Innovative Policy Approaches for Mitigating Antimicrobial Resistance: Polycentric Systems and the Governance of Antimicrobial Usage

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Abstract

Antimicrobial usage (AMU) by humans and animals is driving a worldwide increase in antimicrobial resistance (AMR). The emergence and spread of AMR can render previously treatable infectious diseases untreatable and is forecasted to significantly increase rates of morbidity and mortality worldwide in the coming years. The World Health Organization (WHO) estimates that, by 2050, 10 million people will die each year from AMR. Despite this, current worldwide efforts in response to AMR and AMU remain shockingly inadequate. The cumulative actions of individuals, organizations, and governments that have resulted in the proliferation of AMR could be classified as a collective action problem or a "tragedy of the commons." Polycentric governance has been suggested to address issues involving the tragedy of the commons, or collective action issues, and this concept offers insights into potential AMR management strategies. In this work, we review and apply polycentric governance concepts to AMU and AMR at the local, regional, national, and transnational levels. We discuss the critical components and issues of polycentric governance systems as they pertain to AMR and AMU, which include learning, experimentation, communication, mutual trust, leakage, inconsistent regulatory initiatives, and free riding. This work offers the first application of polycentric governance systems to AMU and AMR, and its findings could be used to inform decision-making processes by public health experts, researchers, and policymakers to mitigate the public health risks of AMR.

Introduction

Antimicrobial resistance (AMR) is a major global public health threat. Over 2.8 million antibiotic-resistant infections occur annually in the United States, resulting in more than 35,000 deaths each year [1]. Internationally, 700,000 people die annually from drug-resistant diseases, and it has been estimated that this could rise to 10 million deaths per year by 2050 [2]. By comparison, the WHO predicts 250,000 deaths each year between 2030 and 2050 due to climate change [3]. Extensive use of antibiotics in medical care and agriculture has played a notable role in the increased proliferation of antimicrobial-resistant bacteria and genes [4, 5]. The emergence of the 2019 novel coronavirus (COVID-19) pandemic also highlighted the widespread empirical prescribing of antibiotics, with 71% of patients in Wuhan, China, reported to have received antibiotic prescriptions [6]. This exemplifies the need for antibiotic stewardship efforts to mitigate the risk of AMR [7]. As a result of the omnipresent usage of antibiotics by both humans and animals, these medicines are detected in aquatic systems at levels associated with environmental concerns [8, 9], with antimicrobial genes found in wastewater and drinking water [10–12]. Thus, the issues surrounding the governance and management of antibiotics and AMR are numerous, potentially affecting all individuals worldwide and particularly those involved with public, animal, and environmental health.

This essay considers an innovative application of the economic science and policy concept of polycentric governance systems to mitigate the public health problem of AMR. As the key components of polycentric governance have not previously been applied to AMU and AMR, we draw from literature on climate change governance, a similar global issue [13–15]. We propose polycentric governance not only as an attempt to resolve issues related to AMU and AMR, but also as a metric to monitor AMR response and management efforts. Thus, this essay proposes a multifaceted framework for understanding and addressing issues of AMU and AMR.

Background on Polycentric Governance Systems

Antibiotics can be viewed as a "common-pool resource," or a resource which benefits wider society and can be utilized by all individual members of society but whose

benefits for the wider population diminish if self-interest is pursued over the greater social good [16]. If clear rights to these resources are not defined, the common-pool resource can be overused to the detriment of all, resulting in a "tragedy of the commons" [17]. Specific to AMR, the inappropriate use of antibiotics is driven by the cumulative actions of individuals, organizations, and governments, as each makes autonomous decisions to benefit themselves, often without consideration for others [13]. For example, these could potentially include the individual insisting on an antibiotic prescription for a cold, the doctor agreeing to a non-indicated prescription, the farmer adding antibiotics to the feed for their overall healthy animals to stimulate growth, and governments and hospital systems allowing antibiotic use when it is not medically necessary. The extensive and often non-indicated use of antibiotics by individual decision-makers, with the corresponding increase in AMR, has depleted the benefit of antibiotics for all and created a major public health crisis that has a far reaching impact [17, 18].

Addressing global common-pool resource problems, such as AMR, involves polycentric governance, which requires collective action [13, 15, 19]. In polycentric governance systems, different government agencies work at varying levels, interacting to address issues at multiple centers, with semi-autonomous decision-making [20]. "Collective action" describes settings in which independent decisions are made that can affect everyone [21]. The theory of collective action predicts that external authority is necessary for individual change, as individual voluntary action will not occur without set rules [13, 22, 23]. Similarly, the common-pool resource research on other complex environmental and public health issues such as climate change indicates that, to avert the public health threat, "many actors at diverse levels need to make costly decisions" [13]. Moreover, as with other collective action issues, the benefits of mitigating the risk of AMR reach everyone, regardless of the individual contributions made to risk reduction [18, 20, 21]. That is, all individuals can benefit from reduced antibiotic usage, even if they do not individually contribute to the reduction efforts.

Yet, questions remain as to how an external authority can influence the collective action issues regarding AMR. Furthermore, the actors engaging with the topic of AMR are diverse. In addition to policymakers, notable actors involved with this issue include those working in the areas of medicine, veterinary medicine, waste disposal, water and wastewater treatment, environmental health, among others [24, 25]. AMR thus demands a polycentric subsystem, with policy actors who oversee different aspects of antibiotic usage for humans and animals, infectious disease control, and environmental concerns. Many have considered the structural features and applications of polycentric systems [26], yet direct application to the specific information concerning AMR is lacking.

Polycentric Governance with Respect to Antimicrobial Resistance

This section discusses the following key characteristics of polycentric governance: experimentation, learning, communication, trust, free riding, leakages, and inconsistent policies [13, 14]. The definition of each characteristic in relation to AMR and the potential measurement and evaluation options are summarized in Table 1 and expanded upon in the following sections.

The technical and scientific approaches that could be taken to successfully mitigate the risk of AMR are unknown. While decreasing the usage of antimicrobial medicines across all sectors is likely necessary, experimentation with different policies is needed to examine techniques from the policy and technical standpoints and determine which could potentially reduce the risks of AMR to public health [24]. Polycentric systems can also "multiply opportunities" for experimentation [14] and may offer a management scenario in which multiple policies can be implemented simultaneously to compare their respective levels of success.

Experimentation with policy solutions can and should occur at the local, national, regional, and international levels. The National Action Plans (NAPs) to address AMR supported by the World Health Organization (WHO) offer an example of experimentation at the national level [27]. For example, the Thailand AMR NAP called for a 20% reduction in human antibiotic usage and 30% reduction in animal antibiotic usage by 2021 [27]. If this ambitious goal is to be met, experimentation is needed to identify the most effective policies for implementation. One primary experimentation effort that could be considered involves innovation in enforcement by the actors themselves, such as imposing fines on those who use antibiotics improperly in hospital or agricultural settings.

Learning occurs "when actors can effectively process new information about problems they care about, and about how actors think about those problems" [26]. When experimentation indicates that a policy or technique has promise, learning and subsequent policy diffusion can occur across the various stakeholders involved with a

Table 1: Characteristics, definition, and potential evaluation opportunities for polycentric governance and AMR

Characteristic	Definition in Relation to Antimicrobial Resistance (AMR)	Potential Opportunities to Measure or Evaluate
Experimentation	Attempting different social and technical solutions at multiple scales of implementation	Evaluate new and emerging efforts, such as developing of WHO AMR National Action Plans
Learning	Effective processing of information by actors involved with the issue	Measure knowledge across sectors and acceptance of new information over time and evaluate how learning is utilized in decision-making
Communication	Exchange of critical information and knowledge successfully within and across sectors and disciplines	Evaluate documents for formal networks and social network mapping for informal networks
Trust	Belief in reciprocal, transparent relationships between those involved with the issue	Consider the level of trust and reciprocity between actors
Free Riding	Individuals that benefit (e.g., taking an antibiotic when not medically indicated) without considering the overall harm from AMR	Measure antibiotic usage patterns by sector and individuals
Leakage	When regulations differ between jurisdictions, users may go to jurisdictions with less strict oversight	Consider the users and traits within and across jurisdictional boundaries
Inconsistent Regulatory Efforts	Policies or rules that differ in design or practice	Measure real-world policy implementation

polycentric governance system [19]. Yet, while all policies can generate errors, "without trial and error, learning cannot occur" [14]. A long period of trial and error will then likely be needed to not only determine AMR and AMU rules or policies that generate minimal levels of success, but to also find rules that generate substantial long-term net benefits. In addition, for long-term behavioral changes, a significant duration may be needed to fully understand the experimental learning. Furthermore, with a serious problem such as AMR, innovation must include both technical and social experimentation and learning.

Communication must occur in a form that includes overall policy directions and guidance and communication regarding implementation to stakeholders. This is not a small task, given the use of antibiotics by nearly everyone in modern society, with significantly greater rates of antibiotic usage found in some developing nations [28]. Furthermore, in emerging nations, societal understanding of the function of these medicines can be lacking, with antibiotics being viewed as supplements or harmless medicines, and regularly prescribed incorrectly by those acting as healthcare providers with insufficient training [29]. The communication of complex issues and rules involving pharmaceutical medicines can also often be

incorrectly communicated by various sources, such as news media [30].

The communication forums surrounding AMR governance, such as the jurisdiction, participation, and decision-making processes, must be considered when evaluating the key structural features. [26]. In addition, for AMR and AMU decision-making, formal and transparent forums should be emphasized over informal and often opaque alternatives. It is also well-known that scientific uncertainty can influence policy making and communication [31]. Thus, it is crucial to engage experts in their respective fields to discuss and explain the uncertainty inherent in the scientific research regarding AMR and AMU. It is important to caution that uncertainty in scientific research has also been used as a tool and rhetorical strategy to hinder regulation by introducing doubt regarding the research [31–33].

To address collective action issues, intergovernmental trust and trust between stakeholders in different sectors must be established, including in the private sector. When trust is present, groups can form that allow for experimentation and learning under the best possible conditions [14]. Trust is directly related to levels of cooperation and reciprocity in a system, which increases overall net benefits [14]. When trust can increase across a system, the net benefits to public health can occur in a common-pool resource system involving polycentric governance.

An increase in trust can lead to "relationship capital," which concerns all relationships between the people and organizations interacting with an organization [34]. This is vital for polycentric systems. In particular, the two largest users of antibiotics [27], the agricultural system and the healthcare system, have likely had limited interaction and low levels of communication regarding AMU and AMR; therefore, increasing trust and showing reciprocity in communication and action are critical for advancing the management of AMR within this system. Trust has been repeatedly shown to play a notable role in long-term relationships [35]. In addition, as meetings have increasingly been conducted via video conferencing, face-to-face interaction has been found to play an increased role in trust and communication [13].

"Free riding" on a common-pool resource such as antibiotics can occur in numerous scenarios [36]. Broadly speaking, this occurs when AMU is not adequately or appropriately decreased by individuals. In these systems, for example, a user such as a medical doctor or a person in the agricultural sector will continue to use antimicrobials to excess or against treatment recommendations. Oversight of free riders is particularly challenging in systems such as the agricultural sector, as the actions of individuals may be difficult or costly to detect. For example, detecting antibiotics in the feed of animals or in the environment around an agricultural setting can be costly given the nature of the complex analytical chemistry required, which could greatly exceed the overall cost of the product.

Major impediments to overcome free riding include individuals who may not understand the public health issues surrounding AMR and the insufficiency of the regulatory system to deter their improper actions [37, 38]. When a patient goes to the doctor, they may insist that a medicine is prescribed to treat their presenting concern, and doctors may comply to ensure satisfied patients. Likewise, those operating agricultural systems may not be properly trained in the multi-faceted aspects of AMR, and thus, to ensure their product has the greatest health and yield, they may insist that their animals continue to receive antimicrobials. Antimicrobial compounds are critical medicines, and their usage will continue to be necessary in medical and agricultural settings, further complicating the free riding possibilities. Antibiotic usage stewardship is key, but again, difficult to implement due to the technical expertise needed and the risk of not using antimicrobials when they are indicated. It is possible that pushback from prescribers will likely continue, as tradition and experience of successful usage lead to a default recommendation of antimicrobial usage.

The collective action research suggests that free riding can be addressed by imposing sanctions on those violating the common pool resource [13]. For example, markets can refuse to sell products from the sellers who are known to violate antibiotic usage in the agricultural sector. In developed nations, medical systems often include oversight by state-level licensing boards and other professional organizations such as healthcare accrediting bodies [39] and these bodies can issue guidance and offer oversight. Furthermore, physicians can deter patients from visiting practitioners known to over-prescribe medicines against best-practice recommendations.

Leakage can occur in relation to AMR when one jurisdiction places stricter AMU requirements than those of surrounding jurisdictions [14]. As a result, some agricultural users may relocate to regions with less strict requirements. Similarly, individuals in the agricultural sector may purchase antibiotics from a jurisdiction with less strict management practices and transport these – potentially illegally – to a jurisdiction with stricter oversight. Likewise, patients who are able to easily choose doctors from different jurisdictions may choose a doctor with lax prescribing requirements. As a result, leakage

could easily become one of the greatest hurdles to reducing the harm of improper AMU patterns.

During experimentation, policies or rules may be inconsistent in design or practice, in particular when implementing complex policies to address complex and highly uncertain scientific issues, such as AMR. The implementation of rules or policies to reduce AMU or mitigate the risk of AMR may also differ in how they are written or intended. Furthermore, the measurement of AMU and AMR is costly and difficult [40], increasing the potential for inconsistent regulatory efforts. Thus, monitoring and evaluating any efforts would be potentially valuable for gauging progress.

Applications of Polycentric Governance to Antimicrobial Resistance

This work considers the key characteristics of polycentric governance systems in the context of AMR management. AMR has the potential to become one of the most severe public health risks of the next 20 years, and we posit that polycentric governance could ensure the necessary progress in this critical area. The primary goal of this work is to outline the key variables and identify the methods with which to measure progress in AMR risk-mitigation on the local, regional, national, and transnational levels. AMR and AMU are progressing at an unsustainable speed, disrupting the treatment of previously treatable diseases [27, 40]. Thus, it is of the utmost importance that we identify the incentives of the relevant actors and the factors that can reduce risk. Self-governance of a system for AMR may, therefore, be too technically complex for users of antimicrobials, and further expertise and guidance is needed.

The sheer scale and scope of the issues surrounding AMR and AMU management is astounding. Unknown numbers of prescribers across all regions of the world may need to make behavioral changes, and AMR has the potential to affect everyone worldwide. Despite efforts such as the WHO's Global Antimicrobial Resistance Surveillance System (GLASS), there are significant challenges with reporting and surveillance in many countries [41]. This further highlights that to allay the risks of AMR, a multi-disciplinary and multifaceted approach is needed for AMR surveillance and the monitoring of strategy effectiveness. To evaluate the success of AMR mitigation efforts, it is necessary to measure the occurrence of AMR and AMU. However, such evaluation is made costly and complex by political, spatial, and temporal considerations and overall scientific uncertainty. Thus, we propose the key characteristics of polycentric governance systems as valuable metrics for the measurement of the structural functionality of the politics and management of AMR, with these metrics to be included in programs such as GLASS.

The role of the individual and their needs may often supersede the needs of the commons during times of great distress, in particular when a complete understanding of the resource degradation is lacking [37]. It is well-known that medical providers can empirically utilize antibiotics for critically ill patients without a definitive diagnosis, as was done for many patients with COVID-19 [7]. Yet, polycentric governance has the potential to address and manage some of these issues in the future.

Traditionally, interaction and cooperation between the medical, agricultural, veterinary medicine, and environmental sectors have been lacking [42, 43]. As a result, trust and communication may also be lacking in this system. Due to the multifaceted nature of AMR, each sector must work concurrently to address the issue, and free riding is a major outcome that will likely need to be addressed. The One Health (OH) approach has been suggested as a method by which to create a collaborative environment across disciplines and sectors [42, 43]; and the OH concept could be enhanced by introducing these polycentric governance strategies when applying OH approaches to collective action issues.

AMR and AMU also intersect with significant issues of poverty and injustice. In many developing nations, those without access to adequate medical care and antibiotics are often sold incomplete courses (for example, when an individual can only afford to buy a few doses of the antibiotic, rather than the full course) or given the incorrect antibiotics due to a lack of testing and medical care [29]. To further complicate the issue, 10% of the drugs prescribed in developing nations are counterfeit [44]. Future inquiries must acknowledge the relationship between socioeconomic status and AMR and AMU practices. In addition, the pricing model of antibiotics does not include all negative externalities, such as antibiotic environmental pollution and AMR [8, 10]. Yet, internalizing those costs into antibiotic pricing may further promote social economic injustice and restrict access to these lifesaving medicines in developing nations, thus lowering the socioeconomic status of individuals and their families.

Conclusion

Significant local, national, and international efforts are needed to address AMR. Inappropriate AMU increases the speed of the negative impacts from improper AMU, and

the rapid development of AMR is now greatly exceeding the rate of advances in new antibiotics. Proper AMU across all sectors will not guarantee the end of AMR, but it could slow the impact. It is now abundantly clear that transnational efforts — such as those for climate change including the International Panel on Climate Change (IPCSS) and the Paris Accord — are required for AMR to reduce damage caused by collective action issues. We have entered a period in which policymaking is required to address the significant worldwide health risks of AMU and AMR. Efforts such as the WHO Global Action Plans are an important step, but much greater efforts are needed. There is a need for both scientific advances in understanding of how to reduce the risks of AMR and the introduction of the social science components of antimicrobial stewardship, and the polycentric system literature offers many insights for the improvement of governance. While it will likely take many decades to fully understand and address AMR, collective action research into learning, experimentation, communication, trust, leakage, inconsistency regulatory initiatives, and free riding may offer insights into how we can measure metrics of success, rather than AMR outcomes alone.

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