Global Governance Mechanisms to Address Antimicrobial Resistance

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ABSTRACT: Since their discovery, antibiotics, and more broadly, antimicrobials, have been a cornerstone of modern medicine. But the overuse and misuse of these drugs have led to rising rates of antimicrobial resistance, which occurs when bacteria adapt in ways that render antibiotics ineffective. A world without effective antibiotics can have drastic impacts on population health, global development, and the global economy. As a global common good, antibiotic effectiveness is vulnerable to the tragedy of the commons, where a shared limited resource is overused by a community when each individual exploits the finite resource for their own benefit. A borderless threat like antimicrobial resistance requires global governance mechanisms to mitigate its emergence and spread, and it is the responsibility of all countries and relevant multilateral organizations. These mechanisms can be in the form of legally binding global governance mechanisms such as treaties and regulatory standards or nonbinding mechanisms such as political declarations, resolutions, or guidelines. In this article, we argue that while both are effective methods, the strong, swift, and coordinated action needed to address rising rates of antimicrobial resistance will be better served through legally binding governance mechanisms.

KEYWORDS: Antimicrobial resistance, global governance, legally binding mechanisms, non-binding mechanisms, AMR

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Antibiotics, and more broadly, antimicrobials, have served as a cornerstone of modern medicine for decades, being used to treat a range of diseases and to support numerous modern medical procedures from organ transplants to chemotherapy. We often see them as a panacea which is why a world without effective antibiotics is unfathomable to many because of the health, social, and economic ramifications of such an occurrence. Yet, this is becoming a reality because of the rise of antibiotic resistance, which occurs when bacteria adapt in ways that render antibiotics ineffective. Around 3.5 billion years of evolution has given bacteria a remarkable ability to evolve, and our persistent misuse and overuse of antibiotics in animal and human health have only aided this rise in resistance by encouraging bacteria to adapt.[1]

The burden of antibiotic resistance, and more broadly, antimicrobial resistance (AMR), has significant impacts on population health,[2,3] global development,[4] and even the world economy.[5] Annual deaths associated with AMR are estimated to be around 25 000 for the European Union alone, with a current worldwide mortality of 700 000 deaths per year.[3] This number is set to increase in the coming years. The World Bank Group's final report on Drug-Resistant Infections outlines the threat they pose to our economic future, stating that if unchecked, AMR spread could cause global gross domestic product reduction in 2050 that is comparable with the 2008-2009 global financial crisis.[5] It could possibly be worse than the 2008 financial crisis because AMR spread causes greater drops in economic growth in low-income countries compared with wealthier countries, widening the gap of economic inequality between countries.[5] The World Bank report concluded that given the significant level of AMR in low-income countries, the impact of AMR on the global economy will result in increased poverty rates, with most of those falling into extreme poverty.

Since their discovery, antibiotics have been heralded as a "miracle drug" that is good for the public, yet, from an economics perspective, they are considered a common good rather than a global public good. The distinction seems minute; however, different frameworks exist in managing public goods versus common goods. The standard definition of a public good is that it must be nonexclusive, meaning if someone wants to use it, they cannot be excluded from it, and nonrivalrous, meaning one person's consumption does not affect another person's consumption.[6]

Although antimicrobial effectiveness (AME) is nonexclusive, in the sense that it can be used by everyone, it is rivalrous. Even prudent use of antibiotics provides an opportunity for bacterial resistance to develop, so one person's consumption does effect another's consumption. As a common good, antibiotic effectiveness is subject to the economic principle of the "tragedy of the commons" where a shared finite resource is squandered by a community when each individual exploits the limited resource for their own benefit.[7] Overexploitation of a shared finite source leads to resource depletion and the collapse of the common good.[8] The conventional example of this is fisheries where overfishing caused by individual self-interest causes depletion. This is an apt comparison with antibiotic effectiveness where overuse of antibiotics leads to resistance and causes antibiotics to no longer be effective.

As a global common good, safeguarding AME and mitigating the threat of AMR are the responsibilities of all countries

and relevant multilateral organizations. A borderless threat like AMR requires global governance mechanisms to mitigate its emergence and spread. This can be in the form of legally binding global governance mechanisms such as treaties and regulatory standards or nonbinding mechanisms such as political declarations, resolutions, or guidelines.

In this article, we argue that while both are effective methods, the strong, swift, and coordinated action needed to address rising rates of AMR will be better served through legally binding governance mechanisms. However, it is important that all solutions to AMR, whether legally binding or nonbinding, will keep in mind the One Health approach—which addresses human health, animal health, and the environment—while recalling that collective action is required in areas of surveillance, infection control, awareness, responsible use, and innovation for successful containment of AMR emergence and spread. These mirror the 5 strategic objectives of World Health Organization's (WHO) Global Action Plan on Antimicrobial Resistance[9] as well as the similar plans of Food and Agricultural Organization (FAO) of the United Nations[10] and the World Organisation for Animal Health (OIE).[11]

Legally Binding Governance Mechanisms

Treaties have long been considered the gold standard in legally binding global governance mechanisms due to their transformative benefits in achieving social goals.[12] They facilitate international cooperation, coordination, and hold countries accountable for the commitments they have made while addressing transnational problems that cannot be tackled by a single country or organization.[13,14] Unlike nonbinding governance mechanisms, treaties have the additional benefit of keeping countries accountable even in the face of government changes. A treaty on managing antimicrobials and containing AMR emergence and spread could help coordinate efforts in this area, especially when combined with strong implementation mechanisms and regulatory functions.

The very first global health treaty negotiated under the auspices of the WHO was the WHO Framework Convention on Tobacco Control (WHO FCTC) which was signed in 2005 by 168 countries and developed in response to the worldwide tobacco epidemic.[15] The 2014 and 2016 WHO FCTC report and impact assessment shows a general downward trend in prevalence of tobacco use among participating countries. However, countries do need to accelerate their implementation efforts if they are to reach the 2025 goal of reducing tobacco use by 30%.[15,16] Progress in the implementation of the WHO FCTC provides supports that a treaty on AMR emergence and spread could find similar success. Due to the ever-evolving threat of AMR, a case can even be made to use the extensive treaty-making power of WHO under Article 21 of its constitution to create an opt-out legally binding treaty rather than an opt-in treaty. With a majority vote of the World Health Assembly, its governing body, Member States can be bound by new regulations on a variety of health issues using Article 21 unless they specifically opt out.[17]

However, new regulations without proper implementation or accountability mechanisms will create ineffective treaties.[18] A study assessed more than 90 treaties on various issues and found that for treaties to be effective and yield positive results, they needed to fulfill the following criteria: (1) address a transnational problem, (2) end goals should justify forcible nature of treaties, (3) have a reasonable chance of achieving benefits, and (4) treaties should be the best mechanism available among alternatives to solve the problem at hand.[19] A treaty on AMR emergence and spread fulfills all these criteria because (1) AMR is a transnational threat, (2) the end goals of reducing the rise of AMR and the coordinated action needed to address this transnational issue justify the forcible nature of a treaty, (3) an AMR treaty can achieve benefits if it incentivizes those with the power to act and institutionalizes accountability mechanisms, and (4) nonbinding governance tools do not have the accountability mechanisms that treaties have to ensure compliance.[19] This 4-step analytic framework confirms that a global health treaty on AMR would yield positive effects and would be one of the few newly proposed global health treaties to do so, irrespective of opt-out or opt-in status.[20]

These positive effects can be supplemented further if we take inspiration from successful treaties such as the Montreal Protocol on ozone depletion. Flexibility and accountability were 2 reasons for the successful ratification and compliance of the Montreal Protocol because it specified that amendments could be made to the original Protocol if two-thirds of signatories supported these changes.[21] Flexibility can also come in the form of how provisions in treaties are met by countries. In terms of AMR, an international treaty does not have to specify the compliance mechanism each country uses to manage antimicrobials and contain resistance and spread, as long as misuse and overuse of antimicrobials in human and animal health decreases. Although in the case of AMR, stewardship, innovation, and access have been shown to be effective methods to combat AMR rise and spread.[22] The Hoffman and Røttingen study which analyzed 90 treaties[19,20] found that international trade and economic treaties tend to be more "successful" at achieving their goals because they had institutional mechanisms for accountability, compliance, and arbitration unlike several international social treaties that were found to be less successful at achieving their goals.

Treaties are not the only legally binding global governance mechanisms used to facilitate international cooperation. The WHO International Health Regulations (2005) (IHR) is a legally binding instrument of international law that seeks to prevent spread of infectious diseases and other health threats to enhance global public health security.[23] Through IHR, 196 State Parties, including 194 Member States, now have a comprehensive legal framework to report to WHO on events that might constitute a public health emergency of international

concern that could severely affect human health and economies. The State Parties' participation and implementation of the IHR, as well as WHO's coordinating role in it, can serve as a template for a legally binding governance mechanism for AMR that is not a treaty.

A legally binding governance tool is a powerful force to facilitate change on a global level, but managing the overuse and misuse of antibiotics through legally binding mechanisms must be balanced with issues around access. Although there has been a rise in antibiotic consumption worldwide, this consumption has been unequal with lower income populations, especially in remote rural areas, often not having access to first-line antibiotics.[24,25] An estimated 5.7 million people die each year from not having access to existing antimicrobials for treatable infectious diseases, and most of those populations are from low-and middle-income countries.[26] Inequitable access can also lead to increased rates of AMR. Any AMR treaty will need to ensure proper stewardship in animal and human health by discouraging low-value antibiotic use and encouraging innovation while keeping in mind issues around access.[24,25]

Nonbinding Global Governance Mechanisms

Binding global governance mechanisms are not the only means of facilitating global cooperation. Nonbinding governing mechanisms such as political declarations, resolutions, or guidelines which are formally approved by intergovernmental organizations are still legal instruments which can foster global consensus and coordinated action on specific issues. Antimicrobial resistance has experienced a groundswell of political support in the past few years starting with the G7 meetings in Germany and Japan, going into the 68th World Health Assembly which endorsed a global action plan to tackle AMR, and culminating with Member States adopting the 71st United Nations (UN) General Assembly (UNGA) Political Declaration of the High-Level Meeting on Antimicrobial Resistance.[27] The high-level meeting marked the fourth time the UNGA met to address a health topic, with Member States reaffirming their commitment to take a coordinated approach to curb AMR in multiple sectors, and pledging to develop national action plans based on the Global Action Plan on Antimicrobial Resistance.[27]

The UNGA Political Declaration on AMR has already shown positive impact with a greater number of countries implementing national action plans to combat AMR emergence and spread. Paragraph 15 of the Political Declaration also established an ad hoc Interagency Coordination Group (IACG) on Antimicrobial Resistance to provide practical guidance on global actions needed to address AMR.[28] The IACG Secretariat is a tripartite of WHO, FAO, and OIE, underlying the multisectoral One Health approach needed to tackle AMR.

Mechanisms such as political declarations offer a nimbler, more adaptive option to the rigidity of legally binding global governance mechanisms such as treaties. Because of their flexibility, nonbinding mechanisms allow for more dynamic discourse and better responsiveness to changing global priorities.[29] They are also easier to modify because amendments do not have to go through ratification. Being voluntary, nonbinding mechanisms can also have stronger implementation language than treaties and bring in civil society organizations and nonstate actors. Ultimately, they provide political and legal significance without incurring the legal consequences of binding governance mechanisms if states fail to meet their commitments.

For all their advantages, nonbinding governance mechanisms are only as effective as their perceived importance. They lack the strength of binding mechanisms like treaties which have legal consequences if countries fail to meet their obligations. Nonbinding mechanisms also lack the credibility of binding instruments because they are not nationally ratified and therefore have no legal effect on national practices. Furthermore, binding legal mechanisms contain financial and logistical support built in for implementation as well as reporting systems, features not often seen in nonbinding governance mechanisms. In terms of AMR, the World Health Assembly Resolution and the UN General Assembly's Political Declaration are the strongest nonbinding global governance mechanisms available and we have used them with the hope that they will encourage global action on curbing AMR. However, due to the escalating danger of AMR to human health, global development, and the world economy, it is imperative we take action in the strongest, most effective way available to us through global governance.

Conclusions

Application of international law to global health is undergoing a transformative time with the WHO emerging as a natural center for lawmaking, negotiations, and global health governance. The WHO FCTC and the IHR stand as a testament to that. Rising rates of AMR emergence and spread, and its danger to global health security, have brought AMR to the forefront of high-level political discussions from the G7 to the World Health Assembly to the UN General Assembly. Global governance mechanisms should be used to regulate a global common good such as AME and to address the growing threat of AMR. Binding and nonbinding global governance strategies can be effective in addressing global health issues but legally binding mechanisms like the Montreal Protocol have shown that they can successfully regulate global common goods such as the ozone layer. However, with climate change, there are viable alternatives to energy production apart from fossil fuels, whereas alternatives to antibiotics, including prebiotics, probiotics, and phage therapy, are still in their experimental stages.[30] This is another reason why immediate action is required to address AMR, and while there are benefits to both governance strategies, the need for strong action to curb AMR resistance leads to the conclusion that legally binding governance

mechanisms on AMR would be one of the most effective ways to maintain AME and manage antimicrobials as a common good.

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Author Contributions

PAP performed the background research and wrote the primary draft of the manuscript with extensive input and revisions by MS and HI.

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