadripartite's ability to fully achieve its One Health vision. First, collaborating on cross-cutting issues like AMR remains challenging due to the organizations' long-standing histories of sectoral separation

(Spencer et al. 2019; Podolsky et al. 2015) – especially since each institution's constitutional mandate limits their ability to work beyond their narrowly defined sectoral scopes (International Court of Justice 1996). Overcoming these divergent mandates will require new rules and governance mechanisms, which must be sanctioned by states (Hanrieder 2015). These mechanisms, moreover, must bridge entrenched systems and patterns of behaviour, including existing resource allocation, decision-making, and accountability mechanisms (Galaz, Leach, and Scoones 2016; Hoffman et al. 2015).

Second, the adoption of One Health principles did not only induce a change to the scope of AMR efforts for these organizations. It also coincided with a transformation to the kind of work that they are engaged in. For example, Overton et al. (2021) note that the WHO only started to progressively transform from a 'whistle blower' alerting the world about public health problems to a 'governing institution' that actively manages those problems in the 2000s (Overton et al. 2021). Thus, as the relevant scope of work for these four organizations slowly expanded from single to multiple sectors, so too did the substantive type of work change from 'whistleblowing' to 'governing'. This transformation adds another challenge for future reforms, where states must now choose whether to confront, embrace, or reject the increasingly political activities of IOs (Wenham, Eccleston-Turner, and Voss 2022). Any of these options will require new rules and mandates that clarify and delimit their purview, while also leveraging their existing momentum and facilitating greater implementation of One Health principles at the global level.

The third factor affecting the Quadripartite Collaboration is the persistence of the issues for which each institution was originally designed to addressed (Wernli et al. 2022). The continued relevance of their institutional mandates for those issues helps their existing systems

resist change and reform. Put differently, each institution is still busy trying to accomplish their original goals. The systems that they have built up over several decades, moreover, still provide a level of efficiency and effectiveness toward them. Waves of pandemics, droughts, food insecurity, climate change, and biodiversity loss all still require these organizations to maintain the systems that they have built up over time. Yet, the interconnection of today's functionally complex challenges, such as climate change, biodiversity loss, zoonoses, and AMR, underscore the need for strong coordinated global responses to manage their interlinked, overlapping, and dynamic causes (Li et al. 2023). The need to address these challenges concurrently in the context of resource constraint institutions raises the bar for One Health principles, which may have to completely transform institutional approaches to managing all of these concurrent problems to unlock the idea's full potential (i.e., to avoid pitfall of falling back into narrowly focused initiatives as opposed to wholistic ones) (Spencer et al. 2019).

These path-dependent constraints make it difficult for the four organizations to work together and govern – not just monitor – AMR through a multisectoral approach while also managing concurrent global challenges. To achieve greater coherence within the regime complex, many persistent path dependent obstacles affecting the implementation of One Health policies must be overcome. This endeavour will require states to also embrace One Health principles and transform the structural limitations that impede the further integration of One Health relevant IOs.

Implementing One Health: from IO ideas to state action

Situating the recent push for One Health within the longer historical trajectory of AMR governance efforts reveals an ongoing transformation to the logic of appropriateness guiding global behaviour around the problem (Gibbs 2014). This transformation was initially driven by

IOs who, guided by One Health ideas, adapted their institutional approaches to AMR governance (Galaz, Leach, and Scoones 2016). In doing so, they have shaped the context where new global AMR governance efforts are now continuing to emerge.

In this context, ongoing negotiations for a new pandemic instrument and revisions to the IHR will serve as critical tests for whether One Health principles can translate from a normative framework for IOs into actionable measures by states (Palkovits, Van Katwyk, and Hoffman 2022). The central question for these negotiations is whether and to what extent states will adopt concrete One Health provisions in these instruments, while facilitating greater collaboration among relevant IOs. This opportunity will further test whether One Health can effectively unite divergent state and sector interests under a shared vision for promoting global health, supported by measurable actions at the national level (Spencer et al. 2019).

Putting One Health principles into practice and achieving more coherent AMR governance is possible. However, this task will be difficult considering the persistent underlying forces that sustain the decentralized regime complex for AMR governance (Lee and Brumme 2013). More specifically, the challenge is to operationalize and institutionalize One Health principles to simultaneously: unite a diverse set of actors; provide coherence to the complex legal system of existing rules; and guide the institutionalization of new mechanisms that comprehensively address the problem's many interlinked facets (Hoffman et al. 2015).

Facing similar challenges over the past decades, recent climate agreements aim to strike a balance between de/centralization to unite the enormous regime complex for climate change governance (Falkner 2016). Somewhat paradoxically, centralization and decentralization are not exclusive and opposite ends of a spectrum but are rather compatible and complementary ways of

achieving institutional objectives (Witesman 2020). An analogous hybrid approach for the regime complex for AMR could provide a promising path forward.

Box 3.2: List of Potential Hybrid Governance Mechanisms for AMR (Weldon et al. 2022)
1. Top-down goals that provide coordination, but which rely on bottom-up implementation to achieve them. 2. Global knowledge sharing and awareness raising mechanisms that are cognizant of location and scale relevant knowledge and evidence. 3. A standardized, consistent, and interoperable global surveillance system. 4. Transparency and accountability mechanisms. 5. A diverse and inclusive multi-stakeholder forum. 6. A global pooled fund for global investments in infection prevention and control, and the innovation and distribution of medical countermeasures including antimicrobials, diagnostics, and alternative therapies. Alternative funding techniques could include a deposit mechanism or multi party-single closing type deals to leverage decentralized funds for AMR initiatives. 7. Global coordination for response to resistant outbreaks.

Limits of a concept

Finally, the history of how One Health ideas propagated through IOs and into IO policy substantiates the foundational constructivist claim that ideas have a significant potential to shape behaviours and actions (Finnemore and Sikkink 1998). Ideas filter our perceptions of the material world and constitute our entire social world (Adler 1997). They frame the problems we see and render intelligible possible solutions. When ideas change to a sufficient extent (both

within individual understandings and across populations), they can lead to entirely new behaviours and actions around a given issue (Hall 1993).

This feature of the relationship between ideas and action, though, begs the questions: can One Health ideas unite interests and transform the underlying structural determinants of AMR, given the current challenges that it faces in catalyzing sufficient global action (Lee and Brumme 2013; Gibbs 2014; Galaz, Leach, and Scoones 2016; Spencer et al. 2019)? Here, I briefly discuss three limitations that, while not fatal, advance constructive theorizing for alternative approaches to inform AMR governance. Indeed, One Health is just one of many recent movements to recognize a more wholistic approach to health and wellbeing. Others include EcoHealth and Planetary Health, which are similar, but have distinct values and assumptions (Lerner and Berg 2017).[22] Crucially, One Health is not a panacea, but together with these other perspectives, offers an opportunity to consider the systemic determinants of health across states and sectors. Outlining the limits of One Health can help situate the idea vis-à-vis other complementary perspectives.

First, it is important to contextualize One Health within the material realities in which it recently became so popular. The idea gained traction within the WHO, FAO, and WOAH when sectoral divisions were preventing coherent and comprehensive policy for complex health issues (Galaz, Leach, and Scoones 2016). One Health principles thus represented an antithesis to their

[22] EcoHealth involves "the health of humans, animals, and ecosystems, including also environmental sustainability and socioeconomic stability in the framework." (Lerner and Berg 2017). It privileges the "relationship between health, ecosystem, and sustainable development, where the latter is based on equity" (Ibid.). Planetary Health, meanwhile, is defined as "the achievement of the highest attainable standard of health, well-being, and equity worldwide through judicious attention to the human systems—political, economic, and social—that shape the future of humanity and the Earth's natural systems that define the safe environmental limits within which humanity can flourish" (Witmee et al. 2015). Planetary health privileges the health of living and future human generations, applied to individuals, communities, and populations. See Lerner and Berg (2017) for a more fulsome comparison of these approaches.

prior policy failures. As a response to persistent sectoral divides, One Health holds potential for guiding better policies for problems with dynamic and far-reaching causes, including AMR.

But insofar as One Health ideas stand to transform AMR governance, the implementation of One Health policies represents an inherently political project (Galaz, Leach, and Scoones 2016; Lee and Brumme 2013). At best, One Health provides an impetus to transform system-wide approaches to health governance at the human-animal-environmental interface. At worst, One Health rhetoric will serve as another vehicle for hollow promises while obscuring global inequities bound up in the cross-cutting social structures that shape human-animal-environmental relations. Indeed, the complexity of today's global challenges and remaining ambiguities around One Health could be strategically leveraged to address the problem in rhetoric only.

At and anywhere in between these two extremes, One Health presents a vision for the future that is rife with political considerations. With tangible effects on global AMR governance already emanating from its logics of appropriateness, One Health is another platform on which social and political aspirations must be negotiated. And despite rhetorical convergence on the need for One Health approaches, uneven distributions of power and interests persist across countries and sectors (Spencer et al. 2019). Even among the Quadripartite, struggles for power and authority linger across groups and subgroups. These turf wars for authority over who owns programs and initiatives are reflected in implementation barriers noted at local levels (dos S. Ribeiro, van de Burgwal, and Regeer 2019). For example, at both global and national levels, conflicts emerge around the proper home for One Health initiatives, with implications for budget lines and distributions of funding across sectors (e.g., animal health sectors may accuse human health sectors of steering important resources away and subordinating animal health priorities when they argue that by virtue of being a determinant of human health, animal health programs

should fall under the remit of human health governance). Such challenges have led scholars to question whether One Health ideas serve to unite or further splinter global efforts (Spencer et al. 2019). Indeed, without confronting the power imbalances affecting these conflicts (e.g., within professional hierarchies; among human, animal, agricultural, and environmental stakeholders; and across countries and populations), an uncritical adoption of One Health principles risks depoliticizing the inherently political objective that is realizing an alternative future.

Relatedly, the concept of One Health does not contain a theory of history. Consequently, it is uncritical of the contingent and changing nature of the subjects of its analysis. One Health takes the domains of human health, animal health, and environmental health as fixed to smooth out the problems that arise at their intersection and from siloed, sector-specific efforts. This assumption is helpful for understanding the challenges that arise across the domains as they currently are. However, this 'locked in time' assumption poses certain limitations. More specifically, what is missing is an understanding of how the specific configuration of these domains came to be, and how they may be changing within a broader historical trajectory. Indeed, the domains of human, animal, and environmental health are all determined by human institutions that shape interspecies and organic-inorganic relations. Without recognizing these broader human institutions, One Health risks decontextualizing its three domains from the various social structures with the power to shape them. For example, contemporary human, animal, and environmental relations are all shaped by human political, cultural, and economic patterns of behavior, including: legacies of colonialism (Büyüm et al. 2020); global capitalism and its logics of production, trade, and consumption (Gill and Benatar 2020); the anarchical system of sovereign states; shifting cultural attitudes (including dietary habits) (Kirchhelle

2019); labor, land, and care practices (Hindmarch and Hillier 2022; Denyer Willis and Chandler 2019); and global movements of people, products, and ideas.

Lastly, by emphasizing the domains of human, animal, environmental health, One Health understates the importance of investigating human-microbial relations. While it is true that microbes spread across One Health's three domains, it is also important to note that, historically, the advent of antimicrobials has had a profound impact in shaping today's human-animal-environmental realities and relationalities. For example, antimicrobials are crucial for facilitating large-scale industrial feed operations, which represent a modern interface for human, animal, and environmental relations. Simultaneously, these industry practices are among the most implicated in the problem of antimicrobial overuse. Thus, one could argue that while a welcomed step, One Health does not go far enough to investigate human, microbial, animal, plant, and environmental relations, which are interdependent, contingent, and continually evolving.

Conclusion

Contemporary global challenges, such as climate change, AMR, and biodiversity loss, are complex, with many dynamic causes and consequences. Crafting institutions commensurate with this complexity requires navigating the structural complexity, interest diversity, and competing norms that sustain the dense, messy, and nebular qualities of contemporary global governance. Any strategy for improvement must be grounded in this complex reality for the nuance of the world, not in simplicity for the convenience of the mind. Nor should 'progress' be equated with 'order'. Instead, in situations characterized by many uncertainties, divergent needs, and uneven capabilities, embracing decentralization and diversity can cultivate multiple pathways to success.

Amid this decentralized governance structure for AMR, a transformation in the behaviour of several IOs has recently affected the logic of appropriateness for global AMR governance,

providing an opportunity to trace the interactions of norms, rationality, and institutional configurations within regime complexes over time. Specifically, One Health norms were leveraged by IOs to reshape the context in which state and non-state actors must now respond to govern the urgent global challenge of AMR.

Indeed, as this case study shows, the social coalescence around an idea within and beyond IOs can shape institutional configurations by justifying convergence and integration among key actors (Wernli et al. 2017). To be sure, the extent to which IOs can transform global politics without concrete state action and support is limited, as evidenced by the persistent structural, functional, and interest diversity preventing genuine One Health action in AMR governance (Podolsky et al. 2015). Yet, crucially, the history of social mobilization around One Health reveals that in the absence of state leadership, IOs can and have shaped the present context where states must now respond to these normative and institutional developments.

Taking a cue from Finnermore and Sikkink (1998), let me conclude with a reminder that every historical narrative demonstrating the effect that ideas can have on behaviour is a story of how the ‘ought to be’ can become the ‘is’. Political philosophy must accompany political analysis when conceptualizing the range of possible and desirable futures. Any project aimed at improving global governance involves some imagining of this kind (e.g., a world with net zero emissions, no poverty, and universal health coverage). The design of equitable, effective, and durable institutions to realize or prevent these goals raises further challenges intrinsic to the political process of achieving social transformation, including whose voices are heard, whose needs are prioritized, and whose interests are elevated over others. Along with One Health, new ideas and approaches can offer opportunities to improve the way we govern multiple complex

problems affecting health and wellbeing. Let us embrace this political challenge and work together to create a healthier and more equitable future for all.

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Chapter 4: "Fit for Purpose?" Assessing the Ecological Fit of the Social Institutions that Globally Govern Antimicrobial Resistance

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A revised version of this chapter, co-authored with Steven J. Hoffman, is forthcoming in *Perspectives on Politics.* This chapter represents the original work of the author.

Chapter Abstract

Antimicrobial resistance (AMR) is an enduring socio-ecological problem arising in the dialectical relationship between human intervention and adaptive microbial behaviors. Like many of today's greatest challenges, AMR demands swift global collective action to mitigate its downstream consequences, including increased morbidity and mortality caused by increasingly or sometimes completely ineffective antibiotic agents. But as a socio-ecological problem, it also requires durable institutions that can guide human-microbial interactions into the future 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 not adept for achieving any of these aims. Advances in biodiversity governance indicate that institutions are more sustainable when they fit the biological features of the problems that they are designed to address – the same way a key *is designed to fit* a specific lock. The concept of ecological fit, defined as the alignment between human social systems and biological ecosystems, offers a powerful lens for designing future institutions for global health. This chapter identifies 18 misfits between the social institutions that govern AMR and the ecological nature of the problem. Drawing similarities between AMR and biodiversity governance, it considers whether strategies previously applied to improve biodiversity governance, and associated challenges therein, can translate into lessons for governing AMR.

Introduction

Like many of today's greatest challenges, mitigating the threats posed by antimicrobial resistance (AMR) requires new ideas and practices for governance (Denyer Willis and Chandler 2019; Weldon et al. 2022). The inability of prevailing policy practices to sufficiently address or even puzzle through anomalies, such as the emergence and re-emergence of mutated zoonotic and resistant disease-variants and the uneven global realities that they create, suggests a problem with the way that global health challenges are conceived (Green 2020). 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 objectives (Oberth 2012). 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 challenge caused by the innate ability for microbes to adapt and develop resistance to human intervention. Framed from this standpoint, AMR is a socio-ecological problem in need of durable institutions to manage the suite of human behaviours with the potential to shape the human-microbial nexus. 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 the challenge, new insights can be generated by considering how well global institutions align with the ecological characteristics of AMR, including the geographical scope, the 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 suited to the problems that they are designed to 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 attempting to govern could significantly improve the likelihood of creating more effective and 'fit for purpose' global health institutions (Léger et al. 2021; Jørgensen et al. 2020; Wallinga, Rayner, and Lang 2015).

This chapter adopts a socio-ecological 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 "glocal" problem inextricably linked to other ecological processes and challenges. Next, drawing on research conducted in a complementary study, it adopts the concept of the regime complex for AMR governance (i.e., the array of global institutions converging around the problem) to frame the current social systems governing it. By systematically comparing the logics of AMR governance with the ecological features of the problem, this chapter 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, since the concept of ecological fit has been extensively used to analyze the socio-ecological challenges associated with biodiversity management, this chapter explores whether strategies previously applied in that setting, and challenges arising therein, can translate into lessons for AMR governance.

Part 1: Adopting a Socio-Ecological Perspective to Investigate AMR

The socio-ecological approach emphasizes the dynamic and complex relationships between 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 approach 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 (Léger et al. 2021; Wallinga, Rayner, and Lang 2015). In contrast with 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, Underdal (2002) 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. The socio-ecological 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 (Banerji et al. 2019; Wallinga, Rayner, and Lang 2015).

By emphasizing the interlinkages between human and ecological systems, the socio-ecological 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 socio-ecological characteristics (Hoffman et al. 2015; Hoffman and Outterson 2015; Nagi et al. 2020; Rogers Van Katwyk, Giubilini, et al. 2020; Rogers Van Katwyk, Weldon, et al. 2020; Wallinga, Rayner, and Lang 2015; Wilson et al. 2021). Specifically, AMR is simultaneously a 1) widespread intersectoral problem 2) global and local – or "glocal" problem; 3) long-enduring process that, because it is caused by the innate evolutionary ability of microbes, is unlikely to ever truly be 'solved' (Rogers Van Katwyk, Giubilini, et al. 2020); 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.

Table 4.1: Ecological Characteristics of AMR

Ecological Characteristic	Explanation	Manifestation as social problems
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	AMR cuts across social boundaries, including sectoral, jurisdictional, and regional divides.

	remain unexposed to the resistant pathogen (Weldon et al. 2022).	
2) Glocal (Global + Local)	Microbial ecologies can be 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 (Green 2020).	AMR links individuals 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.	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.

A starting point for considering how these socio-ecological interdependencies play out in international relations is Robert Cox's 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" (Robert W. Cox 1981, 161). When put in these terms, the socio-ecological approach essentially focuses on the contradictions that arise in the relationship between prevailing systems of human behaviour (i.e., the global political economy and the interstate system) and the biosphere (i.e., the global 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 (Green 2020; Robert W. 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, but the relative importance of which are 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

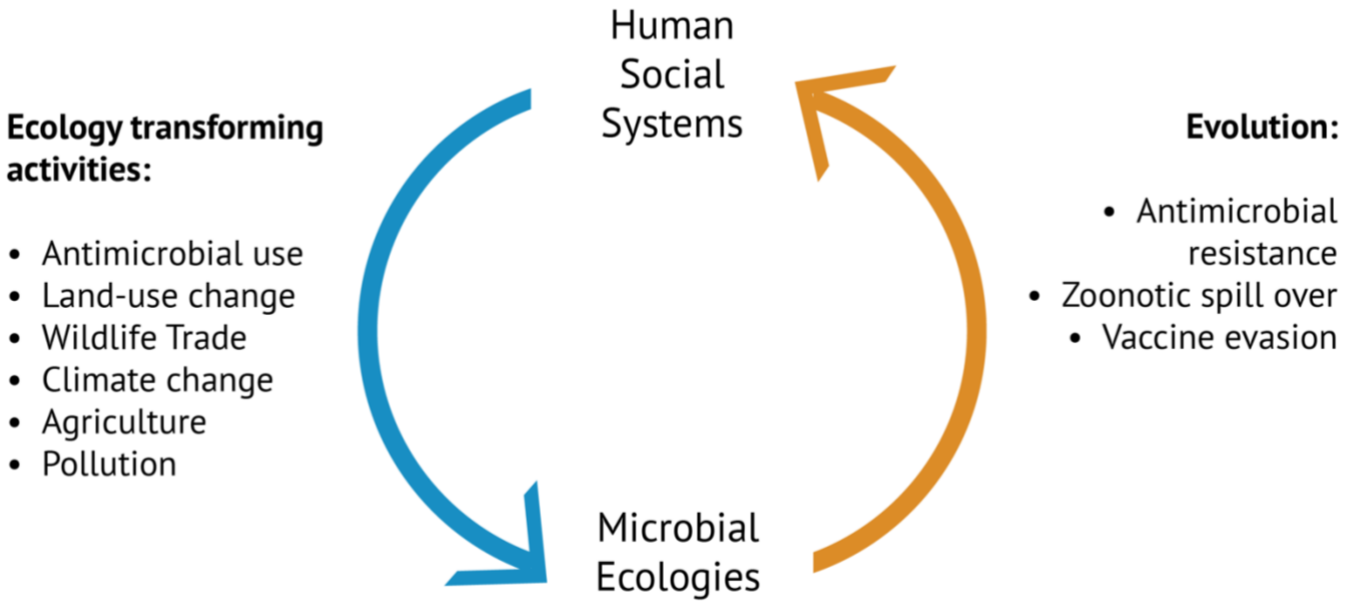
problem-solving approaches that are unquestioning of the changing orders in which they operate, he notes that critical problem-solving perspectives can emerge 'with a normative choice in favour of a social and political order different from the prevailing order' (Robert W. Cox 1981).

Cox's ideas are a useful because they emphasise 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 "humans as removed from nature" or about "nature as something to be controlled by culture" (Agathangelou 2016; Anderson and Perrin 2018; 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 socio-ecological approach directs attention to the way that microbes form part of the natural ecological basis that orders human social relations (Figure 4.1). Since the discovery of effective antimicrobials, societies have formed systems that critically depend upon them in order to function (Chandler 2019). Antimicrobials have attained such an important role in modern societies that they operate like invisible infrastructure that enables more productive food, labor, and healthcare systems. But this dependency, characterized by deeply engrained structures and practices that incentivize antimicrobials use for quick fixes for productivity, abundance, and profits, has generated a wide range of human activities that

affect microbial adaptive behaviours. Specifically, these human activities precipitate biological change and accelerate microbial evolution toward resistance. Antimicrobial resistance, in turn, undermines our social orders which rely upon antimicrobials to provide medical care and avoid more costly investments in sanitation and hygiene (Denyer Willis and Chandler 2019).

Figure 4.1: Socio-Ecological Dynamics of AMR



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 to increase overall agricultural productivity). The increasing failure of antimicrobials, though, now reveals the extent to which those 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 behaviour around antimicrobial use (Denyer Willis and Chandler 2019; Weldon et al. 2022; Chandler 2019), there is an emerging normative project to achieve a new relationship that reduces the rate that humans induce microbial resistance. 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 wholistic perspectives is generating academic projects that aim to grapple with the ecological nature of today's interlinked health challenges, including AMR. There have even been entire journals established to support 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 Chapter 3, AMR is currently governed by a global regime complex. Regime complexes have emerged as a defining feature of global governance in the 21st 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 and legal architectures that structure existing human institutions in the current conjuncture. Although these architectures are evolving, their present historically contingent form represents the socio-ecological niche into which resistant pathogens are currently emerging. Thus, investigating the

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

An international regime is often defined using Stephen Krasner's seminal definition as the "set of implicit or explicit principles, norms, rules, and procedures around which actors' preferences converge in a given area of international relations" (Krasner 1982), where principles are defined as beliefs of fact, causation, and rectitude; norms are the standards of behaviour defined in terms of rights and obligations; rules pertain to specific prescriptions or proscriptions for action; and, finally, procedures are the prevailing practices for making and implementing collective choice. (Krasner 1982; Ruggie 1982; Krasner 2004).

Since Krasner introduced the idea of an international regime in 1983, scholars have used the concept to analyze the global governance of specific issues and domains, including money, trade, the environment, health, and nuclear technology (Ruggie 1982; O. R. Young 2011; Lakoff 2019; Gottemoeller 2015). 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 (Oran R. Young 1996; Aggarwal 1998; Stokke 1997; Rosendal 2001; Oberthür 2002). Specifically, there was a recognition of at least three major limitations which 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 (Raustiala and Victor 2004; Keohane and Nye 2000). 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, Raustiala and 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, rules, norms, 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 socio-ecological approach. 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, 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 (Weldon et al. 2022; Rogers Van Katwyk, Weldon, et al. 2020) 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 3.1).

Some of these elemental regimes have evolved with highly institutionalized agreements with fully spelled out expectations and behaviours. 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 Organization (WHO), which are the legally binding rules that govern how states respond to infectious disease outbreaks, is 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, behaviour in an international regime may be guided by a looser arrangement of principles, rules, norms, and procedures. Such is the case for the humanitarian biomedicine regime, where many rules, norms, principles, and procedures guide actor behaviour, but do not emanate from specific formalized agreements. Instead, these

structures have been shaped historically through informally codified behaviours and sporadic international agreements.

There are several instances of overlapping and sometimes conflicting principles, rules, norms, 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, positive overlaps include the human health security and the trade regimes' shared commitment to minimize the impact of policy interventions on trade (Hoffman, Weldon, and Habibi 2022).

Meanwhile the trade regime's principle that intellectual property rights improve health innovation, as well as the rules within TRIPs that embody that principle, can pose challenges for the development and humanitarian biomedicine regimes' principle of access to medicine as human right (Motari et al. 2021). 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). Other aspects of the trade regime, including its rules and norms around intellectual property, investment, and financing, have also been found to inhibit the achievement of global health goals (Barlow et al. 2017). Where there are growing calls to re-evaluate the priorities of global health governance, there remains a need to determine which principles, norms, rules, and procedures prevail when elemental regimes interact with conflicting perspectives and aims. And where there are calls to identify and transform the suite of human behaviours 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 4.1) and the social systems that currently govern it (Table 3.2), it is possible to consider the ecological fit across these domains. The concept pertains to how well social institutions fit with the problem at hand (Oran R. Young 2002). Specifically, it is defined as "the congruence or compatibility between ecosystems and institutional arrangements created to manage human activities affecting these systems" (Oran R. Young 2002, 20).

The concept of ecological fit has been used extensively to explain governance challenges in biodiversity 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, Hoffman et al. (Hoffman and Silverberg 2018) note several political and technical barriers that prevent the IHR from responding to infectious disease outbreaks promptly, signalling 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.

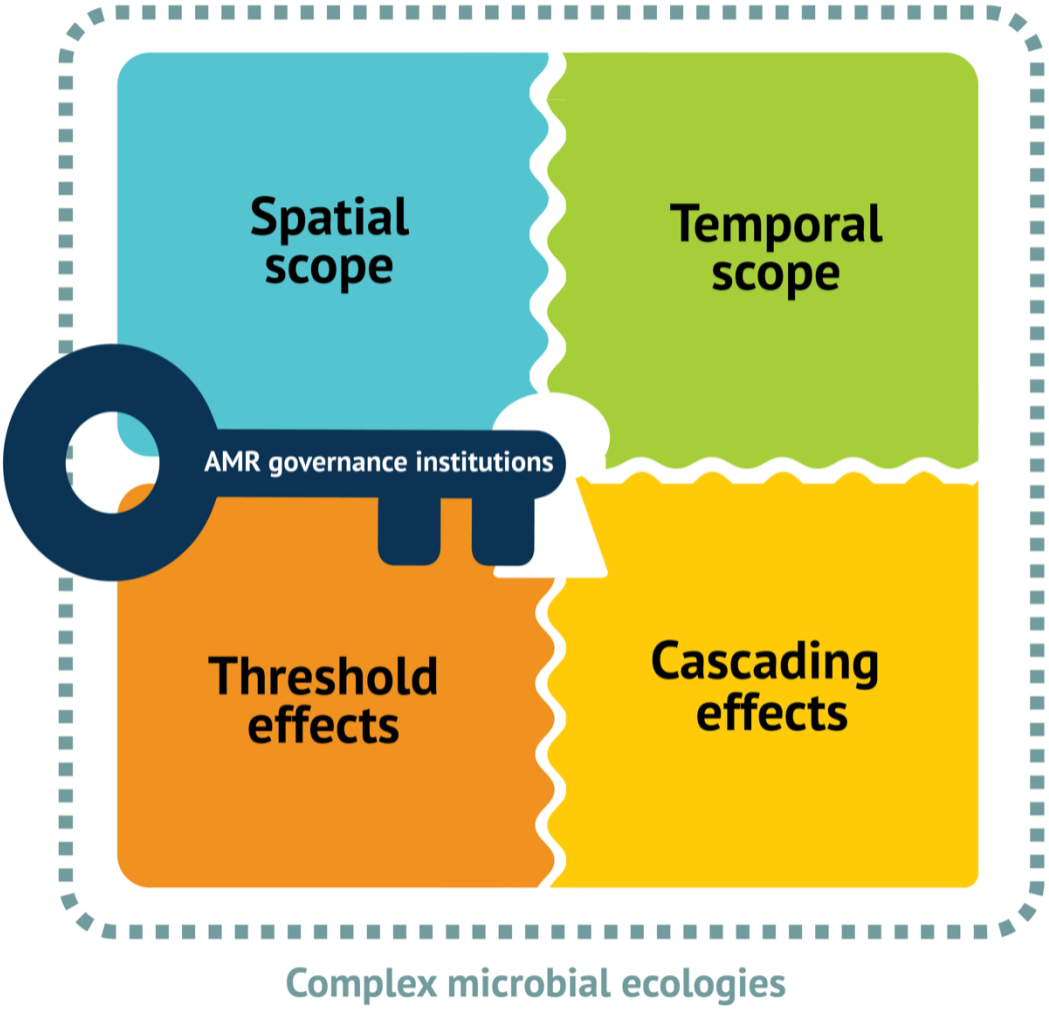
Operationalizing the concept of ecological fit

I follow a relatively simple process to operationalize the concept of ecological fit for application to AMR governance. Specifically, I adopt what Epstein et al. (2015) describe as a straightforward process of "characterizing the attributes of the ecological problem and then comparing these to the attributes of governing institutions." (Epstein et al. 2015, 36). Much has been written about theoretical and practical challenges associated with measuring fit (Epstein et al. 2015; M. Cox 2012; 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 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 socio-ecological 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 global health governance of AMR.

Prior research in biodiversity governance 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 spatial, temporal, threshold, and cascading misfits (Table 4.2). Though a theory-driven analysis, I 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 AMR governance (Figure 4.2; Table 4.2).

Figure 4.2: Unlocking New Approaches for AMR Institutions



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 misfit between the globalizing way that microbes transcend borders and the statist norms and principles that underpin the regime complex for AMR (Wenham, Eccleston-Turner, and Voss 2022; Hoffman, Weldon, and Habibi 2022). This spatial misfit reflects what Wenham et al. (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 (Wenham, Eccleston-Turner, and Voss 2022; Weldon and Hoffman 2021).

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 life-saving products equitably and efficiently. Enduring legacies of colonialism, weak health care 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, little 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 socio-ecological 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, and UN Agency meeting rooms in Geneva and New York, and elsewhere).

Temporal Misfits

Temporal misfits occur when institutional dynamics are too fast or too slow compared to 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. It is worth noting, though, 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 legally binding global framework for AMR, the IHR represent the closest thing to a global regulation for the issue, even though it is not well equipped to govern the challenge. In particular, the primary focus of the IHR, as outlined 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 non-crisis 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. As noted above, another temporal misfit is the slow response time that it can take for the WHO to declare public health emergencies of international concerns (PHEICs). This procedure, which is outlined in Article 12 of the IHR, is used by the WHO to enact emergency global response protocols to emerging disease threats (Hoffman and Silverberg 2018). However, technical and political barriers often prevent a timely declaration of a PHEIC, which hinders an effective global response.

Several market challenges plague the innovation pipeline for new antimicrobial drugs, including the high cost of development and low likelihood of reward for novel antimicrobials (Kesselheim and Outterson 2011). As a result, several public-private partnerships have emerged to address the inability of market mechanisms to develop new antimicrobials fast enough. As demonstrated by ongoing failures to distribute COVID-19 vaccines, the challenge with these non-market mechanisms is that new technologies are not distributed equally or on equal time horizons once discovered.

The inability to replenish the depleting pool of antimicrobial effectiveness and optimally distribute new countermeasures represents another temporal misfit between the social dynamics of drug development and distribution and the socio-ecological factors that accelerate microbial evolutionary processes. Moreover, it signals yet another temporal challenge created by the uneven temporal scales that manifest when microbes spread around the world**.**

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 (Galaz et al. 2008; Folke 2016). 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 (Rogers Van Katwyk, Giubilini, et al. 2020; Chandler 2019; Kirchhelle et al. Forthcoming).

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. One way these misfits can occur is with the overreliance on popular models such as 'the common pool resource' model, which draws attention to 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 common pool resource model, which assumes 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 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).

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). Cascading misfits for AMR draw attention to problematic gaps in global governance around multisectoral 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 function. 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. Specifically, biodiversity, climate change, and zoonotic pandemics all have the potential to accelerate AMR either directly or indirectly (Strathdee, Davies, and Marcelin 2020; Gilchrist et al. 2007; Van Boeckel et al. 2015; Singer et al. 2016). 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.

Table 4.2: Summary of Ecological Misfits for AMR Governance.

Type of Misfit	**Examples in AMR Governance**
Spatial Misfits: Institutional jurisdiction is too small or too large to cover or affect the ecological system which it seeks to govern.	• 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). • Uneven spatial distribution of needs, capabilities, and responsibility to respond, including access to antimicrobials (Laxminarayan et al. 2016). • There is a wide range of national circumstances with little information or evidence on the 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). • Individuals around the world consume antibiotics daily, but governance only occurs in centralized locations, driven by some (powerful) individuals .
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.	• Innovation, driven by IP rights, is not fast enough to replenish depleting stock of effective antimicrobials (Kesselheim and Outterson 2011). • Historically, declarations of PHEICs can be slow, caused by political and technical delays (Hoffman and Silverberg 2018). • 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. • 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).
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 provide buffers against mechanisms that lead to irreversible shifts in ecosystems	• Use and dependence on antimicrobials are themselves caused by 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 over dependence on a technology inherently moving toward a threshold as any use potentially leads to resistance. This points to the need for the regime to focus on social transformation and prevention. • 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). • Collective action framing can cause overfocus on some aspects (e.g., common pool resource framing misses access problems). • AMR challenges are interdependent, focusing on some but not others can cause negative threshold effects (Hoffman and Outterson 2015).

	• Unclear about whether certain contingencies apply, such as declaration of PHEIC even apply if the threshold is crossed and an untreatable disease emerges from AMR.
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)	• No cross sectoral contingency plans. • Zoonotic outbreaks, such as COVID-19, drive antimicrobial usage up (Knight et al. 2021). • Targeting antimicrobial usage in agriculture may undermine food security (World Bank 2017). • Use in many sectors around the world is contributing to AMR spill over in the environment (Singer et al. 2016). • Various unmeasured or unaccounted social equity considerations.

Part 4: Improving the Ecological Fit of AMR Governance Systems

Strategies to mitigate AMR's downstream effects are urgently needed, such as achieving an optimal distribution of new and existing antimicrobials and medical countermeasures to meet existing needs. But global efforts cannot end there. Rather, this investigation has exposed deeper challenges with the current system of global health governance and the way we think about designing the institutions that comprise it. By adopting a socio-ecological perspective and employing the concept of fit, this analysis revealed several areas where the social institutions that govern AMR are at odds with ecological dynamics of microbes in an increasingly interconnected world. The list, while not exhaustive, demonstrates that several misfits can be identified as sites for analysis and areas for improving the design of AMR governance institutions.

Targeting the misfits identified by this analysis will help future institutions to address the underlying socio-ecological causes of AMR. But to do so, it is necessary to first recognize how human activity is embedded within planetary systems comprised partly of invisible microbial ecologies. Framed in this way, the subject of governance transforms beyond just the social

response to infectious disease threats to also encompass the co-evolution of human societies with (and within) microbial ecologies – a concept that Jorgensen et al. call "co-evolutionary governance". In their words, co-evolutionary governance builds on principles of adaptive co-management by recognizing, anticipating, and analyzing "interdependent eco-evolutionary dynamics [and] guide human societies toward identified goals." (Jorgensen p. 485). The idea of co-evolutionary governance recognizes that the evolution of human culture is linked through dialectical interactions with various natural forces of microbial evolution – creating a need for institutions that can sustainably guide these interactions.

For AMR, crafting durable institutions that can sustainably guide human-microbial co-evolution must balance two sets of interrelated needs. On one hand, these institutions must minimize the range of human activities that precipitate and accelerate AMR to limit the emergence of drug-resistant infections (Hinchliffe, Butcher, and Rahman 2018). On the other, they must maximize the ability to protect human health and wellbeing by preserving the effectiveness of existing drugs, optimizing their use and distribution, and developing new antimicrobials, diagnostic technologies, and medical countermeasures to treat pathogenic microbes (Weldon et al. 2022). And in relation to the critical problem-solving approach elaborated above, these two needs should be pursued with one eye on finding strategies that can respond to urgent problems emerging within the current configuration of human-microbial relations, and another eye on adapting to transform this configuration to mitigate the deeper drivers of AMR in the first place (Hoffman, Bakshi, and Rogers Van Katwyk 2019).

The challenge is that to date, AMR governance institutions – embodied by a decentralized regime complex for AMR governance – have emerged with an emphasis on building the capacity needed to solve problems in the socio-political and economic world. Not

only has this aim resulted in a system of governance that is unable to achieve the related goals of sustaining antimicrobial effectiveness and promoting global health for all, but they have also resulted in governance systems that are out of sync with fundamental ecological characteristics of the issue that they are trying to govern. Overcoming these limitations will require reconceptualizing the nature of health problems like AMR and how we address them (Jørgensen et al. 2020; Rochford et al. 2018; Chandler 2019).

Instead of trying to create institutions that solve problems and maintain the status quo of human social systems, we need new systems that can sustainably order and guide human-microbial co-evolution into the future (Jørgensen et al. 2020). The unsustainability of any antimicrobial therapy in the face of inevitable microbial resistance highlights the need for new ideas to change social practices (Denyer Willis and Chandler 2019; Weldon et al. 2022; Jørgensen et al. 2020). These ideas, which inform and shape the way we think about AMR, must sufficiently address the enduring and inevitable nature of the problem and the ways that human activities accelerate adaptive microbial behaviors. Innovation for new antimicrobials will not be enough on its own. While the current pace of antimicrobial innovation needs to be accelerated, without changes to the systems in which antimicrobials are used, this new pace would need to be maintained or accelerated again to keep pace with the rising demand for new therapies.

The process of AMR is inevitable and enduring, but the ways that it manifests as social problems is contingent on the prevailing configuration of human activity and microbial life. As this configuration changes, new institutions must guide human cultural evolution so that it adapts alongside the innate evolutionary tendencies of microbial ecologies. The endeavor to achieve this level of sustainability and adaptability must acknowledge the extent to which existing systems of antimicrobial use accelerate the biological process of microbial evolution and, with it, the

problem of AMR. Specifically, the use of antimicrobials as quick fixes to paper over shortcomings in human health, labor, and agricultural systems has created a global social system that overuses, misuses, and abuses antimicrobials at a rate that is diminishing the resource faster than it can be replenished. Social systems that fit with the evolutionary tendencies of microbial ecologies must, therefore, reduce the demand for antimicrobials in the first place. Among other things, this will require greater investments in hygiene and sanitation, addressing global poverty, and transforming the conditions under which people live and work more broadly. Otherwise, it would be like treating the symptom and not the underlying illness.

Where past institutions have failed to sufficiently manage the dynamics of human-microbial co-evolution, new approaches and policies are needed. Yet, in recognizing a knowledge gap around the exact form of these needed mechanisms, the first step is to generate strategies that can guide their development. Fortunately, it is possible to draw lessons from biodiversity management, where the shift to govern co-evolution is well underway. Learning from biodiversity governance, three interrelated strategies to improve the ecological fit of global health institutions are 1) adopting a mantra of trial and error, 2) diversifying practices, and 4) pursuing stakeholder-led policy experiments.

1) ***Social learning-by-doing guided by a mantra of trial and error.*** Developing more fitting institutions will require normalizing policy experiments, failures, and revisions. In the absence of known policies and approaches, social learning within the broader context of human-microbial co-evolution is needed to drive knowledge generation and evaluation. Current trends in biodiversity management demonstrate that normalizing policy experiments by embracing a mantra of trial, error, and revision can balance the dual

needs of urgent action under conditions of uncertainty and progress toward long-term sustainability (Folke, Colding, and Berkes 2003; Olsson et al. 2007).

2) ***Diversifying practices.*** Relatedly, these policies experiments should seek a wide range of diversified practices. Similar to how biodiversity improves the likelihood of ecosystem resilience, diversity in social systems can unlock multiple pathways to success, generate resilience, and help create and sustain system-wide adaptability and flexibility (Plummer and Armitage 2007). It also enables the creation and implementation of location specific policies, recognizing that there is no one-size-fits-all approach to address AMR across time and space.

3) ***Stakeholder led rules that are flexible, adaptable, and resilient.*** By focusing on mobilizing collaboration across scales of activity, new strategies should aim to build trust, resolve conflicts, and build adaptive capacities through a combined process of institutional development and social learning (Armitage et al. 2009). Rather than command and control modes of governance, principles and techniques from adaptive co-management may help improve the fit between AMR governance institutions and the ecological features of AMR. They could help by improving cross-scale linkages including information flows, flexibility, innovation, and adaptive capacity.

These strategies have helped policymakers design institutions for biodiversity that are more adept at managing complex challenges over time (Armitage et al. 2009). AMR governance needs new approaches, and these strategies can guide the creation of new policies that are focused on improving the sustainability of effective antimicrobial treatments as the human-microbial relationship continues to evolve. For example, they can help improve the ecological fit of governing institutions and their ability to respond to AMR as a complex socio-ecological

problem. They can also help to generate much needed intersectoral contingency plans that can increase the likelihood of effectively responding to the cascading effects of today's interlinked problems. Indeed, improving the ecological fit of AMR institutions will require recognizing how AMR is functionally interdependent with climate change, zoonotic disease, and biodiversity loss. To adequately fit the problem of AMR, governance mechanisms must further unite the regime complex and create institutional linkages that reflect AMR's ecological interdependence with these other challenges.

Whatever approach is taken to improve the ecological fit of AMR institutions, the same political questions remain about the purpose of global health governance and who gets to participate in determining it. Additionally, the strategies mentioned above raise further questions about how success is determined and how valid knowledge gets generated and accepted. Indeed, global health governance must continue to confront these questions since any attempt to govern AMR globally requires a conception of the global public and its objectives, and the process of determining valid knowledge can occlude relevant and location-specific ways of knowing. Some tangible steps have been previously identified, which can help ensure that questions about 'who participates, how, and for what purposes' are answered justly and inclusively in any future global AMR institution. For instance, Weldon et al. (2022) argue that an inclusive global multistakeholder forum and evidence panel could address these political issues head-on by recognizing the inherently political nature of global policymaking and knowledge generation, while committing to a process of equitable goal setting, evidence generation, and policy prioritization through an inclusive global dialogue (Weldon et al. 2022; Tripartite Joint Secretariat on Antimicrobial Resistance 2021; Woolhouse and Farrar 2014).

The implications of this analysis also add new dimensions to the challenge of sovereignty in the Anthropocene, as the social construct continues to contradict the interdependence and interconnectedness of global ecological processes. The many misfits identified here underscore how the principle of sovereignty belies the world's shared vulnerability to infectious disease, as demonstrated by the myriad pathways through which humans, animals, and microbes travel around the world and put all countries at risk. Yet, it is in this very system where immediate solutions will have to be pioneered and implemented by states. Thus, while the strategies outlined above emphasize the need for including non-state actors and recognizing the power imbalances that exist within the prevailing order, the current problem of AMR remains both a problem of and for this system of sovereign states. It is here that the assumption about the fixity of the current state-system, which this chapter initially made to generate solutions for AMR in the current conjecture, must be contextualized within the changing order of human-ecological relations to not reify this system's existence. Indeed, the most fitting relationship between human societies and microbial ecologies may involve new forms of social organization beyond those that currently exist.

Finally, it is important to note that the principles and norms of global health, including the principle of state sovereignty, represent deep-seated conceptions about what is right, desirable, and true for the current architects and beneficiaries of global politics. There is a growing awareness that the principles and norms that underlie our understanding of global health problems often limit the horizon of possible policy responses to those problems (Fehr and Fischbacher 2004; Nyborg et al. 2016). Essentially, they act like lynchpins that hold together the paradigms that people use to make sense of the world (Hall 1993). As such, they are not easily changed, but, crucially, they are also not entirely fixed. And while the specific levers that can

initiate their transformation are unclear, the contradictions in today's prevailing principles and norms merit attention because they represent the ruptures through which new norms and principles may emerge.

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 health governance is serving. But the question also directs our attention in a particular way by pre-empting 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 chapter 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 co-evolution with microbes within planetary systems, 2) minimize the socio-ecological 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 study 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 rules, norms, principles, and procedures by which AMR is globally governed and drew a series of lessons from biodiversity, suggesting that not only is it possible to identify opportunities to tweak the prevailing rules, norms, principles, and procedures by which AMR is currently governed, but it also opened a space to consider new ideas prompted by calls for co-evolutionary governance. Additionally, by adopting a core international relations concept to examine the global social systems emerging around AMR, this chapter sought to help bridge international relations' relative silence about the salience and intensity of today's many pressing ecological challenges, as pointed out by international relations scholars (Agathangelou 2021; Burke et al. 2016). Ultimately, 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.

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Chapter 5: Toward a Safe Antimicrobial Operating Space for Humanity

Chapter Abstract

The Anthropocene is characterized by humanity's escalating interplay with natural systems, ranging in size from miniscule parts of the cell to the planet and its surrounding space. One of the challenges arising from these interactions is antimicrobial resistance (AMR), a growing crisis for humans and human treated animals and plants that underscores the complexity of our relationship with the microbial world. As we use antimicrobials to transform microbial ecosystems, our actions trigger far-reaching and dangerous repercussions on human health and survival. To conclude the dissertation, I propose a new model for understanding and managing AMR. The model defines a safe antimicrobial operating space for humanity, which balances essential human needs and planetary boundaries. Inspired by Kate Raworth's "doughnut economics", the models' safe operating space represents the finite zone in which humans can sustainably use and enjoy antimicrobial effectiveness to support our collective health, wellbeing, and development. The safe antimicrobial operating space has two boundaries: an outer ecological ceiling representing the global maximum for allowable antimicrobial usage, and an inner social floor establishing the minimum baseline for universal antimicrobial access. Akin to a planetary boundary, crossing either limit exposes humanity to dangerous risks associated with abrupt, unpredictable, and irreversible shifts in microbial ecosystems. With a minimum threshold for access, this model seeks to address our Anthropocene paradox of AMR more explicitly, which is characterized by simultaneous overuse and under-provision of antimicrobial drugs globally. The chapter explores the need for robust, polycentric institutions that nurture adaptability, flexibility, and resilience to support sustainable antimicrobial use. This conclusion is an urgent call to redefine our relationship with the microbial world, as we navigate our anthropogenic impacts on the delicate stability of Earth's ecosystems – both vast and microscopic.

Introduction

Antimicrobial resistance (AMR) occurs when microbes, including bacteria, viruses, fungi, and parasites, develop resistance to the drugs and substances designed to kill them or prevent their spread. This natural evolutionary process is accelerated by human actions, especially the use of antimicrobial drugs, such as antibiotics, antivirals, antifungals, and antiparasitics. The same antimicrobial drugs are used across many sectors of human activity, and microbes, including resistant ones, spread quickly across humans, animals, the environment, and the planet. Resistant microbes, even those that initially emerge in animals and the broader environment, often make vital human medical treatments less effective or even completely ineffective in healthcare settings. In 2019, over 1.27 million people worldwide died due to untreatable, drug-resistant infections caused by AMR (Murray et al. 2022). If left unaddressed, AMR could result in up to 10 million deaths per year by 2050, more than the current toll caused by cancer (O'Neill 2016).

In addition to this catastrophic loss of life, AMR underscores the ongoing challenge of navigating our co-evolution with microbes in the Anthropocene era. As we alter invisible microbial worlds, our actions precipitate non-linear transformations and dangerous shifts in their biologies, which, in turn, can boomerang and impact us in profound ways. The COVID-19 pandemic exemplifies this conundrum, as the virus and its variants continue to evolve and subsequently evade vaccinations (Liu et al. 2022).[23] Similarly, disease-causing bacteria and fungi also persist in adapting and developing resistance to our treatments (York 2021). These ongoing and inevitable challenges indicate a need for innovative global policy solutions to manage the enduring and complex relationship between humans and microbes.

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[23] I wish to thank Roojin Habibi for helping me make this connection.

To this end, this aspirational chapter concludes the dissertation by looking toward a future of sustainable human-microbial interactions, drawing upon and synthesizing ideas from previous chapters. It revisits and reframes the social challenges of access, conservation, innovation, and prevention around the transversal challenge of achieving equity in AMR policy, as first introduced in Chapter 1. It also leverages and applies the granular and precise diagnosis of collective action problems for AMR governance derived from Chapter 2. Drawing on Chapter 3, this conclusion advocates for a polycentric approach with minimal but necessary centralization across the vast regime complex for AMR governance. Finally, building on the socio-ecological perspective elaborated in Chapter 4, it proposes durable and fitting institutions for governing the perennial challenge of evolving human-microbial relations.

Building on the conceptual groundwork advanced by the dissertation, this conclusion proposes a new, exploratory model that views AMR as an emergent feature of humanity's transformation of planetary ecologies. By adopting this perspective, the model is able to incorporate and extend Kate Raworth's (2017) ideas on the crucial challenge of balancing essential human needs within finite planetary boundaries – a concept known as "Doughnut Economics". Applying these ideas to the challenge of antimicrobial resistance, the model presented in this chapter defines a safe antimicrobial operating space for humanity and planetary health.

The safe operating space, depicted as "a doughnut" in Figure 5.1, represents the finite zone in which humans can sustainably use and benefit from antimicrobial effectiveness to support our collective health, wellbeing, and development. On the outside, the doughnut is bounded by an ecological limit representing the global maximum for allowable antimicrobial usage. On the inside, the doughnut is bounded by a minimum social limit establishing the

baseline for universal antimicrobial access. Akin to the planetary boundaries proposed by Rockstöm et al. (2009), transgressing either limit exposes humanity to dangerous risks associated with abrupt, often unpredictable, and irreversible shifts in microbial ecologies. Importantly, the safe operating zone encompasses all sectors of human activity, from human health to animal health and agriculture. I propose that this imaginary doughnut is an ideal that signifies our commitment to sustainable practices across these sectors, preserving the effectiveness of antimicrobials for current and future generations.

Unlike existing models focusing solely on maximum boundaries for use (Living with Resistance project 2018), this model includes a minimum boundary for access as both an imperative matter of equity and an integral component of effective mitigation strategies (Årdal et al. 2016; Laxminarayan et al. 2016). With this explicit emphasis on bridging the antimicrobial access gap, I argue that this new framing better captures the complex and dynamic challenges of AMR and can therefore guide better, more equitable policy.

In presenting this new model, my objective is not to define quantitative thresholds. Instead, I aim to conceptually inform debates surrounding planetary boundaries for antimicrobial use. Antimicrobial drugs and substances, used across various sectors of human activity, are potent technologies that transform microbial ecologies. Through these antimicrobials, humanity wields the power to reshape our relationship not only with these microorganisms, but also with other animals, plants, and our shared planetary environment. However, the use of antimicrobials carries significant risk – it is akin to playing with fire. If misused and poorly managed, antimicrobial medicines lose their effectiveness, resulting in harmful consequences such as the 1.27 million lives lost annually to formerly treatable infections. Simultaneously, safeguarding human, economic, and animal welfare calls for greater effort to improve the situation of the

nearly two billion people who still live and die with limited access to essential medicines (Ozawa et al. 2019). Considering these disparities, the model introduced here seeks to address the prevailing social paradox of AMR more explicitly, which is characterized by simultaneous overuse of antimicrobial drugs in some settings and under-provision of antimicrobial drugs in other settings (Hoffman and Outterson 2015).

After providing background on evolving human-microbial relations, this final chapter illustrates "the doughnut model" and conceptually defines a safe antimicrobial operating space for humanity (Figure 5.1). It then demonstrates how the doughnut model can illuminate institutional design principles and techniques for managing antimicrobial use in the Anthropocene. Eight principles are considered to sustain the safe antimicrobial operating space for humanity across global institutions, countries, sectors, populations, and timeframes. These early formulations are presented as a basis for future stakeholder consultation. A brief conclusion ends the chapter and dissertation.

Part 1: Human-Microbe Relations

Microbes are all around us, forming the ecological foundation that shapes human societies and playing a crucial role in our lives. In fact, our bodies regularly contain more microbes than human cells (Sender, Fuchs, and Milo 2016). These microbes often provide symbiotic benefits, such as aiding digestion and enhancing our health (Dethlefsen, McFall-Ngai, and Relman 2007). Interestingly, many of the antimicrobials that we use to fight infections originate from natural substances produced by microbes themselves, which help them compete with other microorganisms (Clardy and Walsh 2004). For example, some bacteria and fungi produce antibacterial substances that we harness to combat bacterial infections, while some

bacteria produce antifungal compounds that we use to treat fungal infections (e.g., the antibiotic *Penicillin* comes from a fungus and the antifungal *Amphotericin B* comes from a bacterium).

Although many microbes are beneficial, some can cause diseases. Throughout history, humans have been vulnerable to these disease-causing microbes. However, recent advances in science, social policy, and public health have improved our ability to survive these germs (Greenwood 2014; Armstrong 1999). Key milestones in these advances include Jenner's smallpox vaccine in 1796, Snow's identification of cholera spread via public infrastructure in 1854, and Fleming's discovery of penicillin in 1927. These breakthroughs, alongside investments in public health and water and sanitation management, better nutrition, and improved living and working conditions, have significantly curbed the impact of infectious diseases in high income countries. However, in many low-income and middle-income countries, antimicrobials are used as substitutes for these other, more costly health improvement measures (Laxminarayan et al. 2016).

In the past century, modern antimicrobials in particular have greatly expanded our ability to intervene in the invisible worlds and complex affairs of microbes. Yet, these advances have only transformed, not ended, our co-evolution with them. Microbes continue to evolve in response to human action, necessitating similar and constant adaptation from human populations. This relationship is especially apparent with antimicrobial use, as this human intervention triggers microbial evolution that, in turn, affects humans through AMR.

The challenge is that we have built social structures centered around effective antimicrobials, using them to paper over shortcomings in labour, care, and land practices and to tailor microbial ecologies for specific human activities like industrial farming (Kirchhelle 2019; Denyer Willis and Chandler 2019). Unfortunately, we often act as if antimicrobials have

permanently tamed microbes, while ignoring the consequences of our actions in pursuit of abundance, productivity, and profits. In reality, the effectiveness of all antimicrobial interventions is limited due to the constant evolution of microbes (Ventola 2015). The effort to avoid squandering these precious resources and diminishing our ability to treat infectious diseases entails a recognition of this fact and a commitment to adapt our social structures and practices accordingly (Jørgensen et al. 2020).

In essence, through antimicrobial overuse and underuse, as well as inadequate innovation and prevention, human societies are accelerating microbial evolution from predominantly symbiotic to predominantly pathogenic. Addressing these challenges is crucial for ensuring a sustainable future for both humans and microbes alike.

Part 2: The Safe Antimicrobial Operating Space for Humanity

To ensure a healthy future for human-microbial co-evolution, maintain the viability of antimicrobial treatments, and protect human health and wellbeing in the Anthropocene, it is crucial that social systems of antimicrobial use stay within the limits of a safe operating space for humanity. This safe antimicrobial operating space can be illustrated as a doughnut, where insufficient antimicrobial provision transgresses the inner social floor, and excessive provision transgresses the outer ecological ceiling (Figure 5.1). Given that microbes can spread easily across humans, animals, plants, and the environment, the safe operating space encompasses all One Health domains, including human, animal, and environmental sectors of human activity.

Mitigating the emergence and risks of drug-resistant pathogens requires striking a balance between access to and conservation of antimicrobial resources (Hoffman et al. 2015). Both access and conservation represent critical strategies to avoid transgressing the doughnut's boundaries, which are characterized by non-linear, socio-ecological tipping points (i.e., distinct

moments capable of catalyzing dynamic causal chains or triggering irreversible shifts when crossed). These tipping points exist across microbiological, ecological, and human societal scales. The emergence of resistance, for instance, represents a biological tipping point. Meanwhile, the moment at which resistant infections become more probable than not represents an ecological tipping point. Crossing these thresholds can precipitate a dramatic change in human societal practices – a social tipping point – where, for example, surgeries may be frequently forgone due to the heightened risk of resistant infections.

Figure 5.1A: The Safe Antimicrobial Operating Space for Humanity

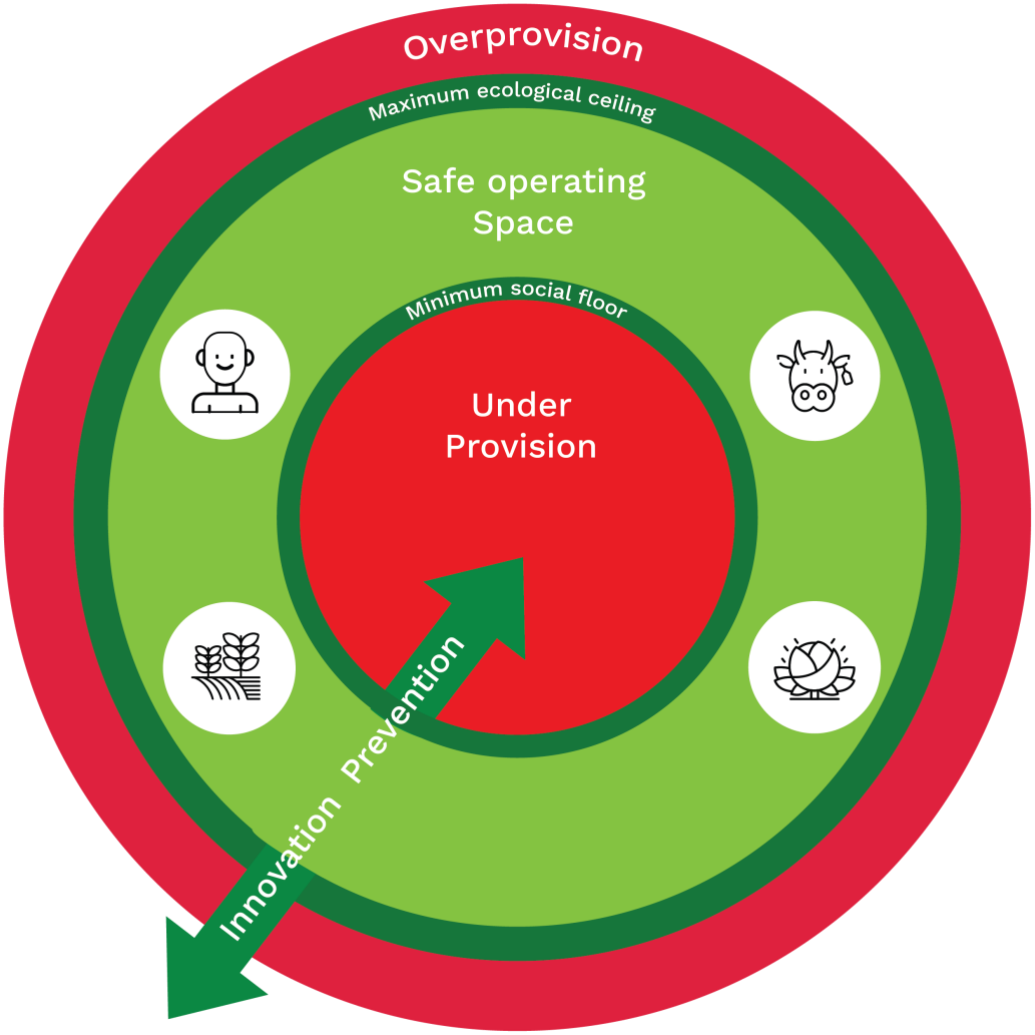
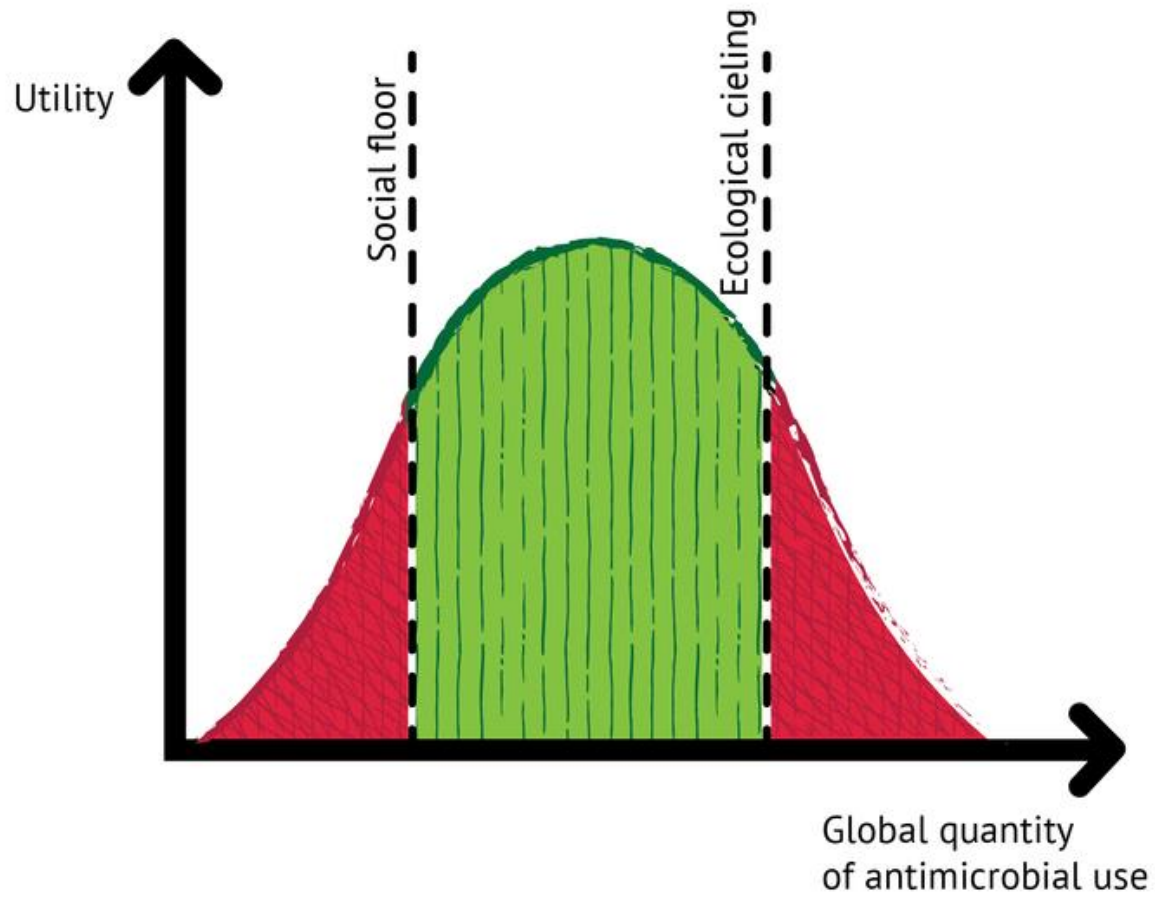


Figure 5.1B: Stylized Cross-Section of the Safe Antimicrobial Operating Space



These tipping points can be breached when antimicrobials are either under or over-used. On one hand, inadequate provision of antimicrobials can lead to the spread of resistant infections and increased mortality rates (Murray et al. 2022). Limited access to effective antimicrobials can also contribute to inappropriate use, which accelerates the development and spread of AMR (Laxminarayan et al. 2016).

Conversely, overprovision of antimicrobials diminishes the resource, with poor coordination and excessive environmental contamination increasing the likelihood of resistance development (Roope et al. 2019). For instance, the use of biosimilar antifungals in crop farming and human medicine has contributed to the rise of resistant fungi that no longer respond to

treatment in hospitals, leading to increased human fatalities (McKenna 2023). In other words, both insufficient and excessive use across populations and sectors render us vulnerable to the consequences of microbial evolution, which manifest as severe health threats such as the emergence of deadly disease variants. Navigating the balance between access and excess poses a complex dilemma, making the safe operating space inherently precarious (Sugden, Kelly, and Davies 2016).

Ensuring universal access to avoid transgressing the inner limit presents a global social challenge. It requires mechanisms to ensure that all individuals have access to a minimum threshold of antimicrobial resources (Årdal et al. 2016). Specifically, improving access globally represents a "weakest link" collective action problem, where the collective outcome is determined by the circumstances of its most vulnerable members. It only takes the emergence and spread of one resistant microbe to undermine the efforts of all – and this is likely to occur in places with poor antimicrobial access where resistance burdens are highest.

Determining who should pay to improve global access and their motivation for doing so remains a complex social issue, influenced by the lingering effects of colonialism and current inequitable economic systems. The fight against malaria serves as an example of the importance of and potential for global cooperation in addressing antimicrobial access, where global initiatives such as the Global Fund to Fight AIDS, TB, and Malaria provide resources to ensure access to antimalarial drugs and preventative tools and strategies in affected regions. Although it may not be in a single person, firm, or country's immediate self-interest to pay for products that they do not immediately benefit from (i.e., paying for someone else's medicine), the positive externalities provided by universal access for all (e.g., reduced prevalence and risk of resistance)

means that it is in everyone's best interest and the collective interest of global society to work toward proving a basic minimum level of antimicrobial access everywhere.

Simultaneously, the social challenge of antimicrobial conservation resembles a global "tragedy of the commons," where limiting individual use is necessary to preserve the collective benefit of sustained antimicrobial effectiveness (Rogers Van Katwyk et al. 2020). This predicament demands collaborative management of the resource to prevent overuse and maintain antimicrobial effectiveness over the long run (Roope et al. 2019).

The size of the metaphorical doughnut, representing the safe operating space, is primarily determined by our ability to balance universal access with conservation of the common-pool resource of antimicrobial effectiveness. Where every use can subtract from the overall stock, sustainability demands that global consumption does not exceed provision. Each use of an antimicrobial, even when prudent and necessary, potentially diminishes this precious and shared resource. Therefore, continuous innovation is essential for replenishing and maintaining the supply of effective antimicrobials (Outterson et al. 2016). Innovation encompasses research and development for new antimicrobial drugs, alternative treatments, diagnostic measures, and social techniques. Collectively, these innovations expand the Doughnut Model's green circle outward, extending the safe operating space and counteracting the microbial evolution that reduces it.

Yet, supporting innovation presents a volunteer's dilemma, raising the question of who should bear the costs of research and development. Although only a few entities need to continually supply new technologies and techniques, all have an incentive to wait and free ride off the efforts of others (Hoffman et al. 2015). Overcoming this dilemma will require mechanisms for coordination and collaboration to distribute responsibilities and burdens globally and equitably.

The market serves as one such mechanism for coordinating investments and distributing rewards for innovation, but it has proven ineffective in maintaining a steady supply of antimicrobials, diagnostic measures, and alternative treatments (Outterson et al. 2015). The pharmaceutical industry's monopolistic tendencies and the time limited monopolies inherent in Intellectual Property Rights, coupled with the inherent market failures associated with the development and production of these essential goods, have resulted in persistent innovation challenges throughout the antimicrobial era. Consequently, government programs, like sponsorships and prizes, have been responsible for producing most of the antimicrobial drugs currently available (Quinn 2013). Similar, global, non-market programs could be warranted to overcome the volunteer's dilemma for innovation, distributing the associated burdens and benefits equitably (Singer, Kirchhelle, and Roberts 2020).

The persistent challenges and inefficiencies in market-driven mechanisms underscore the need for social innovation in AMR management, including novel drug development models. Indeed, scientific innovation for new antimicrobials, while crucial, will not likely suffice on its own. Without deeper changes that affect antimicrobial demand, facilitated by innovative social and behavior-altering techniques, the present (and currently unmet) pace of antimicrobial innovation would need to be continuously maintained or further accelerated to keep pace with rising demand for new treatments.

Preventive measures are therefore essential to reduce antimicrobial demand and increase the likelihood of achieving sustainability (World Health Organization 2012). By implementing prevention strategies, the safe operating space can be extended as the green doughnut expands inward, decreasing the need for antimicrobials (Figure 5.1). Like ensuring access, prevention presents a weakest link challenge, where the effectiveness of global prevention efforts is only as

strong as the most vulnerable point in the system. Comprehensive and collaborative measures to prevent the need for antimicrobial use globally can enhance the sustainability of AMR efforts.

In summary, sustaining the safe operating space requires the effective use of four strategies: 1. achieving universal appropriate access, bringing everyone over the minimum threshold and into the safe zone; 2. supporting appropriate use and conservation, which prevents the transgression of the outer ecological limit; 3. investing in innovation to continually supply antimicrobials at a pace greater than the diminishing rate caused by use; and 4. bolstering infection prevention and innovation for alternatives to reduce the demand and use of antimicrobials. By balancing these four strategies, we can work towards a more effective, equitable, and sustainable approach to managing antimicrobial resistance, ultimately protecting human, animal, and environmental health in the Anthropocene.

However, tackling these areas poses a colossal challenge, necessitating profound, structural, and systemic changes in human societies (Chandler 2019). As with climate governance, individual behaviour-changing strategies alone are insufficient for mitigating and adapting to the risks of AMR (Weldon et al. 2022). We require a collective effort guided by innovative principles and techniques for social transformation, ensuring a just transition to a global social system that supports sustainable antimicrobial use for all.

Employing these strategies on a global scale demands a collective effort to craft and nurture responsive institutions. In an era where human medicines are failing against microbial evolution, there is a need to move beyond the allure of simplistic quick fixes. Instead, our focus should turn toward guiding human cultural adaptation alongside microbial evolution, which requires searching for comprehensive, institutionally grounded approaches rather than silver bullet solutions. Fortunately, history is replete with examples of success in response to failure,

where outcomes have been shaped by the quality of institutional design. Over the long term, robust institutions can equip us to maintain the safe operating space and effectively adapt to the multifaceted risks of AMR.

Part 3: Institutional Design Principles for Sustainable Antimicrobial Use in the Anthropocene

The finite lifespan of all antimicrobial substances, which inevitably lose their effectiveness as microbes evolve, highlights the pressing need for social and structural change to facilitate ongoing mitigation, adaptation, and management. To help achieve this collective effort, the doughnut model representing the safe operating space can help chart a clear roadmap for guiding antimicrobial use in the Anthropocene. Specifically, it offers a concrete platform to connect and extend the extensive literature on crafting institutions for sustainability, including Elinor Ostrom's Nobel Prize-winning work on managing common pool resources (1990). Drawing on her insights as a starting point, the safe operating space illuminates a new outlook on eight fundamental principles for institutional design. As early formulations, the application of the doughnut model to these eight principles are meant to engage future consideration on concrete empirical consideration and content development through appropriate stakeholder consultation.

Table 5.1: Institutional Design Principles for the Safe Antimicrobial Operating Space

Institutional Design Principles	The Safe Antimicrobial Operating Space
1) Clearly defined boundaries	Defining boundaries is crucial in managing shared resources. The doughnut model offers a clear conception of the social floor and ecological ceiling that confine the safe antimicrobial operating space for humanity in the Anthropocene. Given the wide variations in antimicrobial usage worldwide, interpreting and measuring these definitions is a complex task.
2) Congruence between appropriation and provision rules and local conditions	The doughnut model, with its emphasis on a social floor and an ecological ceiling, allows for local adaptation when balancing necessary strategies. The model enables location specific

	priorities, where some places may have poor access to antimicrobials and other may overuse them.
3) Collective-choice arrangements	The doughnut model signifies one shared safe operating space for all sectors of human activity, including human healthcare, animal healthcare, and agriculture. In highlighting this interconnectedness, it emphasizes the need for collective, intersectoral, and inclusive approaches to participatory decision making.
4) Monitoring	The doughnut model can be used to define clear thresholds and an opportunity for quantitative metrics to monitor minimal and maximal usage. More research and stakeholder consultation to quantitatively define the thresholds and tipping points for usage is crucial for tracking, monitoring, and evaluating progress.
5) Graduated sanctions and support	The doughnut model visualizes the consequences of transgressing boundaries, necessitating both sanctions and cooperative support, depending on circumstances. The boundaries of the doughnut help conceptualize proportionality for penalties and support.
6) Conflict resolution mechanisms	With the safe operating space being shared among all populations, sectors, and species, the emergence of divergent interests in different time scales, is inevitable; thus, there is a pressing need for cost-effective and efficient methods to resolve ensuing conflicts within this collectively shared area.
7) Minimal recognition of rights to organize	The doughnut model supports this principle by recognizing a shared responsibility across all sectors within its defined safe operating space. It highlights the need for localized strategies, while ensuring alignment with shared global objectives to maintain the safe space's balance.
8) Nested enterprises	The global AMR landscape already features multiple overlapping centers of authority and decision-making. Nested within the doughnut, a polycentric approach can accommodate local contexts and needs, leverage context-specific knowledge from initiatives already in operation, ensure stakeholder and community-led relevance, and promote adaptability, resilience, and flexibility across different scales and locations (Baird et al. 2019).

1) Clearly defined boundaries

The first step in managing a shared resource is defining its boundaries (Ostrom 1990). Having clearly defined boundaries for managing AMR means staying within the ecological ceiling and social floor of the safe antimicrobial operating space as depicted in the Doughnut Model. This principle offers a pragmatic starting point, delimiting the resource and the thresholds after which use becomes unsustainable. Without this clarity, human tendencies can lean toward overuse and exploitation, potentially leading to irreversible harm or total depletion. Experiences from other areas, such as climate and biodiversity governance, indicate that setting boundaries is essential for maintaining ecological balance (Wilson, Ostrom, and Cox 2013). Applied to AMR management, upholding this principle means to explicitly delineate the limits of antimicrobial use that we must not cross to protect health and sustain the effectiveness of these life-saving drugs.

The doughnut model illuminates this principle by conceptualizing the safe operating space for antimicrobial use. Yet, drawing from experience in other domains such as climate governance, these boundaries will need to be defined in practice. This representation also aids in comprehending the complex socio-ecological dynamics of AMR, with a social floor and ecological ceiling confining the safe antimicrobial operating space for humanity in the Anthropocene. The model also provides a clear vision of the balance we must strike between providing adequate access to antimicrobials and conserving their effectiveness to avoid resistance (i.e., a balance between overuse and underuse). Further, it helps to frame AMR as an intersectoral problem involving the health of humans, animals, and the environment. In other words, the finite space is shared by all sectors of human activity, implying a collective responsibility for sustainability.

2) Upholding one basic principle for sustainability by adapting rules to local circumstances

The cornerstone of sustainability is a simple yet powerful commitment: ensure that our global supply of antimicrobials benefits everyone without depleting the stock. In simple terms, we cannot use more than we have, or at a rate faster than we can resupply. The principle of congruence between appropriation and provision rules and local conditions means that the exact way this commitment is upheld can vary across locations, depending on local cultural, social, economic, and ecological conditions (Ostrom et al. 1999). For AMR, this principle implies that strategies for antimicrobial distribution and use should be compatible with the local healthcare system's capacities, the public's health behavior, and prevalent pathogens.

The doughnut model supports local adaptation by recognizing that situations may vary across populations, with some places living below the social floor and others exceeding the ecological ceiling. In the context of the social floor, the model recognizes the universal need for essential resources like antimicrobials, while simultaneously acknowledging that the methods for achieving universal access might differ based on local socioeconomic conditions, infrastructure, and cultural norms. On the other hand, the ecological ceiling identifies the boundary beyond which antibiotic use becomes dangerous. Importantly, it recognizes that this boundary is based on unique social and ecological environments in different regions. This dual, socio-ecological emphasis enables the doughnut model to offer an adaptable and responsive framework, capable of addressing local complexities.

3) Arranging for intersectoral participation and collective choice

The third principle, collective-choice arrangements, highlights the significance of engaging all relevant stakeholders in decision-making processes that directly affect them. This

principle advocates for a democratic approach that seeks effective, equitable and sustainable governance to reduce AMR, enabling those impacted by specific rules to influence their modifications. In managing shared resources such as antimicrobials, incorporating the perspectives of diverse stakeholders often leads to more robust, effective, and contextually sensitive policies, promoting greater compliance and better overall outcomes (Ostrom et al. 1999). In the context of governance to reduce AMR, this principle calls for the involvement of a wide range of actors – from patients and healthcare professionals to policymakers and agricultural stakeholders – in shaping regulations surrounding antimicrobial use and conservation.

The doughnut model, through its depiction of a single and unified safe operating space for all – encompassing human health, animal health, and agriculture – underscores the profound interconnectedness of these domains. This integrated perspective is critical as it emphasizes how decisions in one sector invariably affect the others. This inherent interdependence of different sectors within the model's single safe zone accentuates the need for inclusivity and cross-sectoral collaboration. By underscoring this interconnectedness, the doughnut model serves as a visual endorsement for collective, intersectoral approaches to decision-making, thereby strengthening the application of the collective-choice arrangements principle in the governance of AMR.

4) Measuring the safe operating space, its thresholds, and its tipping points

Effective management of any shared resource depends on our ability to measure it and monitor its rate of depletion (Freeman III, Herriges, and Kling 2014). This principle holds true in climate governance, a notable example of global common-pool resource management. In climate governance, hard metrics can help motivate action and offer clear indications of progress, such as total atmospheric carbon mass and maximum average temperature increases. Despite the world

falling short of these targets, the very existence of such metrics offers a roadmap for climate action, a necessity not yet available to support AMR governance. Without analogous metrics, our knowledge of the safe antimicrobial operating space remains hazy, and the resulting ambiguity enables contestation over distributions of responsibility.

Currently, empirically defining the safe antimicrobial operating space proves challenging. On one hand, conceptually defining the minimum social threshold to ensure universal access is only somewhat straightforward. For example, we can estimate the number of individuals without antimicrobial access. However, the upper ecological limit is currently elusive. Without concerted research efforts to identify microbial and ecological tipping points, as well as concrete metrics to measure progress, our understanding will remain inadequate to effectively manage the sustainability of antimicrobials. Worse yet, we risk discovering that we have crossed these microbiological and ecological tipping points only after witnessing profound social changes, far too late for effective intervention. Though we have yet to reach a social tipping point, this does not imply that we have not already crossed a microbiological or ecological one. We simply do not know. To continue down our current path is akin to navigating a tightrope in a dark room. Armed with scientific insights to concretely define the limits of the doughnut model, however, we can illuminate the path ahead.

5) Enforcing rules and supporting each other

The fifth of Ostrom's principles, which usually emphasizes rule enforcement, can be broadened to encompass not only enforcement but also support mechanisms. Empirical research on successfully managing shared resources highlights the effectiveness of mechanisms that enforce rules and support actors who struggle to comply with them (Ostrom 1990). While enforcement strategies have been shown to be effective in international law (Hoffman et al.

2022), fostering support and resource sharing is equally vital, given our shared global vulnerability to resistant microbes. Some actors may break rules, not out of disregard, but due to resource limitations that prevent the implementation of cost prohibitive measures. Therefore, it is critical to establish financial and technical support mechanisms to ensure that all can adhere to the rules and adapt to the risk of AMR.

The doughnut model, by displaying a shared safe operating space for all human activity, highlights our shared vulnerability and can promote collaboration, resource-sharing, and mutual support. By adopting an explicitly non-human centric focus, valuable insights to support each other for adaptability can be drawn from unconventional sources, such as the extraordinary evolutionary traits exhibited by microbes themselves. For instance, microbes can rapidly adjust to environmental changes like exposure to antibiotics, as seen in the rapid development of multi-drug resistant bacteria in hospitals. By sharing genetic resources, microbes bolster community-wide resistance against human interventions. In contrast, and as demonstrated by the persistent inequitable distribution of COVID-19 vaccines, human social systems often display selfishness and institutional inertia that resist change, which often exacerbates health crises. By examining the remarkable characteristics of microbes, we can learn not only about their ecology and evolution but also about fostering cohesion, compassion, and resource sharing in social spaces. The socio-ecological perspective of the doughnut model offers a means to consider such strategies to stay within socially and ecologically acceptable limits.

6) Resolving conflicts

The sixth principle emphasizes the importance of conflict resolution mechanisms when managing shared resources. When we consider the complex and interconnected challenges of antimicrobial resistance (AMR), conflicts are inevitable. These conflicts might arise between

different sectors such as healthcare, agriculture, and pharmaceutical production, or among nations with varying levels of economic development, health systems capacities, and AMR burdens. The key is not to avoid conflict, but rather to have robust, fair, and efficient mechanisms in place to address disagreements when they arise. Conflict resolution mechanisms help to maintain trust among stakeholders, prevent escalation of tensions, and ensure that collaborative efforts toward sustainable antimicrobial use are not undermined by disagreements (Ostrom 1990).

The doughnut model's representation of a shared, safe operating space for all human activities is an effective platform for understanding and addressing conflicts. The model visualizes the interconnectedness of all sectors – human health, animal health, agriculture, and the wider environment. It underscores the fact that our fates are tied together within this shared space. Therefore, every conflict that arises, whether between sectors or within them, is not just an isolated problem but a shared challenge that impacts our collective ability to sustain the safe operating space. This understanding of interconnectedness can help foster a sense of shared responsibility, encouraging stakeholders to participate in conflict resolution in a constructive and collaborative manner. Instead of promoting a zero-sum game, where one sector or nation's gain is another's loss, the doughnut model encourages a perspective that values synergistic solutions, understanding that our collective success in preserving this safe operating space depends on our ability to work through conflicts together.

7) Rights to organize

The seventh principle, minimal recognition of rights to organize, emphasizes the need for external authorities to acknowledge and respect the rights of local institutions to devise their own rules regarding the use of common resources. This principle is vital for ensuring that local

institutions have the autonomy and empowerment to devise rules that fit their unique circumstances while respecting collective goals of effective, equitable and sustainable governance of AMR. When applied to AMR, this principle underscores the need for international bodies, national governments, and industry regulators to recognize and respect the rights of local health communities to devise their own rules and strategies for antimicrobial usage.

By acknowledging a shared social foundation and an ecological ceiling, the model suggests that different sectors and communities have the right to organize within these boundaries in a way that suits their specific needs and contexts. The challenge lies in ensuring that the strategies and actions taken at the local level align with and respect the shared global objectives, thus maintaining the balance within the doughnut's safe space.

8) Polycentric governance for AMR

Finally, the eighth principle, nested enterprises, emphasizes that governance activities should be organized in multiple layers of nested enterprises. It recognizes that complex social-ecological systems are best governed when responsibilities, rules, and decision-making processes are distributed across different scales of organization. In the context of AMR, this principle underlines the need for multi-layered antimicrobial stewardship involving local healthcare communities, national health departments, global health institutions, and even environmental and agricultural sectors.

The doughnut model embodies this final concept of nested enterprises. It proposes a holistic view of our shared safe operating space, within which multiple sectors operate at various scales. For instance, a local health department may focus on restricting the use of specific antimicrobials in local hospitals, while a national policy may concentrate on promoting alternative treatments. Simultaneously, international bodies may be engaged in defining global

norms for antimicrobial usage. At each level, the doughnut model serves as a reminder of the shared safe operating space within which these activities are nested, and the need to harmonize them to avoid transgressing the ecological ceiling or falling below the social foundation. This goal oriented, interconnected, and nested structure of governance within the doughnut model ultimately promotes a collaborative and coordinated approach to manage the challenge of AMR.

Conclusion

The challenge of mitigating and adapting to the risks of increasing drug resistance is immense. Contingent on our success is modern medicine's continued ability to treat infectious diseases and conduct life-saving treatments such as chemotherapies and surgeries. If managed appropriately, we can use antimicrobials to protect human and animal health and judiciously support efficiency in food systems, promoting nutrition with less money, space, and energy in a sustainable manner. If not, we may lose a century's worth of health gains.

As an investigation into the immense challenge of AMR, this dissertation analyzed the politics and planetary relations that emerge across human societies and invisible microbial worlds. In expanding political science and international relations into these microbiological and socio-ecological spaces, it identified gaps, challenges, and opportunities for improving AMR governance. It began by crafting and utilizing a novel framework to analyze the granular social and collective action problems presented by the grand challenge of increasing AMR. It moved on to trace the evolution of today's globalized regime complex for AMR governance, combining theoretical perspectives to investigate the array of principles, norms, rules, and procedures for AMR governance. It proceeded to develop and apply a novel, socio-ecological approach to investigate this decentralized governance structure in relation to the ecological problem characteristics of AMR. This final chapter synthesized these perspectives to analyze challenges

and opportunities for governing AMR in the Anthropocene era. Building on the conceptual work advanced throughout the dissertation, this final chapter defined a safe antimicrobial operating space for humanity, emphasizing how this new framing can guide future policy and institutional design. Throughout the dissertation, parallels were drawn between AMR, climate, and biodiversity governance to enhance the rigour of analysis.

The chapters of the dissertation emphasized the urgent need for equity, sustainability, and effective institutional design to address this complex, pressing and multi-faceted challenge. It has emphasized that current and past policies and practices have contributed to the problem, including the overuse of antimicrobials in human and agricultural settings, the inequitable global distribution of access to antimicrobials, underuse of infection prevention approaches including vaccination, and the inadequacy of existing innovation systems. To move forward toward effective governance of AMR, it is essential to learn from these shortcomings and strive to develop more effective and holistic strategies. This entails a shift in priorities from innovation-centered approaches to an approach that also emphasizes prevention, access, and conservation. Although developing cutting-edge treatments remains essential, these resources are maximally effective only if they continue to work and reach those who need them the most. Sustaining the safe operating space will involve re-evaluating economic incentives for drug development and use, as well as fostering global partnerships for equitable antimicrobial distribution (Access to Medicine Foundation 2022).

However, there are major obstacles for redressing these issues. High usage in some areas, not enough in others, and stagnant innovation pipelines present major challenges. Surmounting these will entail a deeper look at their dynamic causes, which often lie in the forces that structure the way we live and work. For example, our agricultural practices, food production, labor

policies, and economic systems too often depend on antimicrobials as quick fixes for profits, productivity, and abundance (Denyer Willis and Chandler 2019; Kirchhelle 2019; Outterson et al. 2016; Singer, Kirchhelle, and Roberts 2019; Weldon et al. 2022). Re-evaluating these priorities and minimizing these dependencies could provide outsized impacts on antimicrobial sustainability in the long run.

While this chapter concludes the dissertation with an optimistic vision for the future, it is important to balance this optimism with a realistic assessment of the many obstacles involved with transforming social systems of antimicrobial use. Achieving change at this scale will require overcoming significant political, social, and economic barriers. These include navigating entrenched interests and path-dependent structures, mobilizing new funding, and fostering collaboration among a diverse range of stakeholders.

Despite these challenges, there are reasons for cautious optimism. The growing awareness of AMR, the escalating momentum to improve global health governance in the wake of COVID-19, and the increasing recognition of holistic and interdisciplinary approaches are generating opportunities for meaningful change. By prioritizing equitable access and distribution, promoting sustainable antimicrobial use, and designing robust, adaptable, and responsive institutions, we can make progress in addressing AMR.

In the face of a continually evolving microbial ecology, our ability to respond to the threat of AMR will depend on our willingness to set collective action goals, learn from past mistakes, collaborate across sectors and borders, and adapt our social ecology to the dynamic nature of the problem. With a pragmatic sense of optimism, we can achieve a healthier future in which AMR is effectively mitigated, and the safe antimicrobial operating space is preserved for generations to come.

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Appendix A

Statement of Authorship for Inclusion in Dissertation

Title of Study:	Analyzing Antimicrobial Resistance as a Series of Collective Action Problems
Publication Status:	Under Review
Publication Details:	Weldon, I., Liddell, K., Rogers Van Katwyk, S., Hoffman, S.J., Minssen, T., Outterson, K., Palmer, S., Viens, A.M., and Viñuales, J. *Policy Studies Journal*.
Student Name:	Isaac Weldon
Supervisor Name:	Steven J. Hoffman
Contribution Statements:	IW, JV, KL, and SJH conceived the study. IW designed the study, led the conceptual development, and conducted the primary research. IW wrote the initial draft under the supervision of KL. All authors were involved in a series of meetings to extract the collective action problems in Table 2.3. The meetings were co-chaired by IW and JV. All authors provided critical feedback on the manuscript. IW integrated contributions and finalized the manuscript.

Signature:  **Date**: October 3, 2023

Supervisor Confirmation

By signing the Statement of Authorship, I am certifying that the student made a substantial contribution to the publication, and that the description described above is accurate.

Signature:  **Date**: October 3, 2023

Appendix B

Statement of Authorship for Inclusion in Dissertation

Title of Study:	Assessing the Ecological Fit of the Social Institutions that Govern Antimicrobial Resistance: A Socio-Ecological Perspective of Human Societies, Microbial Resistance, and Changing Orders
Publication Status:	Forthcoming
Publication Details:	Weldon, I. and Hoffman, S.J. Assessing the Ecological Fit of the Social Institutions that Govern Antimicrobial Resistance: A Socio-Ecological Perspective of Human Societies, Microbial Resistance, and Changing Orders. (Forthcoming). *Perspectives on Politics.*
Student Name:	Isaac Weldon
Supervisor Name:	Steven J. Hoffman
Contribution Statements:	IW conceived, designed, and performed the study and wrote the initial draft. SJH provided critical feedback, edits, and revisions on the manuscript. IW finalized the manuscript.

Signature:  **Date**: October 3, 2023 October 3, 2023

Supervisor Confirmation

By signing the Statement of Authorship, I am certifying that the student made a substantial contribution to the publication, and that the description described above is accurate.

Signature:  **Date**: October 3, 2023 October 3, 2023