Global epistemic authority and its limits: Evidence from the WHO's efforts to preserve antibiotic efficacy

Mirko Heinzel
London School of Economics and Political Science

Mathias Koenig-Archibugi
London School of Economics and Political Science

Abstract:

Many of the problems addressed by international organizations (IOs) are caused by the activities of myriads of individuals, companies, and other societal groups. IOs tackle such problems by facilitating state action or by targeting these societal actors directly. To what extent are they able achieve their goals without the active involvement of governments? We argue that the epistemic authority of IOs puts them in a position to influence societal practices, but this authority needs to be supported by the political authority of governments when the practices entail severe collective action problems. This argument is assessed empirically through an analysis of the World Health Organization (WHO)'s action on one of the most important global cooperation problems: the effort to slow down the rise in antimicrobial resistance. Specifically, we assess the ability of the WHO to shape antibiotic consumption through publishing the AWaRe classification—a list aimed at guiding antibiotic prescription practices globally. We test the impact of this classification through pre-registered analyses of highly disaggregated drug-level data on antibiotic consumption of 274 drugs in up to 93 countries between 2014 and 2023. We show that the WHO's epistemic authority has only been effective in shaping antibiotic use where the WHO could leverage its member states' political authority.

Introduction

Many problems addressed by international organizations (IOs) are generated by the activities of myriads of individuals, companies, and groups. Examples include the emission of ozone-depleting substances and greenhouse gasses, deforestation, human trafficking, the exploitation of workers, gender violence, money laundering, cybercrime, financial market crises, and the marketing of unhealthy foods and drinks. IOs typically tackle these kinds of problems in two ways. The main approach consists of attempts to influence how states deal with such practices, for instance, by encouraging public authorities to adopt more stringent laws and regulations, invest more resources in monitoring and enforcement, and provide positive incentives and support for behavioral change. Working with and through states is the traditional route to impact for IOs since they are intergovernmental creations that specialize in state-facing activities, such as drafting and negotiating international treaties, monitoring compliance with international obligations, and providing funding and technical assistance to governments with less capacity (Abbott and Snidal 1998; Martin and Simmons 2013). The other approach focuses on trying to influence societal practices directly. Some initiatives engage with specific target audiences. For instance, since 2000 the United Nations Global Compact has attracted 13,000 corporate participants, who have committed themselves to embedding environmental, human rights, labor, and anti-corruption principles into their corporate strategies and day-to-day operations, and to reporting on an annual basis about their progress in implementing the principles. But IOs have also been expanding their public outreach capabilities more generally. A study of forty-eight IOs between 1950 and 2015 found an overall trend toward strengthening organizational capacities for public communication, understood as organized communication with any kind of non-governmental audiences (Ecker-Ehrhardt 2018).

The two approaches just described are not mutually exclusive, and some IOs have made considerable efforts to combine them. A prominent example is the World Health Organization (WHO). Many of its activities address governments, most clearly through adopting and managing legal instruments such as the International Health Regulations and the Framework Convention on Tobacco Control. A wide range of other activities target a broader audience. For instance, the WHO's website provides public access to 292 guidelines that include recommendations for clinical practice and public health policy. The organization defines its recommendations as "statements designed to help end-users make informed decisions on whether, when and how to undertake specific actions such as clinical interventions, diagnostic tests or public health measures", with the target audience of many of

those guidelines being explicitly defined as including clinicians as well as officials involved in health policy making. For example, the *WHO guidelines for the prevention of sexual transmission of Zika virus* are designed to "inform national and subnational policy makers, healthcare providers, other healthcare stakeholders and the general public." While most publications of the WHO are technical in nature, some of its activities target virtually everyone in the world. During the COVID-19 crisis, its "Advice for the public" webpages, social media posts, and press conferences had a global reach, while other public communication initiatives were more targeted—for instance, in Mali the WHO prepared risk communication messages that were uploaded onto drones and sent to villages in remote areas (Samaan et al. 2022; Tay 2022; Salama 2022; Muñoz-Sastre, Rodrigo-Martín, and Rodrigo-Martín 2021). While some of these activities have been performed since the early days of the WHO, there has been a qualitative shift more recently. According to David Fidler, the 2003 SARS outbreak represented a watershed event in global health governance (Fidler 2004). Until then, the WHO's role in disease outbreak response was largely limited to handling information provided by and aimed at governments. During the SARS crisis, the WHO secretariat made intense use of non-governmental sources of outbreak data, used its communication networks to spread information widely among a variety of nonstate audiences, and communicated directly to the public, most strikingly by advising against traveling to the Guangdong province of China, Hong Kong, Toronto, and other areas. Fidler interpreted the willingness of the WHO leadership to side-step governments as a crucial step in the shift from a "Westphalian" to a "post-Westphalian" system of global public health (Fidler 2004). The widespread perception of a general shift is reflected in the terminological choices of health policymakers and scholars, who now tend to prefer the expression "global public health" to the older "international public health" (Brown, Cueto, and Fee 2006).

Activities that reach out to nonstate actors directly can be seen as attempts by IOs to grow out of their Westphalian constraints and achieve their goals in a more complex environment. However, there are significant research gaps about the extent to which IOs successfully shape nonstate practices. Determining whether states comply with IO rules and recommendations and whether compliance mitigates the problems targeted by the IO is not easy. However, substantial literature now provides much solid evidence on those questions (Simmons 2010; Hoffman et al. 2022). By contrast, evidence on the impact of IO activities on nonstate practices is much scarcer. Some studies estimate the association between the adoption of IO-sponsored standards and the environmental and social performance of companies (Berliner and Prakash 2015; Erauskin-Tolosa et al. 2020; Thrall 2021). An important body of work uses experimental

designs to examine the effect of IO messages on public opinion. These studies are insightful, but, with some exceptions (Sheen et al. 2023), they focus on how IO endorsement or criticism affects public opinion on *government* policies rather than how they may affect the practices of the public itself.[1] Furthermore, IOs address not only governments and the general public but also specialist nonstate actors, such as health care professionals, engineers, and corporate sustainability managers. In this paper, we contribute to addressing this research gap theoretically and empirically.

Theoretically, we identify a potentially important scope condition for the effect of the epistemic authority of IO on societal practices. We expect such an effect to be weak when the relevant practices involve a diffuse collective action problem. Under such conditions, we hypothesize that the effect of IO's epistemic authority crucially depends on the support provided by the kind of political authority wielded mainly by governments.

Empirically, we examine a particularly important case of IOs dealing with a problem generated by societal practices that are highly diffuse across the world: antimicrobial resistance (AMR) (Baekkeskov et al. 2020). AMR occurs when microbes become resistant to antimicrobial medicines. While AMR is a natural process, it is accelerated by the use, and especially the overuse and misuse, of antibiotics in health care and farming. Thus, preserving the efficacy of antibiotics crucially depends on influencing how they are used by millions of health care professionals and, ultimately, billions of individuals around the world. The WHO considers AMR to be one of the top health threats facing humanity. It directly caused 1.27 million deaths and was associated with a further 3.68 million deaths in the year 2019 (Murray et al. 2022). The death toll includes 214,000 newborns killed each year by blood infections caused by resistant pathogens (Laxminarayan et al. 2016). If projections are correct, and the international community does not make substantial progress toward slowing down AMR, it could cause 10 million deaths annually by 2050 and a cumulative GDP loss of approximately US$85 trillion between 2015 and 2050 (Review on Antimicrobial Resistance 2016; Ahmed et al. 2018).

The WHO convened discussions on antibiotic use since the 1950s but intensified its action in the 2010s (Podolsky 2018). An important element of its response was the creation of the "AWaRe" classification in 2017 to guide the responsible prescription of antibiotics

[1] This applies to the studies of Chapman (2012), Linos (2013), Kreps and Wallace (2016), Bearce and Cook (2018), Greenhill (2020), Koliev, Page, and Tallberg (2022), Chapman and Li (2023), and Kobayashi et al. (2023). Anjum, Chilton, and Usman (2021) examine how UN endorsement affects public support for state policy reforms aimed at changing societal practices.

globally. It has been updated bi-annually by the WHO Expert Committee on Selection and Use of Essential Medicines. AWaRe stands for Access, Watch, and Reserve, and the framework divides antibiotic medicines into a group that has low resistance potential and is recommended as first or second choice treatment for common infections, a group for which use needs to be carefully monitored, and a group that needs to be used only as a last resort. The AWaRe list has become a standard reference point for monitoring antibiotic use in various settings.[2] However, no systematic evidence exists on whether it has affected antibiotic use patterns.

The AWaRe framework is implemented in a public database that can be accessed by national governments and various kinds of health professionals—doctors, nurses, pharmacists, hospital managers, medical associations, and medical training institutions. We formulate and test two sets of hypotheses. The first states that the per capita consumption of an antibiotic drug decreases when it is listed as a Watch or Reserve antibiotic in the WHO's AWaRe guidelines. These hypotheses concern the impact of the epistemic authority of the WHO in general, without distinguishing between governmental and nongovernmental targets. The second set of hypotheses states that, when antibiotics are listed as Watch or Reserve antibiotics in the AWaRe guidelines, the per capita consumption of these antibiotics decreases in countries that implement national action plans on AMR. The implementation of an AMR national action plan indicates that the government resolved to use its political authority to modify societal practices regarding antibiotic use.

We test these hypotheses through a pre-registered difference-in-difference analysis of highly disaggregated drug-level consumption data—including up to 274 antibiotics in up to 93 countries between 2014 and 2023. Our dataset on antibiotic consumption is drawn from the proprietary IQVIA MIDAS® dataset licensed by the company IQVIA. We pre-registered[3] our analysis on August 29, 2023, and attained access to the data on September 20, 2023.

We find that the WHO's epistemic authority by itself has been insufficient to induce reductions in the use of Watch and Reserve antibiotics. However, this overall outcome masks significant differences among national contexts. In countries implementing national action plans, the AWaRe classification appears to have worked as a backstop preventing increased Watch antibiotic use. We substantiate these results through a pre-registered placebo test and several new difference-in-difference estimators. Finally, we conduct exploratory tests that

[2] See, for instance, Hsia et al. (2019); Knowles et al. (2020); Adekoya et al. (2021); Hillock et al. (2021); Kalungia et al. (2022); Abdelsalam Elshenawy, Umaru, and Aslanpour (2023); Mudenda et al. (2023).
[3] https://osf.io/7z6xe/?view_only=916f35b85a3e4a0b937229e67c7ab335

further support the critical role played by state agency in ensuring that the WHO's epistemic authority affects health care behavior on the ground.

Overall, these findings indicate that, in a domain marked by severe collective action problems such as AMR, the exercise of epistemic authority needs to be combined with the exercise of political authority to shift entrenched societal practices.

Theoretical background and hypotheses

Scholars have long debated what kind of authority IOs have, if any. Most generally, authority involves "the subordination of an individual's judgment or will to that of another person in a way that is binding, independent of the particular content of what that person says or requires" (Green 1998, 584). Michael Zürn (2018) has provided a valuable map of analytical perspectives on how the concept has been used and developed in the literature on global governance. He distinguishes between three perspectives. The first perspective sees authority as emerging from a contractual negotiation of roles and responsibilities that serve the predefined interests of all parties, albeit not necessarily equally (Lake 2010; Hooghe, Lenz, and Marks 2019). The second perspective sees authority as emerging from a process of socialization into legitimacy beliefs and as sustained by habitualization (Hurd 1999; Barnett and Finnemore 2004; Pouliot 2016). Zürn builds on both perspectives to develop a third conception, which he calls "reflexive authority." In contrast to the first perspective, reflexive authority is based not on a strategic calculus but on the recognition that limitations in decision-making capacities, such as bounded rationality, make it necessary to trust actors with a reputation for superior expertise and impartiality. In contrast to the second perspective, reflexive authority is never fully internalized since the credentials and trustworthiness of the authority are checked continuously, even if the reasons behind specific decisions and opinions are not. Typically, a reflexive authority "requests"—as opposed to "commands"—that a certain action is taken in the pursuit of a collective goal. Zürn argues that reflexive authority best describes the relationship between most IOs and other actors as it evolved during the twentieth century (Zürn 2018, 37-50).

Zürn also elaborates on two forms that authority—and specifically reflexive authority—can take: political and epistemic. Political authority is the right to make decisions that are binding for a collective (which may or may not be accompanied by the right to enforce compliance). Epistemic authority is the belief that an actor's interpretations, positions, and requests should be followed because of the superior knowledge and impartiality of that actor (Zürn 2018, 50-3). The difference between political and epistemic authority is concisely conveyed by the distinction between being "in authority" and being "an authority" (Friedman 1973). In some

cases, an organization may be officially assigned the role of providing authoritative interpretations and guidance by a political authority, in which case it becomes what Zürn calls a "politically assigned epistemic authority." An example of this type of authority is the Organization of Economic Cooperation and Development (OECD), which evaluates and compares the performance of national educational systems (Zürn 2018, 52-3). Empirical studies show that IO's epistemic authority is widely recognized by national policymakers around the world (Liese et al. 2021).

These concepts have a straightforward application to the governance of antibiotic use. Most generally, the Constitution of the WHO explicitly gives the organization the mandate to act as a global epistemic authority in the field of health. Crucially, this mandate is not limited to maintaining a relationship with governments—it includes, for instance, the function "to assist in developing an informed public opinion among all peoples on matters of health".[4] As noted in the Introduction, one of the many ways the organization has performed such functions is by developing and publishing nearly 300 guidelines on a wide range of areas of clinical practice and health policy for the use of policy-makers and a broad range of health-related professionals. These "are widely regarded by physicians and health services throughout the world as standard guides to practice" (Jacobson 1984, 124). The WHO attained this privileged position by acting as global convenor of multinational epistemic communities of specialists in specific health areas and supporting them in the development of science-based and evidence-led consensus documents (Haas 1992; Haas 2023).

The widespread attention given to WHO guidelines does not mean they always gain universal acceptance—occasionally, they attract criticism and resistance (e.g., Abeysinghe 2015; Lewis 2022). During the COVID-19 pandemic, the WHO was attacked by powerful politicians (Johnson 2020; Pevehouse 2020; Yang 2021). But such episodes occur against the backdrop of a widespread expectation that the WHO should—and usually does—provide impartial guidance that adequately reflects the best available scientific evidence. International surveys suggest that the WHO largely meets that expectation. Among representative samples of citizens of 45 countries covered in the seventh wave of the World Value Survey, the WHO

[4] Other expertise-based tasks attributed to the organization by the Constitution include the function "to act as the directing and co-ordinating authority on international health work", "to promote co-operation among scientific and professional groups which contribute to the advancement of health", "to propose conventions, agreements and regulations, and make recommendations with respect to international health matters…", "to promote and conduct research in the field of health", "to promote improved standards of teaching and training in the health, medical and related professions", "to provide information, counsel and assistance in the field of health", "to develop, establish and promote international standards with respect to food, biological, pharmaceutical and similar products", and to perform other expertise-focused tasks.

enjoys the highest level of confidence among the six global IGOs included in the survey (Haerpfer et al. 2022). It also enjoys the highest level of confidence among the 599 members of the political and societal elite in five countries interviewed for the LegGov Elite Survey: 83 percent reported having a great deal or quite a lot of confidence in the WHO (Dellmuth et al. 2022, 82).

The features that generally confer authority and credibility to WHO guidelines are also present in the creation and management of the AWaRe classification of antibiotics. The classification was introduced by the WHO Expert Committee on the Selection and Use of Essential Medicines at its 21st meeting, which took place from 27 to 31 March 2017. This expert committee meets periodically to review and update the WHO Model List of Essential Medicines (EML) and the WHO Model List of Essential Medicines for Children (EMLc) (WHO 2001). The participants in the 2017 meeting consisted of 15 members (medical experts from as many countries), three temporary advisors, one observer, and representatives of WHO regional offices and other IOs. The work was supported by eight members of the WHO Secretariat, mainly from its Department of Essential Medicines and Health Products (WHO 2017, xix-xx). The work of the expert committee built on a previously published *WHO List of critically important antimicrobials for human medicine*, which aims to preserve medically important antimicrobials used in food animal production, as well as reviews provided by an external university department and two specialist WHO departments. The committee assigned antibiotics to one of three groups: the Access group includes first- and second-choice antibiotics for the empirical treatment of most common infectious syndromes; the Watch group includes those with higher resistance potential and whose use as first- and second-choice treatment should be limited to a small number of syndromes or patient groups; and the Reserve group includes antibiotics to be used mainly as "last-resort" treatment when the alternatives would be inadequate or have already failed, for instance in life-threatening infections due to multidrug-resistant bacteria. The WHO aims for at least 60 percent of total antibiotic consumption to consist of Access group antibiotics (WHO 2020, 111).

The expert committee introduced the classification "[t]o assist in the development of tools for antibiotic stewardship at local, national and global levels" (WHO 2017, 64), and it emphasized that "[a]ntibiotic use is a complex interplay between patients, prescribers and nonprescriber health-care professionals, all influenced by their environment (system organization, culture, regulation). An antibiotic stewardship program must target the general public, health-care professionals (whether they prescribe or not), and policy-makers. It must

try to change behavior – a notoriously difficult process – by acting at the level of both the individual and the system" (WHO 2017, 67).

The first set of hypotheses we consider assumes that the epistemic authority of the WHO is sufficient to trigger the process that leads to behavior change by persuading all relevant stakeholders—regulators, health-care professionals, and patients—that the inappropriate use of antibiotics on the Watch and Reserve lists poses unacceptable risks for their continued efficacy and availability when they are really needed.

H1a (Watch): When antibiotics are listed as Watch antibiotics in the WHO's AWaRe classification, countries decrease per capita consumption of these antibiotics.

H1b (Reserve): When antibiotics are listed as Reserve antibiotics in the WHO's AWaRe classification, countries reduce per capita consumption of these antibiotics.

Our second set of hypotheses assumes that the WHO's epistemic authority is important but insufficient to produce change. The expert committee itself hinted at the reasons in its report: antibiotic stewardship programs "can have a positive impact provided that sufficient resources are made available and are sustainable and that there is strong political and institutional support" (WHO 2017, 67).

We argue that the epistemic authority of IOs is unlikely to generate major changes when it addresses a diffuse and severe collective action problem. In such situations, it needs to be backed by political authority, i.e., the authority to make binding decisions for the whole group. In the following, we illustrate such a situation by providing more detail on the motivations and interactions underlying the AMR problem.

Reducing the inappropriate use of antibiotics is very challenging because of the combination of two factors. First, antibiotic use is a highly decentralized practice involving billions of patients, health-care workers, and sellers. Second, individual and collective benefits are less aligned with each other compared to other areas of health care regulation, such as the safety of drugs, medical procedures, and medical devices. Abstention from consumption requires individual patients to run an individual risk (complications from a missed bacterial infection) to make a small contribution to a public good (preserving drug efficacy for a longer period). Prescribers and sellers are often unwilling to withhold individual benefits from patients for several potential reasons. First, health professionals may focus on the individual's immediate welfare rather than a more abstract and long-term collective good (Krockow, Tarrant, and

Colman 2022). This focus would be especially pronounced in settings with widespread poverty and a lack of publicly funded health care, because the inability to work and hospitalization expenses could have a catastrophic impact on household finances (Nabirye et al. 2023; Broom et al. 2020). Second, health care professionals may be risk averse because they worry about the legal and personal repercussions of not providing access to a treatment that might prevent serious complications (Stivers 2007). Third, in many settings, health care professionals gain financially from prescribing and selling antibiotics (Lin et al. 2020; Blaser et al. 2021; Servia-Dopazo and Figueiras 2018; Auta et al. 2019; Batista et al. 2020; Khan et al. 2022). Moreover, the easy availability of antibiotics means that refusing to prescribe or sell them does not guarantee non-use. As a pharmacy professional in Eritrea described a typical situation, "If you try to teach the patient about antibiotic resistance and you told them they do not need antibiotics, they leave your pharmacy and get the medicine next door" (cited by Bahta et al. 2021, 4).

For all these reasons, gaining knowledge of which antibiotics are unlikely to worsen AMR does not necessarily affect the choices of health care workers and patients.[5] When collective action problems are severe, epistemic authority is insufficient—political authority is also required.

In a few areas of global health, states have delegated some political authority to the WHO, defined as the right to make collectively binding decisions. Such political authority is most evident in the power conferred by the International Health Regulations (IHR) to the WHO Director-General to declare a public health emergency of international concern and to issue temporary and standing recommendations on what actions the member states should take to address the crisis. If a government takes measures that are more stringent than those recommended by the WHO and that significantly interfere with international traffic, it has a legal obligation to justify them to WHO using scientific reasoning and evidence, and the WHO can request that the government reconsiders the application of the measures. The degree of political authority the WHO wields remains very limited: member states were entitled to opt out of the IHR for a period after its adoption, and the WHO Director-General has no means of

[5] In principle, alerting the public and health workers to the dangers of AMR might even backfire, as noted by some of the most vocal supporters of decisive action against antibiotic misuse: "Perhaps the major risk from predicting a post-antibiotic era that leads to public alarm is that this may also drive individual behavior that makes good antimicrobial stewardship difficult, that is, it increases demand for broad-spectrum antibiotics that, from a society perspective, we would prefer to hold in reserve" (Fowler, Walker, and Davies 2014, 7)

enforcing compliance with their provisions (Davies, Kamradt-Scott, and Rushton 2015; Worsnop et al. 2023).

In relation to AMR, the WHO does not even have this limited degree of political authority. Its recommendations in this area are not based on a legally binding treaty like the IHR but on the general mandate conferred by the WHO Constitution. To spur action on this issue, in 2015, the WHO adopted a Global Action Plan (GAP) on AMR that requested all member states to create national action plans (NAPs) and implement thirty-one key actions to raise awareness, increase surveillance, reduce infection, optimize antimicrobial medicines use, and increase sustainable investment (WHO 2015). One of the actions requested is the "development and implementation of national and institutional essential medicine lists guided by the WHO Model Lists of Essential Medicines, reimbursement lists and standard treatment guidelines to guide purchasing and prescribing of antimicrobial medicines, and regulation and control of promotional practices by industry" (WHO 2015, 17). The WHO, the Food and Agriculture Organization and the World Organization for Animal Health periodically ask governments to provide information on which AMR-relevant policies have been adopted and implemented, through a Tripartite AMR Country Self-assessment Survey (TrACSS), and the WHO publishes the information in its website (WHO-FAO-OIE 2022). Despite the standardized format of the TrACSS, the WHO does not aggregate the responses into a single and easily comparable index of AMR policy action, in constrast to other instances of "governance by indicators" in global health (Kentikelenis and Seabrooke 2022).

Many governments heeded the WHO's request and created NAPs (Munkholm and Rubin 2020; Patel et al. 2023). By adopting such plans, states agreed to use their political authority in support of the policies recommended by the WHO. In principle, governments possess regulatory instruments suitable to address the collective action problem of antibiotic use (Rogers Van Katwyk et al. 2019; Lim et al. 2020). For instance, they can impose sanctions on practices such as selling drugs without a prescription and invest resources into the surveillance of compliance. They can also provide positive incentives for behavior change. For example, as part of the UK Five Year Antimicrobial Resistance Strategy, in 2015 the National Health Service of England included an antibiotic prescribing element to the national "quality premium", which provides financial rewards to the bodies organizing healthcare services in each local area. To qualify for such financial rewards, primary care prescribers were asked to meet reduction targets for all antibiotics, with more stringent targets applied to a set of broad-spectrum antibiotics (Anyanwu et al. 2020; Gotham et al. 2021).

By adopting and implementing a NAP aligned with the GAP, states confer to WHO the status of what earlier has been referred to as a "politically assigned epistemic authority" in the field of AMR (Zürn 2018, 52-3). We expect that this mix of epistemic authority provided by WHO and the political authority wielded by governments directs antibiotic use patterns in a more sustainable direction. However, the combination developed unevenly worldwide because some governments implemented NAPs later than others or not at all. Heinzel and Koenig-Archibugi (2023) show that NAP implementation is affected by the bureaucratic capacity of the government and implementation by regional peers. The uneven take-up of NAPs signifies differences in governments' use of their political authority in the service of tackling AMR. We are specifically interested whether NAP implementation facilitates the effect of the AWaRe classification on antibiotic use and formulate the following hypotheses:

H2a (Watch): When antibiotics are listed as Watch antibiotics in the WHO's AWaRe classification, countries that implement AMR national action plans reduce per capita consumption of these antibiotics.

H2b (Reserve): When antibiotics are listed as Reserve antibiotics in the WHO's AWaRe classification, countries that implement AMR national action plans reduce per capita consumption of these antibiotics.

Research Design

We estimate two-way fixed effects (TWFE) models using IQVIA MIDAS proprietary quarterly pharmaceutical sales data, licensed from IQVIA, for 274 molecules (listed in Appendix) in Kilograms for 93 countries for the period Q1 2014 to Q2 2023.IQVIA MIDAS is the world's most comprehensive dataset of historical drug volumes and sales, and previous releases of the dataset have been used by other researchers studying patterns of antibiotic use (Klein et al. 2018; Klein et al. 2021; Browne et al. 2021; Bortone et al. 2021; Nandi, Pecetta, and Bloom 2023; Simmons et al. 2021). MIDAS data is updated Monthly and Quarterly and retroactive backdata changes can be applied,

We preregistered our empirical analyses before observing the data.[6] We did not alter the choices made in the pre-registration and label all additional analyses as exploratory throughout

[6] https://osf.io/7z6xe/?view_only=916f35b85a3e4a0b937229e67c7ab335

the paper. The pre-registration was uploaded on August 29, 2023, and we ~~received~~ licensed and received access to the data on September 20, 2023.

The unit of analysis is the country-drug-year. In our request to IQVIA, we included 297 antibiotic molecules. These molecules were selected based on two sources. First, we included all antibiotics listed in the three available versions of the AWaRe classification (2017, 2019, and 2021). Our main models rely on these antibiotics. Second, we included all antibiotics listed by Klein et al. (2018) and Klein et al. (2021) in their studies of global antibiotic consumption. We included these additional antibiotics to conduct a placebo check, which is discussed in more detail below. IQVIA delivered data on 274 drugs—the remaining antibiotics were not included in the IQVIA MIDAS data and are, thus, absent from our study. We exclude all drugs not listed in the 2017, 2019, or 2021 AWARE classifications for the main models.

The delivered data included 93 countries. Nineteen of these countries are part of two aggregated regions, "Central America" and "West Africa." Central America includes seven countries, and West Africa contains 12 countries. Due to a lack of country-level covariates, identifying specific control variables and some independent variables is difficult for these countries. Therefore, we excluded them from the primary analyses but present robustness checks that include them where possible. The countries in our sample cover approximately 80% of global antibiotic consumption in 2017 (Browne et al. 2021).

Our primary dependent variable of interest is antibiotic consumption (in defined daily doses [DDD] per 1000 people per day) of a given drug in a given country and year. IQVIA data are widely employed in studies of drug consumption and are generally considered the most comprehensive source of drug consumption data. One limitation is that the data are based on drug sales rather than actual consumption. At our request, IQVIA delivered data in kilograms. We estimate DDD per 1000 people per day by drawing on the WHO/ATC list for DDD, Klein et al. (2018) and Klein et al. (2021). The WHO ATC/DDD list is the authoritative source for the recommended dosage of many drugs. Where DDD values are unavailable from the WHO list, we rely on Klein et al.'s estimations of DDD for additional antibiotics. For 19 drugs, we could not identify a DDD value from Klein et al. or WHO/ATC. We imputed these values in 9 of these cases, making some basic assumptions.[7] For the remaining 10 antibiotics, we could not identify DDD values and, hence, dropped them from the analysis. The Appendix displays a full list of the coding choices.

[7] Specifically, we identified combination antibiotics including these drugs and calculated the likely DDD value based on existing information of the other part of the combination.

The first AWARE classification was adopted in 2017, and, as discussed, the goal formulated by the WHO was 60% Access antibiotics by 2023. To ensure that we had substantial pre-treatment coverage, we licensed data from 2014-2023. We licensed the latest available data from IQVIA which was Q1 and Q2 data for 2023. Existing analyses of monthly antibiotic consumption patterns imply a cyclical pattern where consumption increases in winter and decreases in summer (Nandi, Pecetta, and Bloom 2023). In other words, the Q1 and Q2 values tend to be very similar to the Q3 and Q4 values. Therefore, we multiplied the 2023 estimates by 2 to get the full 2023 value. Where IQVIA delivered data on multiple methods of administration for the same drugs, we aggregate the data to the country-drug-year level.

We employ four primary independent variables to operationalize our main theoretical arguments. We include a variable coded as one if the WHO listed a given drug as a Reserve antibiotic in a given year and as zero otherwise (H1a). Moreover, we create a binary variable coded as one if the WHO listed a given drug as a Watch antibiotic in a given year and as zero otherwise (H1b).

Additionally, we employ two binary interaction variables to operationalize the political support variables. As discussed, we operationalize political will through countries' implementing national action plans to combat AMR. This measure is based on the TrACSS survey conducted by the WHO, FAO, and OIE. Specifically, the survey asks countries to indicate the status of their NAPs. Countries can choose between five answer categories: (a) the country has no NAP, (b) a NAP is being developed, (c) a NAP has been adopted, (d) a NAP was approved, budgeted, is aligned with GAP objectives and has an operational plan, and (e) a NAP was approved, has funding, involves relevant sectors, and monitoring and evaluation is in place. We take answers of (d) or (e) as an indication that countries were implementing their NAP. We conducted online searches for countries with NAPs before 2016 to identify the first known implementation date based on academic articles, official evaluations, and other official sources. We then build two more variables based on this implementation indicator. The first variable is coded as one if a given drug was listed as a Reserve antibiotic by the WHO in a given year and the country was implementing a national action plan on AMR in the same year and as zero if one or both of these conditions are not fulfilled (H2a). The second variable is coded as one if a given drug was listed as a Watch antibiotic by the WHO in a given year and the country was implementing a national action plan on AMR in the same year and as zero if one or both of these conditions are not fulfilled (H2b).

Our country-drug fixed effects control for time-invariant differences in consumption between countries and particular drugs. We also include year fixed effects to control for

common shocks. Nevertheless, time-varying confounders are still of concern. To account for such time-varying confounders at the country level, we control for logged population, logged GDP per capita and economic growth (all from World Bank 2023), government health expenditure as a share of total health expenditure (IHME 2023), and electoral democracy and bureaucratic quality proxied by criteria for appointment decisions in the state administration (both from Coppedge et al. 2021). Health spending data from IHME is only available until 2019 as of July 2023. Therefore, we rely on projected health spending by IHME for 2020-2022. We lag all independent and control variables by one year.

Results

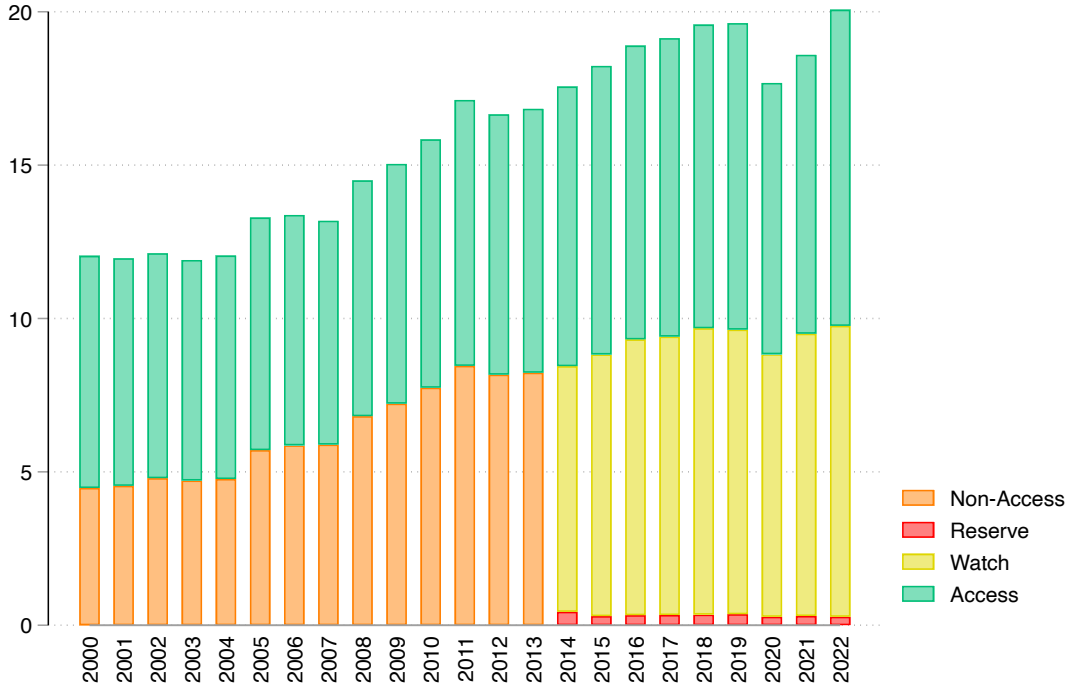
Before discussing the results from our statistical analyses, we highlight some broad patterns in global antibiotic consumption. Browne et al. (2021) estimate that the global volume of antibiotic consumption increased by 46 percent between 2000 and 2018. In this paper, however, we are interested in consumption levels of the three WHO categories of Access, Watch, and Reserve. To this end, we used two sources. First, Klein et al. (2018) and Klein et al. (2021) present data on antibiotics consumed in 93 countries between 2000 and 2015 based on earlier data licensed from IQVIA.[8] Second, we included the same antibiotics in our request to extend these data to 2022. Since IQVIA MIDAS data is dynamic, backdata changes can be applied retroactively and, therefore, the data we obtained show minor differences from the data presented by Klein et al. (2021) for the two overlapping years, 2014 and 2015. For the purpose of displaying the long-term trend, we adjust earlier values from Klein et al. based on the average difference between the two estimations in these two years.

Figure 1 displays the global volume of consumption of different categories of antibiotics in 93 countries between 2000 and 2022[9]. The overall use of Watch antibiotics increased until 2018 and then seems to have stabilized, except for a temporary drop in the COVID-19-year 2020. Trends can also be assessed by considering what percentage of total consumption is made up of Access antibiotics. As noted earlier, the WHO aims for it to be at least 60 per cent (WHO 2020). Figure A1 in the Appendix shows that percentage for all years since 2000. While the percentage of Access antibiotics consumed globally in the early 2000s was approximately 63%, that number decreased to around 57% by 2005 and 50% by 2013. Since then, the percentage

[8] We extracted these data from the website resistancemap.org.
[9] Since full 2023 data was not yet available at the time of conducting the analysis, we exclude them from the visualization (but include them in the regression models).

of Access antibiotics has been somewhat stable and there appears to be a slow-down of the trend of increasing consumption of Watch antibiotics globally.

Figure 1: Access antibiotics consumed 2000 to 2022 in 93 countries (in DDD per 1000 people per day)



Source of data: *IQVIA MIDAS® Quarterly sales data in KG, reflecting estimates of real-world activity. Copyright IQVIA. All rights reserved.*Note: Data before 2013 is based on (adjusted) estimates from Klein et al. (2021) based on IQVIA MIDAS—extracted from resistancemap.org. As IQVIA updates their earlier data in later years when new data becomes available, we adjust these estimates based on differences in overlapping years between the data we obtained and Klein et al. (2021). Klein et al. (2021) only distinguish between Access and non-Access antibiotics. Therefore, we only disaggregate the non-Access category into Watch and Reserve when using the data from 2014 onwards.

The overall descriptive patterns we have presented could hide substantial heterogeneity in antibiotic consumption and the trajectories of different countries. WHO epistemic authority might have provided an important backstop against a further increase in the consumption of Watch and Reserve antibiotics. We probe this question in more detail in the remainder of the paper. Whereas Figure 1 shows the sum of all relevant antibiotics used across all countries in the sample, the next part of the analysis implements fixed effects regressions and uses country-molecule level estimates of antibiotic consumption in DDD per 1000 people per day. While these models increase causal leverage, they hide substantial heterogeneity in the importance of some countries. In other words, whether China reduces the consumption of a particular Watch antibiotic per 1000 people per day is arguably much more relevant for addressing the problem

of AMR than if a smaller country like Belgium does. Despite this downside, we selected our model specification to increase our ability to understand whether the AWaRe classification had a causal effect on antibiotic consumption.

Table 1 displays the results of a sequence of models. Model 1 includes only measures of Watch and Reserve antibiotics. Model 2 incorporates the country-level control variables. These two regressions can be seen as tests for Hypotheses 1 and 2. Model 3 also includes the binary variable indicating whether a given country implemented a national action plan against AMR. Models 4 and 5 focus on governments' support for the WHO's global agenda. To this end, we display the interaction between the classification, Reserve or Watch, and the implementation of an NAP. Model 5 also includes our country-level control variables.

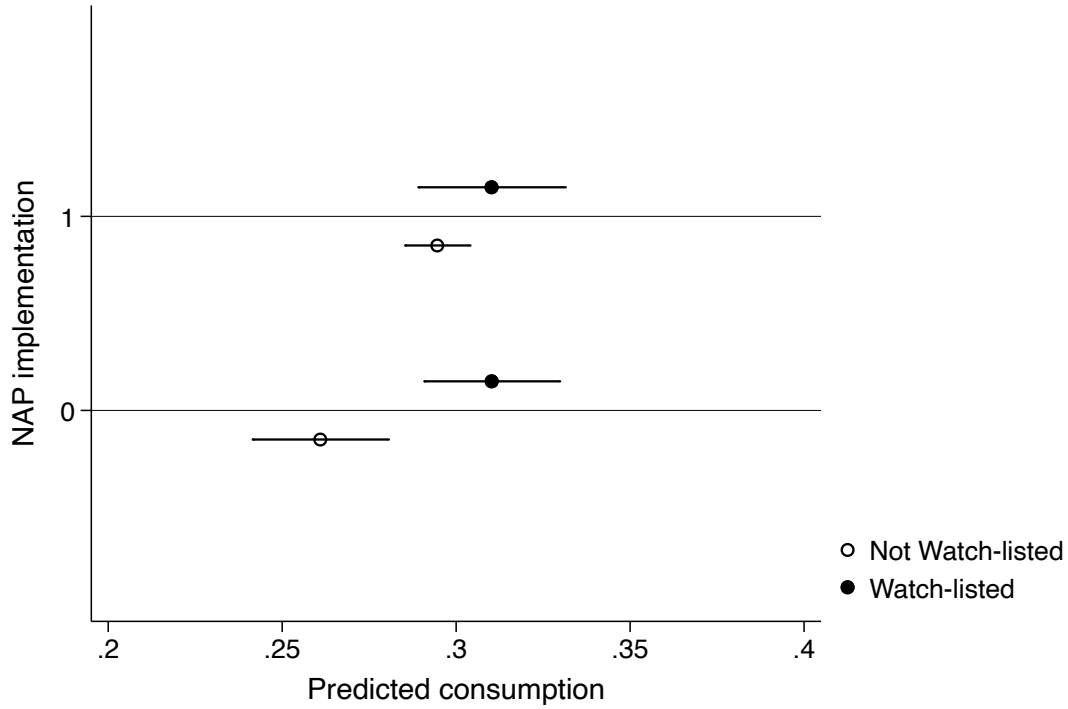
The results presented in Table 1 show some clear patterns. First, the epistemic authority of the WHO does not seem to lead by itself to improved antibiotic use. On average, consumption of an antibiotic in a country appears to have increased when listed as Watch. The effect size, 0.0233 DDD per 1000 people per day, is the equivalent of around 10% of the mean antibiotic consumption in a given country-molecule-year. In other words, Models 1 and 2 indicate that after being listed as a Watch antibiotic, sales of a drug increased by approximately 10% per year, on average in the countries in the sample. Second, there is evidence that WHO expertise on AMR seems to have curbed the growth in Watch antibiotics in countries where governments were implementing action plans on AMR. On average, our models estimate that the consumption of Watch-listed antibiotics decreases by around 0.037 DDD per 1000 people per day in countries implementing a national action plan once they have been listed as Watch antibiotics. However, this decrease is insufficient to curb the overall increase in Watch antibiotics even among countries implementing a NAP. To ease the interpretation of these results, we display the predicted values of each level of the Watch * NAP implementation interaction coefficients in Figure 2 (based on the fully specified Model 5). The results show that, on average, countries increase their consumption of Watch antibiotics, even after these drugs were listed in the classification. However, the increases do not materialize in countries implementing a NAP. While these countries appear to still expand their consumption of antibiotics, on average, they appear to do so using mainly antibiotics in the Access category. Hence, there are no statistically significant differences between antibiotics listed as Watch and not listed as Watch in countries implementing their NAPs.

Table 1: Assessing the impact of the WHO AWARE classification.

	(1)	(2)	(3)	(4)	(5)
Watch	0.0233*	0.0237*	0.0226*	0.0549***	0.0547***
	(0.0101)	(0.0106)	(0.0109)	(0.0146)	(0.0143)
Reserve	0.0006	-0.0011	-0.0012	-0.1266	-0.1307
	(0.0248)	(0.0265)	(0.0268)	(0.1416)	(0.1435)
NAP implementation			0.0355**	0.0328***	0.0338***
			(0.0128)	(0.0091)	(0.0098)
Watch * NAP implementation				-0.0362**	-0.0371**
				(0.0117)	(0.0117)
Reserve * NAP implementation				0.1510	0.1538
				(0.1413)	(0.1432)
Government health expenditure		-0.1343+	-0.0978		-0.0901
(% of total)		(0.0707)	(0.0808)		(0.0765)
Democracy		-0.1592	-0.1621		-0.1657
		(0.1011)	(0.1036)		(0.1068)
Bureaucratic quality		0.0137+	0.0122		0.0114
		(0.0082)	(0.0085)		(0.0088)
GDPpc (log)		0.0607*	0.0488+		0.0541+
		(0.0281)	(0.0275)		(0.0283)
Population (log)		-0.0734	-0.1110		-0.1119
		(0.1390)	(0.1545)		(0.1574)
Economic growth		0.0010	0.0012+		0.0012+
		(0.0007)	(0.0007)		(0.0007)
Country-drug fixed effects	Yes	Yes	Yes	Yes	Yes
Year fixed effects	Yes	Yes	Yes	Yes	Yes
Observations	55940	52798	51368	51510	51368
R^2	0.923	0.922	0.922	0.922	0.922

Source of consumption data: *IQVIA MIDAS® quarterly sales data in KG for Q1 2014 to Q2 2023, [93] countries, reflecting estimates of real-world activity. Copyright IQVIA. All rights reserved.*
Country-drug clustered standard errors in parentheses; $^{+}$ $p < 0.10$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Figure 2: Plotting the interaction between Watch antibiotics and NAP implementation.

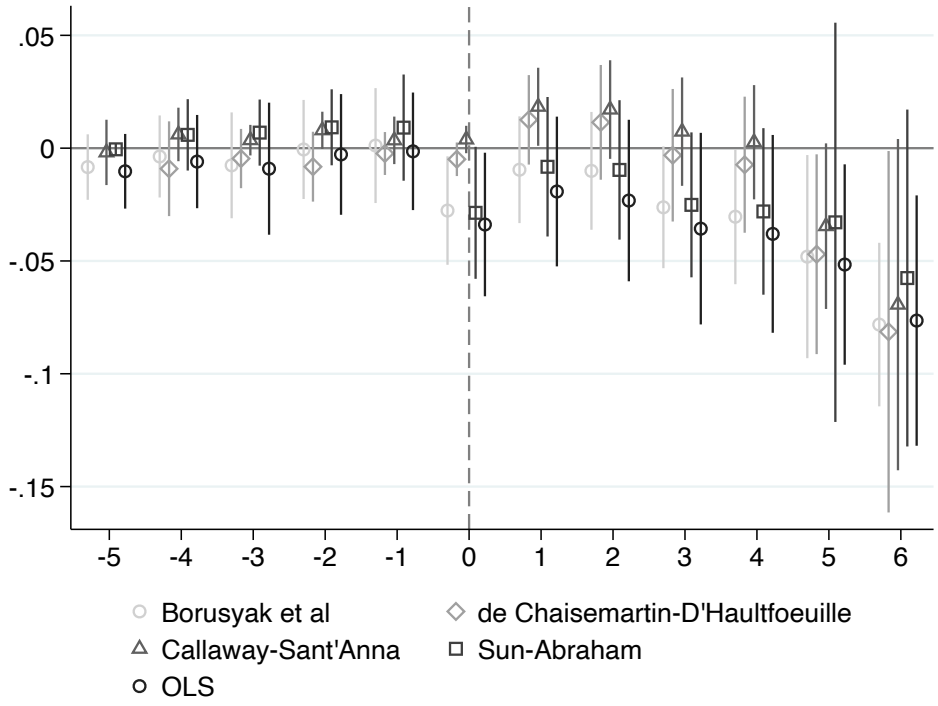


Source of consumption data: *IQVIA MIDAS® quarterly sales data in KG for Q1 2014 to Q2 2023, [93] countries, reflecting estimates of real-world activity. Copyright IQVIA. All rights reserved.*

Methodological debates on TWFE models have recently called these approaches into question. Specifically, the authors highlight three issues that could potentially threaten the validity of the conclusions drawn from TWFE models (Blackwell and Glynn 2018; Goodman-Bacon 2021; Imai and Kim 2021). First, TWFE models are a weighted average of individual two-time-period difference-in-difference estimates. With staggered adoption, the weights can be negative and can skew estimates. Second, the estimates rely on the assumption that treatment assignment is unrelated to past values of the dependent variable. Third, the models assume treatment effect homogeneity—treatment effects should not vary across years. Scholars have proposed a range of estimators meant to remedy these problems. Each of these estimators has benefits and drawbacks, and the literature has not converged on one approach. Hence, we compare our OLS estimates (based on Model 4) with the four most commonly used estimators (De Chaisemartin and d'Haultfoeuille 2020; Callaway and Sant'Anna 2021; Sun and Abraham 2021; Borusyak, Jaravel, and Spiess 2023) and display the results in an event plot in Figure 3. This plot also allows us to probe the main identifying assumption of TWFE models—common trends, which are present if the treated units would have behaved like the non-treated units without the treatment.

Figure 3 substantiates the relative ineffectiveness of the AWaRe classification. The pre-treatment trends are insignificant in all five estimators, and the estimates are, in fact, relatively precise zeroes. These findings strengthen the confidence that we can interpret our estimates as causal effects. The estimators generally show similar treatment effects over time, although most are more conservative than OLS. The OLS estimates are statistically significant in the initial year and years five and six after the treatment. The Sun and Abraham (2021) estimator is only statistically significant ($p < 0.05$) in the initial year of treatment introduction. The estimator by De Chaisemartin and d'Haultfoeuille (2020) is statistically significant in years five and six after the treatment. The approach by Borusyak, Jaravel, and Spiess (2023) shows statistically significant treatment effects in the year when the treatment is introduced and in years four, five, and six. Finally, the estimator by Callaway and Sant'Anna (2021) shows no statistically significant treatment effects at $p < 0.05$. In sum, these estimates appear to imply that we see some small reductions in consumption of Watch-listed antibiotics, and these are somewhat robust across estimators.

Figure 3: Testing robustness to various TWFE estimators.



Source of consumption data:*IQVIA MIDAS® quarterly sales data in KG for Q1 2014 to Q2 2023, [93] countries, reflecting estimates of real-world activity. Copyright IQVIA. All rights reserved.*.

So far, our models appear to show a small causal effect of the AWaRe classification but only in countries with politically committed governments and not in a magnitude that would have curbed the overall rise in the consumption of Watch antibiotics during the period under

investigation. To further substantiate the causal effect, we conducted a pre-registered placebo check. The main threat to inference is that national health systems independently identified some antibiotics they wanted to reduce and that these independent decisions are responsible for the small effect we observe. The placebo check uses a study by Klein et al. (2021). For the purpose of creating that study, three experts who had previously participated in producing the WHO's AWaRe list as members and advisors of the 21st Expert Committee on the Selection and Use of Essential Medicines[10] classified a number of antibiotics that had not been included in the WHO list. We assume that they applied the same classification criteria used in the WHO process, with the crucial difference that the outcome was not published by WHO. We re-estimate our models focusing on the antibiotics included by Klein et al. but not by the WHO to estimate whether the inclusion in the WHO list drives our effects. Since the list by Klein et al. has only been produced once, we re-estimate the models separately with treatments starting in the three years the WHO has published the AWaRe classification. As the list only includes two Reserve antibiotics, we group the Reserve and Watch groups in some models and exclude Reserve antibiotics in others. Table 2 presents the results. The interactions fail to attain statistical significance at conventional thresholds in all six models. These results indicate that the impact we identified in previous models was actually due to the WHO's AWaRe classification and not because of an independent decision by countries to curb the rise of problematic antibiotics.

[10] Sumanth Gandra, Céline Pulcini, and Mike Sharland.

Table 2: Placebo check.

	(6) 2017	(7) 2017	(8) 2019	(9) 2019	(10) 2021	(11) 2021
Watch & Reserve	0.0356**		0.0432***		0.0347***	
	(0.0113)		(0.0125)		(0.0093)	
Watch		0.0218**		0.0283***		0.0089*
		(0.0076)		(0.0082)		(0.0040)
NAP implementation	0.0020	0.0034	0.0035	0.0036	0.0035	0.0033
	(0.0049)	(0.0038)	(0.0034)	(0.0032)	(0.0031)	(0.0030)
Watch & Reserve * NAP implementation	0.0022		-0.0011		-0.0019	
	(0.0040)		(0.0021)		(0.0014)	
Watch * NAP implementation		-0.0006		-0.0024		-0.0014
		(0.0026)		(0.0016)		(0.0011)
Government health expenditure (% of total)	0.0336*	0.0324*	0.0323*	0.0326*	0.0326*	0.0326*
	(0.0165)	(0.0161)	(0.0161)	(0.0161)	(0.0154)	(0.0155)
Democracy	-0.0041	-0.0036	-0.0036	-0.0037	-0.0039	-0.0041
	(0.0122)	(0.0123)	(0.0123)	(0.0122)	(0.0121)	(0.0123)
Bureaucratic quality	-0.0005	-0.0004	-0.0004	-0.0004	-0.0004	-0.0004
	(0.0014)	(0.0014)	(0.0014)	(0.0014)	(0.0014)	(0.0014)
GDPpc (log)	-0.0108*	-0.0105*	-0.0104*	-0.0102*	-0.0102*	-0.0104*
	(0.0051)	(0.0051)	(0.0051)	(0.0051)	(0.0050)	(0.0050)
Population (log)	0.0232	0.0230	0.0233	0.0239	0.0239	0.0235
	(0.0199)	(0.0199)	(0.0195)	(0.0198)	(0.0195)	(0.0200)
Economic growth	-0.0000	-0.0000	-0.0000	-0.0000	-0.0000	-0.0000
	(0.0001)	(0.0001)	(0.0001)	(0.0001)	(0.0001)	(0.0001)
Country-drug fixed effects	Yes	Yes	Yes	Yes	Yes	Yes
Year fixed effects	Yes	Yes	Yes	Yes	Yes	Yes
Observations	16503	16503	16503	16503	16503	16503
R^2	0.969	0.968	0.969	0.968	0.968	0.968

Source of consumption data: *IQVIA MIDAS® quarterly sales data in KG for Q1 2014 to Q2 2023, [93] countries, reflecting estimates of real-world activity. Copyright IQVIA. All rights reserved.*Country-drug clustered standard errors in parentheses; $^{+}$ $p < 0.10$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

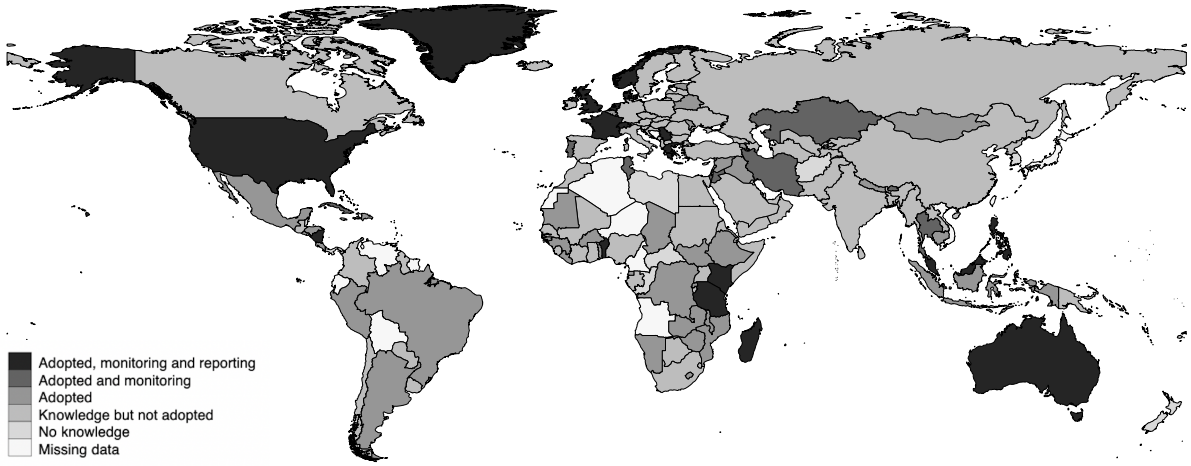
To summarize, we presented three main results in this section. First, the rise in the global consumption of Watch antibiotics seems to have slowed down or stopped, but the world has still lingered below the WHO-promoted 60% threshold of Watch antibiotics over total consumption since the mid-2000s. Second, the WHO's efforts to change prescription practices have had some small effects on the behavior of medical professionals in member states, but only in those member states that were politically committed to supporting the WHO agenda by implementing NAPs. Third, the magnitude of the effects is insufficient to create meaningful movement towards the target of 60% consumption of Watch antibiotics.

Exploratory analyses

Our findings indicate that the AWaRe framework helps achieve the aims of the WHO only in countries with politically supportive governments. We conducted further analyses to understand why this synergy materializes. We can posit three necessary conditions for its emergence: (1) the WHO has to raise awareness of the AWaRe framework among member states; (2) these member states need to be convinced to adopt the classification; and (3) member states need to be able to steer prescribers within their borders to change prescription behavior. The influence of the WHO could be stifled at each step: (1) governments may lack knowledge of the classification, implying limited dissemination capacity on the part of the WHO; (2) governments may have knowledge of the classification but be unwilling and/or unable to use it in their domestic medicines policies; (3) governments may have adopted the classification but lack the capacity to change the behavior of prescribers, sellers, and users.

We rely on self-reported data from the TRACSS surveys to probe these explanations. As part of the survey, governments inform the WHO about their knowledge and adoption of the AWaRe classification. Figure 4 displays countries' responses to the latest round of the TRACSS surveys. The data shows that the vast majority of countries know the classification. Therefore, the capacity of the WHO to raise awareness seems sufficient. However, the data also show that many countries have not adopted the classification six years after its initial publication.

Figure 4: Countries' adoption of AWARE classification (in 2022).



We test whether the limited influence of the classification is driven mainly by this lack of adoption or an inability to shape societal practices once the classification is adopted. To this

end, we re-estimate our models with one modification: we now interact Watch and Reserve status with a new variable, AWaRe adoption, coded as one if a given country indicated in a TRACSS survey that it has adopted the classification (Table 3). We display four regression models. The first includes only the Watch, Reserve, and AWaRe adoption variables. The second model further includes our control variables and the NAP implementation variable. Model three interacts the Watch and Reserve variables with AWaRe adoption. Model four, finally, is the fully specified regression, including control variables.

The results indicate that the national adoption of the AWaRe classification is followed by a substantial change in the use of antibiotics. The coefficient for the interaction is statistically significant ($p < 0.05$) and substantial. Countries adopting the AWaRe classification consume, on average, 0.271 (95% CIs: 0.283 to 0.258) DDDs per 1000 people in antibiotics after these drugs have been listed in the Watch category. Countries that have not adopted the classification nationally consume, on average, 0.324 (95% CIs: 0.301 to 0.347) DDDs per 1000 people in the same antibiotics. In other words, countries' adoption of the classification in their national medicines policies decreases the consumption of Watch antibiotics by 17% on average.

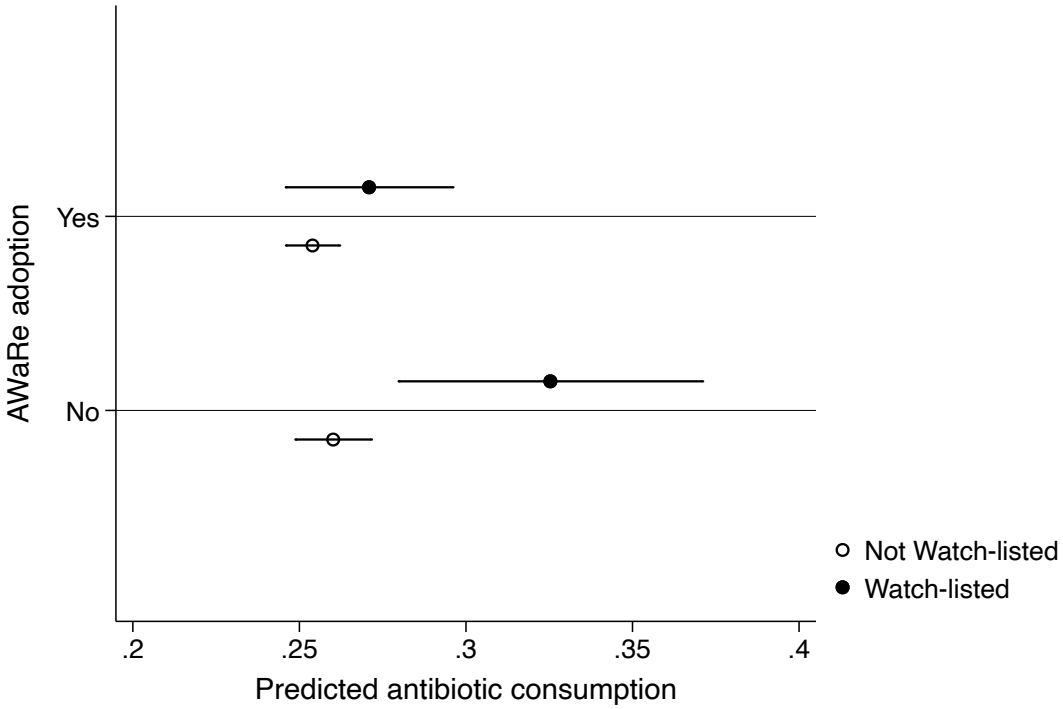
Again, we display predicted values to ease the interpretation of the interaction (Figure 5). The coefficients show that consumption of Watch antibiotics is much more likely than consumption of Access antibiotics in countries that have not adopted the AWaRe classification. However, once countries adopt it, we see substantial decreases in the sold volume of Watch antibiotics.

Table 3: Assessing the impact of the adoption of the WHO AWARE classification

	(12)	(13)	(14)	(15)
Watch	0.0275*	0.0261+	0.0640*	0.0636*
	(0.0137)	(0.0139)	(0.0253)	(0.0251)
Reserve	0.0311+	0.0305+	0.0328	0.0318
	(0.0184)	(0.0185)	(0.0235)	(0.0236)
AWaRe adoption	-0.0191*	-0.0172+	-0.0092	-0.0071
	(0.0085)	(0.0096)	(0.0064)	(0.0076)
Watch * AWaRe adoption			-0.0450*	-0.0463*
			(0.0228)	(0.0222)
Reserve * AWaRe adoption			-0.0039	-0.0035
			(0.0155)	(0.0157)
NAP implementation		0.0199*		0.0188*
		(0.0098)		(0.0096)
Government health expenditure (% of total)		0.1146		0.1229
		(0.1206)		(0.1201)
Democracy		-0.1743		-0.1772
		(0.1125)		(0.1125)
Bureaucratic quality		0.0093		0.0104
		(0.0089)		(0.0088)
GDPpc (log)		-0.0285		-0.0301
		(0.0445)		(0.0447)
Population (log)		0.0032		-0.0015
		(0.1950)		(0.1949)
Economic growth		0.0009		0.0009
		(0.0008)		(0.0008)
Country-drug fixed effects	Yes	Yes	Yes	Yes
Year fixed effects	Yes	Yes	Yes	Yes
Observations	32480	32332	32480	32332
R^2	0.942	0.943	0.942	0.943

Source of consumption data: *IQVIA MIDAS® quarterly sales data in KG for Q1 2014 to Q2 2023, [93] countries, reflecting estimates of real-world activity. Copyright IQVIA. All rights reserved.*Country-drug clustered standard errors in parentheses; $^{+}$ $p < 0.10$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Figure 5: Plotting the interaction between Watch and AWaRe adoption



Source of consumption data: *IQVIA MIDAS® quarterly sales data in KG for Q1 2014 to Q2 2023, [93] countries, reflecting estimates of real-world activity. Copyright IQVIA. All rights reserved.*Copyright IQVIA.

In a final step, we conduct exploratory analyses to understand what drives whether governments use their political authority to implement the AWaRe classification domestically. The WHO lacks means of enforcement that allow IOs to induce compliance from member states. IOs often need to rely on sympathetic interlocutors in national policy circles that advocate for IO policy advice and translate it to local contexts (Chwieroth 2007; Broome and Seabrooke 2015; Woods 2018; Arpac and Bird 2009; Heinzel and Liese 2021). We conjecture that participation in the process of creating the AWaRe classification is a powerful socializing experience that creates sympathetic interlocutors that serve as policy entrepreneurs in domestic policymaking on AMR. As discussed, the AWaRe classification is published by the WHO Expert Committee on the Selection and Use of Essential Medicines. The committee included fifteen individuals from fifteen different countries in 2017 (Argentina, Australia, China, France, Ghana, Morocco, Pakistan, Peru, South Africa, Sri Lanka, Switzerland, Tanzania, Thailand, UK, USA) (WHO 2017). Eight of these experts returned for the 2019 committee, which included thirteen experts from eleven countries (Canada, China, Italy, Pakistan, Peru, South Africa, Sri Lanka, Switzerland, Thailand, 2x UK, 2x USA)(WHO 2019). Eight experts from the 2019 committee also appear in the 2021 participant list. The 2021 committee again

includes fifteen individuals from fourteen countries (Australia, Cameroon, China, Ghana, Italy, Kenya, Netherlands, Pakistan, Peru, South Africa, Sri Lanka, Tunisia, 2x UK, USA) (WHO 2021). All members of these committees hold academic positions at national universities or are medical doctors at national hospitals (or both). We test whether countries whose experts are participating in the committee are more likely to engage with the AWaRe classification.

We estimate cross-sectional OLS models as data on AWaRe adoption is not available over a substantial time period. We cluster standard errors at the level of 20 sub-regions. Our main dependent variable is a score of the highest level of engagement with the AWaRe classification governments reported in the 2019-2022 TRACSS surveys. We created an adoption score that ranges from 1 (no knowledge) to 5 (adopted, monitoring and reporting). Our main independent variable is a binary indicator measuring whether a given country had at least one national in one of the three committees. Table 4 displays the results from five models. Model 16 includes only our main variable of interest, committee membership. Model 17 further incorporates region fixed effects. In Model 18, we account for our primary control variables. In Model 19, we also incorporate three models adjusting for political will that may affect both committee membership and engagement with the AWaRe classification. Finally, in Model 20, we also include the Access share to control for differential costs of adjustment of countries. All control variables are measured in 2016, the year before the first AWaRe classification.

The models provide evidence consistent with the argument that having a national expert in the committee increases the engagement of countries with the AWaRe classification. The coefficient is positive and substantial across model specifications. The difference between countries with and without an expert on the committee is statistically significant in all four models and the coefficient is substantial (around one standard deviation). We caution against overinterpreting these final results as they are based on cross-sectional models and may be affected by omitted variable bias. That said, the models imply that countries with an expert on the committee have an around 25-40% higher score in AWaRe engagement than countries without such an expert.

Table 4: Drivers of AWARE adoption

	(16)	(17)	(18)	(19)	(20)
Committee membership	1.1720***	1.1435***	0.8154**	0.7800**	0.6642*
	(0.2985)	(0.2838)	(0.2554)	(0.2555)	(0.3005)
Government health expenditure (% of total)			0.8220	0.6261	-1.1680
			(0.5126)	(0.5124)	(0.9832)
Democracy			0.1366	0.0487	0.6597
			(0.6753)	(0.6713)	(0.9397)
Bureaucratic quality			0.0523	0.0339	-0.0499
			(0.1134)	(0.1189)	(0.1949)
GDPpc (log)			-0.0890	-0.0715	-0.0365
			(0.0899)	(0.0936)	(0.2525)
Population (log)			0.1565*	0.1424*	0.2305+
			(0.0594)	(0.0510)	(0.1069)
Economic growth			-2.1531	-2.1372	-23.5543*
			(2.2138)	(2.4212)	(7.7236)
NAP (adoption)				-0.1402	0.2903
				(0.2183)	(0.6546)
NAP (implementation)				0.5631**	0.1995
				(0.1811)	(0.5727)
Antibiotic consumption (total)				0.0174	-0.0026
				(0.0115)	(0.0189)
Antibiotic consumption (share of Access antibiotics)					0.7722
					(1.1852)
Region fixed effects	No	Yes	Yes	Yes	Yes
Observations	184	184	167	167	64
R^2	0.106	0.224	0.262	0.291	0.485

Source of consumption data: *IQVIA MIDAS® quarterly sales data in KG for Q1 2014 to Q2 2023, [93] countries, reflecting estimates of real-world activity. Copyright IQVIA. All rights reserved.*Region clustered standard errors in parentheses; $^{+}$ $p < 0.10$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Overall, the results from our exploratory analyses imply that the main obstacle to the effectiveness of the AWaRe classification is the lack of widespread adoption among WHO member states. The WHO's ability to shape the behavior of prescribers, sellers, and uses independently of their government is very limited. To affect change in societal practices, the epistemic authority of the WHO needs to be supported by the political authority of governments. Finally, we provide some initial evidence that, in order to galvanize that political authority, the WHO relies crucially on sympathetic interlocutors that participate directly in its committees and can advocate for policy change at the national level.

Robustness checks

In addition to the tests reported in this article, we conducted several additional exploratory robustness checks included in the supplementary Appendix. First, in our main models we restricted the sample to all drugs that were consumed at least once in each country and were ever listed on the AWaRe classification. To ensure that these sample restrictions do not drive our results, we expanded the sample to include all drugs that we have data for. The results in that expanded sample are substantively similar (Table A1). Second, we test whether alternative measures of our dependent variable attain different results. Hence, we re-estimate our models using overall consumption, consumption per 1000 people, and consumption per capita as dependent variables (Table A2). The results hold in all but one case. The Watch*NAP implementation coefficient fails to attain statistical significance when using overall consumption as a dependent variable (Model 25). Third, our data on antibiotic consumption counts the number of defined daily doses consumed in a country. Hence, it may be more accurately modelled using a Poisson distribution. To account for this possibility, we re-estimate the regressions using Poisson-pseudo maximum likelihood models (Table A3). These estimations do not lead to different results. Fourth, we alter the time fixed effects to account for drug-specific time shocks by including drug-year fixed effects (Table A4). This approach does not change the conclusions we can draw from the data. Fifth, in our main models, we employ country-drug fixed effects. We also conduct robustness checks with country-clustered standard errors (Table A5) and the results remain consistent. Sixth, we control for previous levels of antibiotic consumption by controlling for a lagged dependent variable (Table A6). The findings are not affected by this choice. Finally, we also display the list of drugs included in the study (Table A7).

Conclusion

Some of the most important global problems are generated or exacerbated by practices of non-state actors. IOs address these problems by enlisting state support and by attempting to shape these actors' behavior directly. While many studies have demonstrated how IOs can influence state actions, less is known about their impact on the behavior of non-state actors. This paper has examined this question in relation to one of the most important IOs, the WHO. We have argued that the epistemic authority of the WHO is widely recognized not only by governments but also by health care professionals worldwide; however, by itself this authority should be insufficient to produce meaningful changes in the behavior of those professionals in the

presence of severe and diffuse collective action problems, such as those involving the use of antibiotics and the protection of antibiotic efficacy. In such circumstances, the knowledge diffused by the WHO needs to be supported by the political authority of member states. The paper assessed this argument through a pre-registered observational analysis of whether the adoption of the WHO's AWaRe classification—aimed at curbing the rise in antimicrobial resistance—led to a meaningful change in the sale of 274 antibiotics in 93 countries between 2014 and 2023. Our main findings are, first, that the AWaRe list has not had an unconditional effect on the behavior of health care professionals globally and, second, that it has served as a backstop in countries where governments are politically committed to addressing AMR. Furthermore, we found that the AWaRe classification has led to some small reductions in prescriptions in the minority of countries that have incorporated it into their national medicines policy. Finally, we found evidence that the political will to throw the weight of national political authority behind the AWaRe classification crucially depends on the participation of national experts in WHO decision-making committees.

These findings have implications for several current debates. First, they highlight that persuading government to formally incorporate the AWaRe classification in national policy frameworks may be a particularly important way of advancing the goals of the WHO's global action plan on AMR and slowing down the loss of antibiotic efficacy. This insight can be valuable for international policy-makers who may have to prioritize among the numerous policy measures that the global action plan asks member states to implement (WHO 2015; Munkholm and Rubin 2020; Patel et al. 2023).

Second, our findings provide insights on the state of global health governance more generally. Buoyed by developments in the early 2000s, prominent scholars pointed at an unfolding transition towards a "post-Westphalian" or post-international system of global public health (Fidler 2004; Ruger 2008; Kirton and Cooper 2009). Other scholars cautioned that such claims were "premature" and that states remain central (Ricci 2009). The evidence we presented indicate that the relationship is not zero-sum: both the epistemic authority of the main IGO in the health domain and the political authority wielded by states turned out to be necessary to mitigate the difficult problem of curbing the overuse and misuse of antibiotics. Future research on other health issues could provide further evidence relevant to our argument about the intensity of the collective action problem resulting from diffuse healthcare choices.

Third, polycentric governance is a lively area of research across most areas of international relations,[11] but an important ingredient of global polycentrism remains empirically underexplored: the capacity of IOs to translate the epistemic authority they have in the eyes of societal groups and individuals into desired behavioral changes, even in the context of inaction by government actors. An important emerging body of research examines, often using experimental methods, whether IO positions and communications affects citizen attitudes but—as noted in the introduction—the attitudes of interest are almost always about government action rather than about the behavior of the citizens themselves. We hope that, by generating insights on the effect of IO epistemic authority on societal practices in relation to an important global challenge, our study will inspire other researchers to give this potential route of IO impact the attention that it deserves.

References:

Abbott, Kenneth W, and Duncan Snidal. 1998. "Why states act through formal international organizations." *Journal of Conflict Resolution* 42 (1):3-32.

Abdelsalam Elshenawy, Rasha, Nkiruka Umaru, and Zoe Aslanpour. 2023. "WHO AWaRe classification for antibiotic stewardship: Tackling antimicrobial resistance–a descriptive study from an English NHS Foundation Trust prior to and during the COVID-19 pandemic." *Frontiers in Microbiology* 14.

Abeysinghe, Sudeepa. 2015. *Pandemics, Science and Policy: H1N1 and the World Health Organisation*. Basingstoke: Palgrave Macmillan.

Adekoya, Itunuoluwa, Darshanand Maraj, Liane Steiner, Hannah Yaphe, Lorenzo Moja, Nicola Magrini, Graham Cooke, Mark Loeb, and Nav Persaud. 2021. "Comparison of antibiotics included in national essential medicines lists of 138 countries using the WHO Access, Watch, Reserve (AWaRe) classification: A cross-sectional study." *The Lancet Infectious Diseases* 21 (10):1429-1440.

Ahmed, Syud Amer, Enis Barış, Delfin S Go, Hans Lofgren, Israel Osorio-Rodarte, and Karen Thierfelder. 2018. "Assessing the global poverty effects of antimicrobial resistance." *World Development* 111:148-160.

Aligica, Paul D, and Vlad Tarko. 2012. "Polycentricity: From Polanyi to Ostrom, and beyond." *Governance* 25 (2):237-262.

Anjum, Gulnaz, Adam Chilton, and Zahid Usman. 2021. "United Nations endorsement and support for human rights: An experiment on women's rights in Pakistan." *Journal of Peace Research* 58 (3):462-478.

Anyanwu, Philip Emeka, Koen Pouwels, Anne Walker, Michael Moore, Azeem Majeed, Benedict WJ Hayhoe, Sarah Tonkin-Crine, Aleksandra Borek, Susan Hopkins, and Monsey Mcleod. 2020. "Investigating the mechanism of impact and differential effect of the Quality Premium scheme on antibiotic prescribing in England: A longitudinal study." *BJGP Open* 4 (3).

[11] See for instance Ostrom (2010); Aligica and Tarko (2012); Jordan et al. (2018); Kim (2020); Gadinger and Scholte (2023).

Arpac, Ozlem, and Graham Bird. 2009. "Turkey and the IMF: A case study in the political economy of policy implementation." *The Review of International Organizations* 4:135-157.

Auta, Asa, Muhammad Abdul Hadi, Enoche Oga, Emmanuel O Adewuyi, Samirah N Abdu-Aguye, Davies Adeloye, Barry Strickland-Hodge, and Daniel J Morgan. 2019. "Global access to antibiotics without prescription in community pharmacies: A systematic review and meta-analysis." *Journal of Infection* 78 (1):8-18.

Baekkeskov, Erik, Olivier Rubin, Louise Munkholm, and Wesal Zaman. 2020. "Antimicrobial resistance as a global health crisis." *Oxford Research Encyclopedia of Politics* https://doi.org/10.1093/acrefore/9780190228637.013.1626.

Bahta, Merhawi, Dawit G Weldemariam, Sirak Tesfamariam, Eyasu H Tesfamariam, and Mulugeta Russom. 2021. "Determinants of dispensing antibiotics without prescription in Eritrea: A mixed-method qualitative study on pharmacy professionals' perspective." *BMJ Open* 11 (8):e049000.

Barnett, Michael, and Martha Finnemore. 2004. *Rules for the World: International Organizations in Global Politics*. Ithaca, NY: Cornell University Press.

Batista, Ana Daniela, Daniela A. Rodrigues, Adolfo Figueiras, Maruxa Zapata-Cachafeiro, Fátima Roque, and Maria Teresa Herdeiro. 2020. "Antibiotic dispensation without a prescription worldwide: A systematic review." *Antibiotics* 9 (11):786.

Bearce, David H, and Thomas R Cook. 2018. "The first image reversed: IGO signals and mass political attitudes." *The Review of International Organizations* 13 (4):595-619.

Berliner, Daniel, and Aseem Prakash. 2015. "'"Bluewashing" the Firm? Voluntary Regulations, Program Design, and Member Compliance with the United Nations Global Compact." *Policy Studies Journal* 43 (1):115-138.

Blackwell, Matthew, and Adam N Glynn. 2018. "How to make causal inferences with time-series cross-sectional data under selection on observables." *American Political Science Review* 112 (4):1067-1082.

Blaser, Martin J, Melissa K Melby, Margaret Lock, and Mark Nichter. 2021. "Accounting for variation in and overuse of antibiotics among humans." *BioEssays* 43 (2):2000163.

Bortone, Barbara, Charlotte Jackson, Yingfen Hsia, Julia Bielicki, Nicola Magrini, and Mike Sharland. 2021. "High global consumption of potentially inappropriate fixed dose combination antibiotics: Analysis of data from 75 countries." *PLoS One* 16 (1):e0241899.

Borusyak, Kirill, Xavier Jaravel, and Jann Spiess. 2023. "Revisiting Event Study Designs: Robust and Efficient Estimation." *Review of Economic Studies* forthcoming.

Broom, Alex, Katherine Kenny, Emma Kirby, Nimesh George, and Mahati Chittem. 2020. "Improvisation, therapeutic brokerage and antibiotic (mis) use in India: A qualitative interview study of Hyderabadi physicians and pharmacists." *Critical Public Health* 30 (1):16-27.

Broome, André, and Leonard Seabrooke. 2015. "Shaping policy curves: Cognitive authority in transnational capacity building." *Public Administration* 93 (4):956-972.

Brown, Theodore M, Marcos Cueto, and Elizabeth Fee. 2006. "The World Health Organization and the transition from "international" to "global" public health." *American Journal of Public Health* 96 (1):62-72.

Browne, Annie J, Michael G Chipeta, Georgina Haines-Woodhouse, Emmanuelle Kumaran, Bahar H Kashef Hamadani, Sabra Zaraa, Nathaniel J Henry, Aniruddha Deshpande, Robert C Reiner Jnr, Nicholas PJ Day, Alan D. Lopez, Susanna Dunachie, Catrin E. Moore, Andy Stergachis, Simon I. Hay, and Christiane Dolecek. 2021. "Global antibiotic consumption in humans, 2000 to 2018: A spatial modelling study." *The Lancet* 5 (12):e893-e904.

Callaway, Brantly, and Pedro HC Sant'Anna. 2021. "Difference-in-differences with multiple time periods." *Journal of Econometrics* 225 (2):200-230.
Chapman, Terrence L. 2012. *Securing Approval: Domestic Politics and Multilateral Authorization for War*. Chicago: University of Chicago Press.
Chapman, Terrence L, and Huimin Li. 2023. "Can IOs influence attitudes about regulating "Big Tech"?" *The Review of International Organizations* 18:725–751
Chwieroth, Jeffrey. 2007. "Neoliberal economists and capital account liberalization in emerging markets." *International Organization* 61 (2):443-463.
Coppedge, Michael, John Gerring, Carl Henrik Knutsen, Staffan I. Lindberg, Jan Teorell, Nazifa, Alizada, Michael Bernhard David Altman, Agnes Cornell, M. Steven Fish, Lisa Gastaldi, Haakon Gjerløw, Adam Glynn, Allen Hicken, Garry Hindle, Nina Ilchenko, Joshua Krusell, Anna Luhrmann, Seraphine F. Maerz, Kyle L. Marquardt, Kelly McMann, Valeriya Mechkova, Juraj Medzihorsky, Pamela Paxton, Daniel Pemstein, Josefine Pernes, Johannes von Romer, Brigitte Seim, Rachel Sigman, Svend-Erik Skaaning, Jeffrey Staton, Aksel Sundstrom, Eitan Tzelgov, Yi-ting Wang, Tore Wig, Steven Wilson, and Daniel Ziblatt. 2021. V-Dem [Country-Year/Country-Date] Dataset v11.1. Varieties of Democracy Project.
Davies, Sara E, Adam Kamradt-Scott, and Simon Rushton. 2015. *Disease Diplomacy: International Norms and Global Health Security*. Baltimore: Johns Hopkins University Press.
De Chaisemartin, Clément, and Xavier d'Haultfoeuille. 2020. "Two-way fixed effects estimators with heterogeneous treatment effects." *American Economic Review* 110 (9):2964-96.
Dellmuth, Lisa, Jan Aart Scholte, Jonas Tallberg, and Soetkin Verhaegen. 2022. *Citizens, Elites, and the Legitimacy of Global Governance*. Oxford: Oxford University Press.
Ecker-Ehrhardt, Matthias. 2018. "International organizations "going public"? An event history analysis of public communication reforms 1950–2015." *International Studies Quarterly* 62 (4):723-736.
Erauskin-Tolosa, Artitzar, Eugenio Zubeltzu-Jaka, Iñaki Heras-Saizarbitoria, and Olivier Boiral. 2020. "ISO 14001, EMAS and environmental performance: A meta-analysis." *Business Strategy and the Environment* 29 (3):1145-1159.
Fidler, David. 2004. *SARS, Governance and the Globalization of Disease*. Basingstoke and New York: Palgrave Macmillan.
Fowler, Tom, David Walker, and Sally C Davies. 2014. "The risk/benefit of predicting a post-antibiotic era: Is the alarm working?" *Annals of the New York Academy of Sciences* 1323 (1):1-10.
Friedman, Richard B. 1973. "On the concept of authority in political philosophy." In *Concepts in Social and Political Philosophy*, edited by Richard E. Flathman, 121-46. New York: Macmillan.
Gadinger, Frank, and Jan Aart Scholte, eds. 2023. *Polycentrism: How Governing Works Today*. Oxford: Oxford University Press.
Goodman-Bacon, Andrew. 2021. "Difference-in-differences with variation in treatment timing." *Journal of Econometrics* 225 (2):254-277.
Gotham, Dzintars, Lorenzo Moja, Maarten van der Heijden, Sarah Paulin, Ingrid Smith, and Peter Beyer. 2021. "Reimbursement models to tackle market failures for antimicrobials: Approaches taken in France, Germany, Sweden, the United Kingdom, and the United States." *Health Policy* 125 (3):296-306.
Green, Leslie. 1998. "Authority." In *Routledge Encyclopedia of Philosophy*, edited by Edward Craig, 584-586. London and New York: Routledge.

Greenhill, Brian. 2020. "How can international organizations shape public opinion? Analysis of a pair of survey-based experiments." *The Review of International Organizations* 15 (1):165-188.
Haas, Peter M. 2023. "Preserving the epistemic authority of science in world politics." In *Professions and Proficiency*, edited by Johannes Glückler, Christopher Winch and Anna Mateja Punstein, 135-155. Cham: Springer.
Haas, Peter M. 1992. "Introduction: Epistemic communities and international policy coordination." *International Organization* 46 (1):1-35. doi: 10.1017/S0020818300001442.
Haerpfer, C. , R. Inglehart, A. Moreno, C. Welzel, K. Kizilova, Diez-Medrano J., M. Lagos, P. Norris, E. Ponarin, and B. Puranen, eds. 2022. *World Values Survey: Round Seven - Country-Pooled Datafile Version 5.0*. Madrid, Spain & Vienna, Austria: JD Systems Institute & WVSA Secretariat.
Heinzel, Mirko, and Mathias Koenig-Archibugi. 2023. "Soft governance against superbugs: How effective is the international regime on antimicrobial resistance?" *Review of International Organizations* Published online 30 September.
Heinzel, Mirko, and Andrea Liese. 2021. "Managing performance and winning trust: How World Bank staff shape recipient performance." *The Review of International Organizations* 16 (3):625-653.
Hillock, Nadine T, Erin Connor, Courtenay Wilson, and Brendan Kennedy. 2021. "Comparative analysis of Australian hospital antimicrobial utilization, using the WHO AWaRe classification system and the adapted Australian Priority Antimicrobial List (PAL)." *JAC-Antimicrobial Resistance* 3 (1):dlab017.
Hoffman, Steven J, Prativa Baral, Susan Rogers Van Katwyk, Lathika Sritharan, Matthew Hughsam, Harkanwal Randhawa, Gigi Lin, Sophie Campbell, Brooke Campus, and Maria Dantas. 2022. "International treaties have mostly failed to produce their intended effects." *Proceedings of the National Academy of Sciences* 119 (32):e2122854119.
Hooghe, Liesbet, Tobias Lenz, and Gary Marks. 2019. *A Theory of International Organization*. Oxford: Oxford University Press.
Hsia, Yingfen, Brian R Lee, Ann Versporten, Yonghong Yang, Julia Bielicki, Charlotte Jackson, Jason Newland, Herman Goossens, Nicola Magrini, and Mike Sharland. 2019. "Use of the WHO Access, Watch, and Reserve classification to define patterns of hospital antibiotic use (AWaRe): An analysis of paediatric survey data from 56 countries." *The Lancet Global Health* 7 (7):e861-e871.
Hurd, Ian. 1999. "Legitimacy and authority in international politics." *International Organization* 53 (2):379-408.
IHME. 2023. *Financing Global Health*. Seattle, WA: Institute for Health Metrics and Evaluation, University of Washington. Available from http://vizhub.healthdata.org/fgh/.
Imai, Kosuke, and In Song Kim. 2021. "On the use of two-way fixed effects regression models for causal inference with panel data." *Political Analysis* 29 (3):405-415.
IQVIA. IQVIA MIDAS data obtained under license, reflecting estimates of real-world activity. Copyright IQVIA. All rights reserved
Jacobson, Harold K. 1984. *Networks of Interdependence: International Organizations and the Global Political System*. New York: Alfred A. Knopf.
Johnson, Tana. 2020. "Ordinary patterns in an extraordinary crisis: How international relations makes sense of the COVID-19 pandemic." *International Organization* 74 (S1):E148-E168.

Jordan, Andrew, Dave Huitema, Harro Van Asselt, and Johanna Forster, eds. 2018. *Governing Climate Change: Polycentricity in Action?* Cambridge: Cambridge University Press.

Kalungia, Aubrey C, Moses Mukosha, Chiluba Mwila, David Banda, Matthews Mwale, Solomon Kagulura, Olanyika O Ogunleye, Johanna C Meyer, and Brian Godman. 2022. "Antibiotic use and stewardship indicators in the first-and second-level hospitals in Zambia: Findings and implications for the future." *Antibiotics* 11 (11):1626.

Kentikelenis, Alexander E, and Leonard Seabrooke. 2022. "Governing and measuring health security: The global push for pandemic preparedness indicators." *Global Policy* 13 (4):571-578.

Khan, Mishal, Afifah Rahman-Shepherd, Sothavireak Bory, Sophea Chhorn, Anna Durrance-Bagale, Rumina Hasan, Sotheara Heng, Socheata Phou, Chanra Prien, and Ari Probandari. 2022. "How conflicts of interest hinder effective regulation of healthcare: An analysis of antimicrobial use regulation in Cambodia, Indonesia and Pakistan." *BMJ Global Health* 7 (5):e008596.

Kim, Rakhyun E. 2020. "Is global governance fragmented, polycentric, or complex? The state of the art of the network approach." *International Studies Review* 22 (4):903-931.

Kirton, John J, and Andrew F. Cooper. 2009. "Innovation in global health governance." In *Innovation in Global Health Governance: Critical Cases*, edited by Andrew F. Cooper and John J. Kirton, 309-340. Farnham and Burlington: Ashgate.

Klein, Eili Y, Maja Milkowska-Shibata, Katie K Tseng, Mike Sharland, Sumanth Gandra, Céline Pulcini, and Ramanan Laxminarayan. 2021. "Assessment of WHO antibiotic consumption and access targets in 76 countries, 2000–15: An analysis of pharmaceutical sales data." *The Lancet Infectious Diseases* 21 (1):107-115.

Klein, Eili Y, Thomas P Van Boeckel, Elena M Martinez, Suraj Pant, Sumanth Gandra, Simon A Levin, Herman Goossens, and Ramanan Laxminarayan. 2018. "Global increase and geographic convergence in antibiotic consumption between 2000 and 2015." *Proceedings of the National Academy of Sciences* 115 (15):E3463-E3470.

Knowles, Rebecca, Mike Sharland, Yingfen Hsia, Nicola Magrini, Lorenzo Moja, Amani Siyam, and Elizabeth Tayler. 2020. "Measuring antibiotic availability and use in 20 low-and middle-income countries." *Bulletin of the World Health Organization* 98 (3):177.

Kobayashi, Yoshiharu, Menevis Cilizoglu, Tobias Heinrich, and William Christiansen. 2023. "No entry in a pandemic: Public support for border closures." *American Journal of Political Science* Published online April 23.

Koliev, Faradj, Douglas Page, and Jonas Tallberg. 2022. "The domestic impact of international shaming: Evidence from climate change and human rights." *Public Opinion Quarterly* 86 (3):748-761.

Kreps, Sarah E, and Geoffrey PR Wallace. 2016. "International law, military effectiveness, and public support for drone strikes." *Journal of Peace Research* 53 (6):830-844.

Krockow, Eva M, Carolyn Tarrant, and Andrew M Colman. 2022. "Prosociality in the social dilemma of antibiotic prescribing." *Current Opinion in Psychology* 44:164-169.

Lake, David A. 2010. "Rightful rules: Authority, order, and the foundations of global governance." *International Studies Quarterly* 54 (3):587-613.

Laxminarayan, Ramanan, Precious Matsoso, Suraj Pant, Charles Brower, John-Arne Røttingen, Keith Klugman, and Sally Davies. 2016. "Access to effective antimicrobials: A worldwide challenge." *The Lancet* 387 (10014):168-175.

Lewis, Dyani. 2022. "Why the WHO took two years to say COVID is airborne." *Nature* 604 (7904):26-31.
Liese, Andrea, Jana Herold, Hauke Feil, and Per-Olof Busch. 2021. "The heart of bureaucratic power: Explaining international bureaucracies' expert authority." *Review of International Studies* 47 (3):353-376.
Lim, Jane Mingjie, Shweta Rajkumar Singh, Minh Cam Duong, Helena Legido-Quigley, Li Yang Hsu, and Clarence C Tam. 2020. "Impact of national interventions to promote responsible antibiotic use: A systematic review." *Journal of Antimicrobial Chemotherapy* 75 (1):14-29.
Lin, Leesa, Ruyu Sun, Tingting Yao, Xudong Zhou, and Stephan Harbarth. 2020. "Factors influencing inappropriate use of antibiotics in outpatient and community settings in China: A mixed-methods systematic review." *BMJ Global Health* 5 (11):e003599.
Linos, Katerina. 2013. *The Democratic Foundations of Policy Diffusion: How Health, Family, and Employment Laws Spread across Countries*. Oxford: Oxford University Press.
Martin, Lisa L, and Beth A Simmons. 2013. "International organizations and institutions." In *Handbook of International Relations. Second Edition*, edited by Walter Carlsnaes, Beth A. Simmons and Thomas Risse, 326-351. London: SAGE.
Mudenda, Steward, Eustus Nsofu, Patience Chisha, Victor Daka, Billy Chabalenge, Webrod Mufwambi, Henson Kainga, Manal HG Kanaan, Ruth L Mfune, and Florence Mwaba. 2023. "Prescribing patterns of antibiotics according to the WHO AWaRe classification during the COVID-19 pandemic at a teaching hospital in Lusaka, Zambia: Implications for strengthening of antimicrobial stewardship programmes." *Pharmacoepidemiology* 2 (1):42-53.
Munkholm, Louise, and Olivier Rubin. 2020. "The global governance of antimicrobial resistance: A cross-country study of alignment between the global action plan and national action plans." *Globalization and Health* 16 (1):1-11.
Muñoz-Sastre, Daniel, Luis Rodrigo-Martín, and Isabel Rodrigo-Martín. 2021. "The Role of Twitter in the WHO's Fight against the Infodemic." *International Journal of Environmental Research and Public Health* 18 (22):11990.
Murray, Christopher JL, Kevin Shunji Ikuta, Fablina Sharara, Lucien Swetschinski, Gisela Robles Aguilar, Authia Gray, Chieh Han, Catherine Bisignano, Puja Rao, and Eve Wool. 2022. "Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis." *The Lancet* 399 (10325):629-655.
Nabirye, Christine, Laurie Denyer Willis, Susan Nayiga, Miriam Kayendeke, Sarah G Staedke, and Clare IR Chandler. 2023. "Antibiotic 'entanglements': Health, labour and everyday life in an urban informal settlement in Kampala, Uganda." *Critical Public Health* 33 (1):95-104.
Nandi, Arindam, Simone Pecetta, and David E Bloom. 2023. "Global antibiotic use during the COVID-19 pandemic: Analysis of pharmaceutical sales data from 71 countries, 2020–2022." *Eclinicalmedicine* 57.
Ostrom, Elinor. 2010. "Polycentric systems for coping with collective action and global environmental change." *Global Environmental Change* 20:550-557.
Patel, Jay, Anne Harant, Genevie Fernandes, Ambele Judith Mwamelo, Wolfgang Hein, Denise Dekker, and Devi Sridhar. 2023. "Measuring the global response to antimicrobial resistance, 2020–21: A systematic governance analysis of 114 countries." *The Lancet Infectious Diseases* 23 (6):706-718.
Pevehouse, Jon CW. 2020. "The COVID-19 pandemic, international cooperation, and populism." *International Organization* 74 (S1):E191-E212.

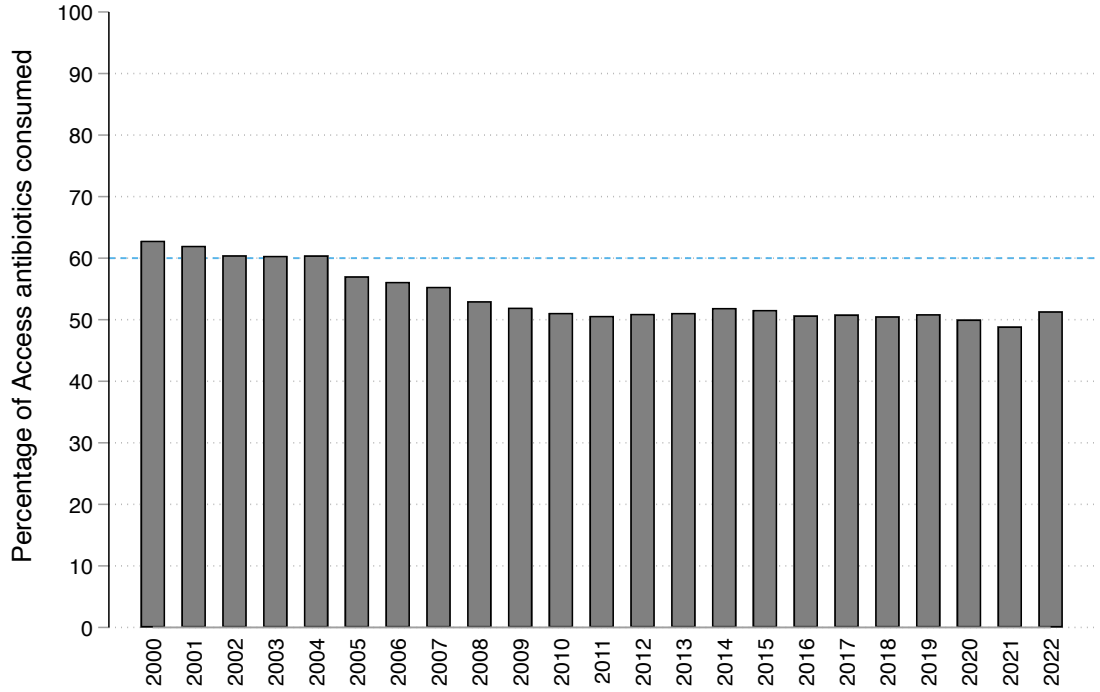
Podolsky, Scott H. 2018. "The evolving response to antibiotic resistance (1945–2018)." *Palgrave Communications* 4 (1):1-8.
Pouliot, Vincent. 2016. "Hierarchy in practice: Multilateral diplomacy and the governance of international security." *European Journal of International Security* 1 (1):5-26.
Review on Antimicrobial Resistance. 2016. *Tackling Drug-Resistant Infections Globally: Final Report and Recommendations*. London: Wellcome Trust.
Ricci, James. 2009. "Global health governance and the state: Premature claims of a post-international framework." *Global Health Governance* 3 (1):1-18.
Rogers Van Katwyk, Susan, Jeremy M Grimshaw, Miriam Nkangu, Ranjana Nagi, Marc Mendelson, Monica Taljaard, and Steven J Hoffman. 2019. "Government policy interventions to reduce human antimicrobial use: A systematic review and evidence map." *PLoS Medicine* 16 (6):e1002819.
Ruger, Jennifer Prah. 2008. "Normative foundations of global health law." *The Georgetown Law Journal* 96 (2):423–443.
Salama, Amir H. Y. 2022. "Exploring the multimodal representation of Covid-19 on the official homepage of World Health Organization (WHO): A social-semiotic approach." In *Pandemic and Crisis Discourse: Communicating COVID-19 and Public Health Strategy*, edited by Andreas Musolff, Ruth Breeze, Kayo Kondo and Sara Vilar-Lluch, 31–46. London: Bloomsbury Academic.
Samaan, Gina, Michelle McPherson, Johan Eidman, Offeibea Obubah, Jean-Pierre Baptiste, Lianne Kuppens, Kai Von Harbou, Miftahul Fahmi Sembiring, Shambhu Acharya, and Peter Graaff. 2022. "The World Health Organization's actions within the united nations system to facilitate a whole-of-society response to COVID-19 at country level." *Frontiers in Public Health* 9:831220.
Servia-Dopazo, Miguel, and Adolfo Figueiras. 2018. "Determinants of antibiotic dispensing without prescription: A systematic review." *Journal of Antimicrobial Chemotherapy* 73 (12):3244-3253.
Sheen, Greg Chih-Hsin, Hans H Tung, Chien-Huei Wu, and Wen-Chin Wu. 2023. "WHO approves? Relative trust, the WHO, and China's COVID-19 vaccines." *The Review of International Organizations* 18 (3):499-521.
Simmons, Beth A. 2010. "Treaty compliance and violation." *Annual Review of Political Science* 13:273-296.
Simmons, Bryony, Koya Ariyoshi, Norio Ohmagari, Celine Pulcini, Benedikt Huttner, Sumanth Gandra, Giovanni Satta, Lorenzo Moja, Michael Sharland, and Nicola Magrini. 2021. "Progress towards antibiotic use targets in eight high-income countries." *Bulletin of the World Health Organization* 99 (8):550.
Stivers, Tanya. 2007. *Prescribing under Pressure: Parent-physician Conversations and Antibiotics*. Oxford: Oxford University Press.
Sun, Liyang, and Sarah Abraham. 2021. "Estimating dynamic treatment effects in event studies with heterogeneous treatment effects." *Journal of Econometrics* 225 (2):175-199.
Tay, Dennis. 2022. "Covid-19 press conferences across time: World Health Organization vs. Chinese Ministry of Foreign Affairs." In *Pandemic and Crisis Discourse: Communicating COVID-19 and Public Health Strategy*, edited by Andreas Musolff, Ruth Breeze, Kayo Kondo and Sara Vilar-Lluch, 13–30. London: Bloomsbury Academic.
Thrall, Calvin. 2021. "Public-private governance initiatives and corporate responses to stakeholder complaints." *International Organization* 75 (3):803-836.

WHO-FAO-OIE. 2022. *Global Database for the Tripartite Antimicrobial Resistance (AMR) Country Self-assessment Survey (TrACSS)*. https://amrcountryprogress.org/ (last accessed August 9, 2022).
WHO. 2001. *Revised procedure for updating WHO's Model List of Essential Drugs. Report by the Secretariat, EB 109/8*. Geneva: World Health Organization.
WHO. 2015. *Global Action Plan on Antimicrobial Resistance*. Geneva: World Health Organization.
WHO. 2017. *The Selection and Use of Essential Medicines: Report of the WHO Expert Committee, 2017 (including the 20th WHO Model List of Essential Medicines and the 6th Model List of Essential Medicines for Children)*. Geneva: World Health Organization.
WHO. 2019. *Executive Summary. The Selection and Use of Essential Medicines 2019. Report of the 22nd WHO Expert Committee on the Selection and Use of Essential Medicines, 1-5 April 2019*. Geneva: World Health Organization.
WHO. 2020. *Thirteenth General Programme of Work (GPW13): Metadata for Impact Measurement Indicators*. Geneva: World Health Organization.
WHO. 2021. *Executive summary. The Selection and Use of Essential Medicines 2021. Report of the 23rd WHO Expert Committee on the Selection and Use of Essential Medicines, virtual meeting, 21 June–2 July 2021*. Geneva: World Health Organization.
Woods, Ngaire. 2018. *The Globalizers: The IMF, the World Bank, and Their Borrowers*. Ithaca: Cornell University Press.
World Bank. 2023. *World Development Indicators*. http://datatopics.worldbank.org/world-development-indicators/.
Worsnop, Catherine Z, Samuel Nass, Karen Ann Grépin, and Kelley Lee. 2023. "An analysis of WHO's Temporary Recommendations on international travel and trade measures during Public Health Emergencies of International Concern." *BMJ Global Health* 8 (7):e012615.
Yang, Hai. 2021. "Contesting legitimacy of global governance institutions: The case of the World Health Organization during the coronavirus pandemic." *International Studies Review* 23 (4):1813-1834.
Zürn, Michael. 2018. *A Theory of Global Governance: Authority, Legitimacy, and Contestation*. Oxford: Oxford University Press.

Appendix: The Power of Expertise: Evidence from the World Health Organization's AWaRe Classification

Table of Contents

Figure A1: Percentage of Access antibiotics over total consumption, 2000-2022



Source of consumption data: *IQVIA MIDAS® quarterly sales data in KG for [Q1 2000 to Q4 2022], [93] countries, reflecting estimates of real-world activity. Copyright IQVIA. All rights reserved.*

Table A1: Alternative sample

	(21)	(22)	(23)	(24)
Watch	0.0170***	0.0171***	0.0306**	0.0305**
	(0.0048)	(0.0048)	(0.0119)	(0.0118)
Reserve	-0.0244	-0.0243	0.0150	0.0149
	(0.0336)	(0.0337)	(0.0102)	(0.0102)
NAP implementation	0.0088***	0.0091**		0.0066+
	(0.0026)	(0.0028)		(0.0035)
AWaRe adoption			-0.0026	-0.0020
			(0.0022)	(0.0028)
Watch * NAP implementation	-0.0116***	-0.0121***		
	(0.0033)	(0.0033)		
Reserve * NAP implementation	0.0314	0.0311		
	(0.0330)	(0.0332)		
Watch * AWaRe adoption			-0.0238*	-0.0243*
			(0.0107)	(0.0105)
Reserve * AWaRe adoption			-0.0039	-0.0039
			(0.0072)	(0.0072)
Government health expenditure (% of total)		-0.0347		0.0456
		(0.0259)		(0.0425)
Democracy		-0.0548		-0.0668
		(0.0361)		(0.0431)
Bureaucratic quality		0.0043		0.0039
		(0.0027)		(0.0031)
GDPpc (log)		0.0151+		-0.0091
		(0.0082)		(0.0144)
Population (log)		-0.0252		0.0010
		(0.0481)		(0.0691)
Economic growth		0.0003		0.0003
		(0.0002)		(0.0003)
Country-drug fixed effects	Yes	Yes	Yes	Yes
Year fixed effects	Yes	Yes	Yes	Yes
Observations	154780	154344	89380	88944
R^2	0.925	0.925	0.944	0.944

Source of consumption data: *IQVIA MIDAS® quarterly sales data in KG for Q1 2014 to Q2 2023, [93] countries, reflecting estimates of real-world activity. Copyright IQVIA. All rights reserved.*. Country-drug clustered standard errors in parentheses; $^{+}$ $p < 0.10$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table A2: Alternative dependent variables

	(25)	(26)	(27)	(28)	(29)	(30)
Watch	388389.6868	0.0180***	17.9795***	2516318.3846	0.0232*	23.2079*
	(268096.4923)	(0.0047)	(4.7104)	(1574705.1176)	(0.0092)	(9.1529)
Reserve	-1202555.5252	-0.0294	-29.3872	-99460.4284	0.0116	11.6247
	(1362203.7325)	(0.0380)	(38.0199)	(612929.9462)	(0.0086)	(8.6032)
NAP implementation	1215055.3499***	0.0096**	9.5740**	1146476.0417***	0.0069*	6.8706*
	(284316.8132)	(0.0030)	(2.9530)	(319939.1267)	(0.0035)	(3.4871)
Watch * NAP implementation	-431143.3520	-0.0123***	-12.2825***			
	(388871.2947)	(0.0037)	(3.6832)			
Reserve * NAP implementation	679846.6644	0.0355	35.5471			
	(1327150.3420)	(0.0370)	(36.9539)			
AWaRe adoption				-98252.2355	-0.0026	-2.5777
				(214017.8931)	(0.0028)	(2.7888)
Watch * AWaRe adoption				-2942685.8698*	-0.0169*	-16.9115*
				(1334811.3526)	(0.0081)	(8.1022)
Reserve * AWaRe adoption				-491122.2029	-0.0013	-1.2717
				(375946.9862)	(0.0057)	(5.7200)
Government health expenditure (% of total)	1579876.7892	-0.0373	-37.2757	7057783.5934	0.0449	44.8649
	(2828124.5613)	(0.0278)	(27.7887)	(6222238.3524)	(0.0438)	(43.8384)
Democracy	-1.4411e+07*	-0.0575	-57.4529	-2.1042e+07+	-0.0647	-64.6728
	(7056396.8219)	(0.0371)	(37.0525)	(11106962.7553)	(0.0410)	(41.0492)
Bureaucratic quality	56958.1545	0.0046	4.5749	-95080.7146	0.0038	3.7923
	(174497.8256)	(0.0030)	(3.0052)	(271032.4855)	(0.0032)	(3.2255)
GDPpc (log)	744514.5738	0.0190+	19.0289+	687858.0509	-0.0110	-10.9965
	(1069406.8704)	(0.0099)	(9.8779)	(4827513.9620)	(0.0163)	(16.2978)
Population (log)	10909875.3298**	-0.0365	-36.4835	13229029.7934*	-0.0006	-0.5596
	(3829468.8830)	(0.0541)	(54.1183)	(5723348.6883)	(0.0712)	(71.1557)
Economic growth	-2078.3962	0.0004+	0.3971+	-16160.4392	0.0003	0.3270
	(30086.2780)	(0.0002)	(0.2298)	(68647.1866)	(0.0003)	(0.3035)
Country-drug fixed effects	Yes	Yes	Yes	Yes	Yes	Yes
Year fixed effects	Yes	Yes	Yes	Yes	Yes	Yes
Observations	53442	53442	53442	32332	32332	32332
R^2	0.948	0.922	0.922	0.950	0.943	0.943

Source of consumption data: *IQVIA MIDAS® quarterly sales data in KG for Q1 2014 to Q2 2023, [93] countries, reflecting estimates of real-world activity. Copyright IQVIA. All rights reserved.*. Country-drug clustered standard errors in parentheses; + $p < 0.10$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table A3: Poisson-pseudo maximum likelihood models

	(31)	(32)	(33)	(34)
Watch	0.1708***	0.1694***	0.2176**	0.2073**
	(0.0455)	(0.0458)	(0.0669)	(0.0642)
Reserve	-0.7383+	-0.7228+	0.3721	0.3945
	(0.4204)	(0.4024)	(0.2740)	(0.2842)
NAP implementation	0.0789**	0.0811***		0.0652*
	(0.0242)	(0.0243)		(0.0310)
Watch * NAP implementation	-0.1354**	-0.1401**		
	(0.0477)	(0.0467)		
Reserve * NAP implementation	0.9256**	0.9351**		
	(0.3586)	(0.3462)		
AWaRe adoption			-0.0424+	-0.0332
			(0.0219)	(0.0215)
Watch * AWaRe adoption			-0.1616**	-0.1622**
			(0.0556)	(0.0546)
Reserve * AWaRe adoption			-0.0298	-0.0179
			(0.1638)	(0.1558)
Government health expenditure (% of total)		-0.4173		0.5737
		(0.2857)		(0.4915)
Democracy		-0.4306+		-0.6355+
		(0.2499)		(0.3521)
Bureaucratic quality		0.0320		0.0365
		(0.0258)		(0.0308)
GDPpc (log)		0.2031+		-0.2062
		(0.1094)		(0.2155)
Population (log)		-0.1380		0.0546
		(0.4157)		(0.5691)
Economic growth		0.0048*		0.0031
		(0.0019)		(0.0024)
Country-drug fixed effects	Yes	Yes	Yes	Yes
Year fixed effects	Yes	Yes	Yes	Yes
Observations	53590	53442	32480	32332
R^2	0.681	0.681	0.684	0.684

Source of consumption data:*IQVIA MIDAS® quarterly sales data in KG for Q1 2014 to Q2 2023, [93] countries, reflecting estimates of real-world activity. Copyright IQVIA. All rights reserved.*. Country-drug clustered standard errors in parentheses; + $p < 0.10$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table A4: Alternative fixed effects (at drug-year level)

	(35)	(36)	(37)	(38)
NAP implementation	0.0255***	0.0257***		0.0223*
	(0.0073)	(0.0076)		(0.0104)
Watch * NAP implementation	-0.0302**	-0.0322***		
	(0.0092)	(0.0093)		
Reserve * NAP implementation	-0.0138	-0.0138		
	(0.0100)	(0.0101)		
AWaRe adoption			-0.0060	-0.0045
			(0.0081)	(0.0095)
Watch * AWaRe adoption			-0.0527*	-0.0526*
			(0.0250)	(0.0243)
Reserve * AWaRe adoption			-0.0315	-0.0305
			(0.0277)	(0.0278)
Government health expenditure (% of total)		-0.0617		0.1400
		(0.0678)		(0.1213)
Democracy		-0.1053		-0.1884
		(0.0871)		(0.1159)
Bureaucratic quality		0.0154*		0.0114
		(0.0077)		(0.0091)
GDPpc (log)		0.0424+		-0.0291
		(0.0251)		(0.0467)
Population (log)		-0.0279		-0.0139
		(0.1392)		(0.2083)
Economic growth		0.0010		0.0009
		(0.0006)		(0.0009)
Country-drug fixed effects	Yes	Yes	Yes	Yes
Drug-year fixed effects	Yes	Yes	Yes	Yes
Observations	53310	53162	32220	32072
R^2	0.949	0.950	0.945	0.946

Source of consumption data: *IQVIA MIDAS® quarterly sales data in KG for Q1 2014 to Q2 2023, [93] countries, reflecting estimates of real-world activity. Copyright IQVIA. All rights reserved.*. Country-drug clustered standard errors in parentheses; $^{+}$ $p < 0.10$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table A5: Alternative standard errors (at country-level)

	(39)	(40)	(41)	(42)
Watch	0.0491***	0.0493***	0.0640**	0.0636**
	(0.0127)	(0.0129)	(0.0230)	(0.0225)
Reserve	-0.0780	-0.0805	0.0328	0.0318
	(0.0984)	(0.0988)	(0.0326)	(0.0329)
NAP implementation	0.0250*	0.0262**		0.0188+
	(0.0098)	(0.0096)		(0.0112)
Watch * NAP implementation	-0.0323**	-0.0337**		
	(0.0111)	(0.0116)		
Reserve * NAP implementation	0.0963	0.0974		
	(0.0963)	(0.0966)		
AWaRe adoption			-0.0092	-0.0071
			(0.0070)	(0.0074)
Watch * AWaRe adoption			-0.0450+	-0.0463+
			(0.0242)	(0.0231)
Reserve * AWaRe adoption			-0.0039	-0.0035
			(0.0107)	(0.0111)
Government health expenditure (% of total)		-0.1021		0.1229
		(0.1177)		(0.1574)
Democracy		-0.1574		-0.1772+
		(0.0949)		(0.0932)
Bureaucratic quality		0.0125		0.0104
		(0.0096)		(0.0100)
GDPpc (log)		0.0521		-0.0301
		(0.0360)		(0.0540)
Population (log)		-0.1000		-0.0015
		(0.1307)		(0.1354)
Economic growth		0.0011		0.0009
		(0.0007)		(0.0009)
Country-drug fixed effects	Yes	Yes	Yes	Yes
Year fixed effects	Yes	Yes	Yes	Yes
Observations	53590	53442	32480	32332
R^2	0.922	0.922	0.942	0.943

Source of consumption data: *IQVIA MIDAS® quarterly sales data in KG for Q1 2014 to Q2 2023, [93] countries, reflecting estimates of real-world activity. Copyright IQVIA. All rights reserved.*Country clustered standard errors in parentheses; + $p < 0.10$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table A6: Including lagged dependent variable

	(43)	(44)	(45)	(46)
Watch	0.0196**	0.0188**	0.0305*	0.0316**
	(0.0062)	(0.0061)	(0.0122)	(0.0121)
Reserve	-0.0029	-0.0027	0.0245*	0.0248*
	(0.0192)	(0.0194)	(0.0117)	(0.0117)
NAP implementation	0.0044	0.0063		0.0011
	(0.0036)	(0.0038)		(0.0040)
Watch * NAP implementation	-0.0176**	-0.0170**		
	(0.0057)	(0.0057)		
Reserve * NAP implementation	0.0116	0.0112		
	(0.0206)	(0.0208)		
AWaRe adoption			-0.0016	-0.0004
			(0.0048)	(0.0047)
Watch * AWaRe adoption			-0.0324*	-0.0345**
			(0.0132)	(0.0131)
Reserve * AWaRe adoption			-0.0157	-0.0167
			(0.0115)	(0.0118)
Lagged Dependent Variable	0.6053***	0.6069***	0.6514***	0.6560***
	(0.0434)	(0.0442)	(0.0785)	(0.0805)
Government health expenditure (% of total)		-0.0036		0.1827+
		(0.0453)		(0.1043)
Democracy		-0.0727+		-0.0468
		(0.0403)		(0.0463)
Bureaucratic quality		0.0150***		0.0162**
		(0.0043)		(0.0053)
GDPpc (log)		-0.0222		-0.0549+
		(0.0144)		(0.0299)
Population (log)		-0.1117		-0.1145
		(0.0719)		(0.0955)
Economic growth		0.0003		0.0006
		(0.0006)		(0.0010)
Country-drug fixed effects	Yes	Yes	Yes	Yes
Year	Yes	Yes	Yes	Yes
Observations	48231	48083	29232	29084
R^2	0.963	0.964	0.972	0.973

Source of consumption data:*IQVIA MIDAS® quarterly sales data in KG for Q1 2014 to Q2 2023, [93] countries, reflecting estimates of real-world activity. Copyright IQVIA. All rights reserved.*. Country-drug clustered standard errors in parentheses; $^{+}$ $p < 0.10$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table A7: Included molecules and DDD values

Molecule list	*Method*	*DDD value*
ACETYL KITASAMYCIN	All	1.20
ACETYLSPIRAMYCIN	All	3.00
AMIKACIN	All	1.00
AMOXICILLIN	All	2.25
AMOXICILLIN + CLAVULANIC ACID	All	1.50
AMOXICILLIN + CLOXACILLIN	All	3.00
AMOXICILLIN + DICLOXACILLIN	All	3.00
AMOXICILLIN + FLUCLOXACILLIN	All	3.00
AMOXICILLIN + METRONIDAZOLE	All	3.00
AMPICILLIN	All	6.00
AMPICILLIN + CLAVULANIC ACID	All	6.00
AMPICILLIN + CLOXACILLIN	All	6.00
AMPICILLIN + DICLOXACILLIN	All	6.00
AMPICILLIN + FLUCLOXACILLIN	All	6.00
AMPICILLIN + OXACILLIN	All	6.00
AMPICILLIN + SULBACTAM	All	6.00
ANTOFLOXACIN	All	0.50
ARBEKACIN	All	0.20
ASPOXICILLIN	All	4.00
ASTROMICIN	All	0.40
ASTROMICIN	Enteral	0.40
ASTROMICIN	Parenteral	0.40
AVIBACTAM + CEFTAZIDIME	All	6.00
AZITHROMYCIN	All	0.40
AZITHROMYCIN + CEFIXIME	All	0.40
AZLOCILLIN	All	12.00
AZTREONAM	All	2.11
BACAMPICILLIN	All	1.20
BALOFLOXACIN	All	0.20
BEKANAMYCIN	All	0.50
BEKANAMYCIN	Enteral	0.50
BENZATHINE-BENZYLPENICILLIN	All	2.00
BENZATHINE-BENZYLPENICILLIN	Enteral	2.00
BETAMIPRON + PANIPENEM	All	2.00
BIAPENEM	All	1.20
CARBENICILLIN	All	12.00
CARUMONAM	All	2.00
CEFACETRILE	All	1.00
CEFACLOR	All	1.00
CEFADROXIL	All	2.00
CEFALEXIN	All	2.00
CEFALORIDINE	All	3.00
CEFALOTIN	All	4.00
CEFAMANDOLE NAFATE	All	6.00
CEFAPIRIN	All	4.00
CEFATHIAMIDINE	All	4.00
CEFATRIZINE	All	1.00
CEFAZEDONE	All	3.00
CEFAZOLIN	All	3.00
CEFBUPERAZONE	All	2.00
CEFCAPENE PIVOXIL	All	0.45
CEFDINIR	All	0.60
CEFDITOREN PIVOXIL	All	0.40
CEFEPIME	All	4.00
CEFETAMET PIVOXIL	All	1.00
CEFIDEROCOL	All	NA
CEFIXIME	All	0.40
CEFMENOXIME	All	2.00
CEFMETAZOLE	All	4.00
CEFMINOX	All	4.00
CEFODIZIME	All	2.00
CEFONICID	All	1.00
CEFOPERAZONE	All	4.00
CEFORANIDE	All	4.00
CEFOSELIS	All	3.30
CEFOTAXIME	All	4.00
CEFOTETAN	All	4.00
CEFOTIAM	All	2.60
CEFOTIAM HEXETIL	All	2.60
CEFOXITIN	All	6.00
CEFOZOPRAN	All	4.00
CEFPIRAMIDE	All	2.00

CEFPIROME	All	4.00
CEFPODOXIME PROXETIL	All	0.40
CEFPROZIL	All	1.00
CEFRADINE	All	2.00
CEFROXADINE	All	2.10
CEFSULODIN	All	4.00
CEFTAROLINE FOSAMIL	All	1.20
CEFTAZIDIME	All	4.00
CEFTERAM PIVOXIL	All	0.40
CEFTEZOLE	All	3.00
CEFTIBUTEN	All	0.40
CEFTIZOXIME	All	4.00
CEFTOBIPROLE MEDOCARIL	All	1.50
CEFTOLOZANE + TAZOBACTAM	All	3.00
CEFTRIAXONE	All	2.00
CEFUROXIME	All	1.75
CHLORAMPHENICOL	All	3.00
CHLORTETRACYCLINE	All	1.00
CICLACILLIN	All	2.00
CILASTATIN + IMIPENEM	All	2.00
CILASTATIN + IMIPENEM + RELEBACTAM	All	2.00
CINOXACIN	All	1.00
CIPROFLOXACIN	All	0.80
CLARITHROMYCIN	All	0.75
CLINDAMYCIN	All	1.50
CLOFOCTOL	All	1.50
CLOMETOCILLIN	All	1.00
CLOXACILLIN	All	2.00
COLISTIN	All	0.09
COLISTIN	Enteral	0.09
COLISTIN	Parenteral	0.27
DALBAVANCIN	All	1.50
DALFOPRISTIN + QUINUPRISTIN	All	1.50
DAPTOMYCIN	All	0.28
DELAFLOXACIN	All	0.75
DEMECLOCYCLINE	All	0.60
DIBEKACIN	All	0.14
DICLOXACILLIN	All	2.00
DIRITHROMYCIN	All	0.50
DORIPENEM	All	1.50
DOXYCYCLINE	All	0.10
ENOXACIN	All	0.80
ERAVACYCLINE	All	NA
ERTAPENEM	All	1.00
ERYTHROMYCIN	All	1.33
ERYTHROMYCIN STINOPRATE	All	1.00
ETIMICIN	All	0.50
FAROPENEM	All	0.75
FIDAXOMICIN	All	0.40
FLEROXACIN	All	0.40
FLOMOXEF	All	2.00
FLUCLOXACILLIN	All	2.00
FLUMEQUINE	All	1.20
FLURITHROMYCIN	All	0.75
FOSFOMYCIN	Enteral	3.00
FOSFOMYCIN	Parenteral	8.00
FURAZIDIN	All	0.30
FURBENICILLIN	All	1.50
FUSIDIC ACID	All	1.50
GARENOXACIN	All	0.40
GATIFLOXACIN	All	0.40
GEMIFLOXACIN	All	0.32
GENTAMICIN	All	0.24
GREPAFLOXACIN	All	0.40
GUAMECYCLINE	All	NA
ISEPAMICIN	All	0.40
JOSAMYCIN	All	2.00
KANAMYCIN	All	1.00
KANAMYCIN	Enteral	1.00
KANAMYCIN	Parenteral	1.00
KITASAMYCIN	All	1.20
LASCUFLOXACIN	All	0.08
LATAMOXEF	All	4.00
LEFAMULIN	All	NA
LENAMPICILLIN	All	1.00

LEVOFLOXACIN	All	0.41
LEVONADIFLOXACIN	All	NA
LINCOMYCIN	All	1.80
LINEZOLID	All	1.20
LOMEFLOXACIN	All	0.40
LORACARBEF	All	0.60
LYMECYCLINE	All	0.60
MECILLINAM	All	1.20
MELEUMYCIN	All	1.30
MEROPENEM	All	3.00
MEROPENEM + VABORBACTAM	All	3.00
METACYCLINE	All	0.60
METRONIDAZOLE	All	1.50
METRONIDAZOLE	Parenteral	1.50
METRONIDAZOLE	Enteral	1.50
METRONIDAZOLE + SPIRAMYCIN	All	3.00
MEZLOCILLIN	All	6.00
MICRONOMICIN	All	0.24
MIDECAMYCIN	All	1.10
MINOCYCLINE	All	0.20
MINOCYCLINE	Enteral	0.20
MINOCYCLINE	Parenteral	0.20
MOXIFLOXACIN	All	0.40
NAFCILLIN	All	3.00
NEMONOXACIN	All	NA
NEOMYCIN	All	1.00
NEOMYCIN	Enteral	1.00
NEOMYCIN	Parenteral	1.00
NETILMICIN	All	0.35
NIFURTOINOL	All	0.16
NITROFURANTOIN	All	0.20
NORFLOXACIN	All	0.80
NORVANCOMYCIN	All	1.30
OFLOXACIN	All	0.40
OLEANDOMYCIN	All	1.00
OMADACYCLINE	All	0.20
ORITAVANCIN	All	1.20
ORNIDAZOLE	Enteral	1.00
ORNIDAZOLE	Parenteral	1.00
OXACILLIN	All	2.00
OXOLINIC ACID	All	1.00
OXYTETRACYCLINE	All	1.00
PAROMOMYCIN	All	3.00
PAZUFLOXACIN	All	1.00
PEFLOXACIN	All	0.80
PENAMECILLIN	All	1.05
PENICILLIN G	All	3.60
PENICILLIN G + PROCAINE	All	0.60
PENICILLIN G + STREPTOMYCIN	All	1.00
PENICILLIN V	All	2.00
PHENETICILLIN	All	1.00
PIPEMIDIC ACID	All	0.80
PIPERACILLIN	All	14.00
PIPERACILLIN + TAZOBACTAM	All	14.00
PIROMIDIC ACID	All	2.00
PIVAMPICILLIN	All	1.05
PIVAMPICILLIN + PIVMECILLINAM	All	0.83
PIVMECILLINAM	All	0.60
PLAZOMICIN	All	NA
POLYMYXIN B	All	0.15
POLYMYXIN B	Enteral	0.15
POLYMYXIN B	Parenteral	0.15
PRISTINAMYCIN	All	2.00
PROPICILLIN	All	0.90
PRULIFLOXACIN	All	0.60
RIBOSTAMYCIN	All	1.00
RIFABUTIN	All	0.15
RIFAMPICIN	All	0.60
RIFAMYCIN	All	0.60
RIFAMYCIN	Enteral	0.60
RIFAMYCIN	Parenteral	0.60
RIFAXIMIN	All	0.60
ROKITAMYCIN	All	0.80
ROLITETRACYCLINE	All	0.35
ROSOXACIN	All	0.30

ROXITHROMYCIN	All	0.30
RUFLOXACIN	All	0.20
SARECYCLINE	All	0.10
SECNIDAZOLE	All	2.00
SISOMICIN	All	0.24
SITAFLOXACIN	All	0.10
SPARFLOXACIN	All	0.20
SPECTINOMYCIN	All	3.00
SPIRAMYCIN	All	3.00
STREPTOMYCIN	Parenteral	1.00
SULBACTAM	All	1.00
SULBENICILLIN	All	15.00
SULFADIAZINE	All	1.60
SULFADIAZINE + TRIMETHOPRIM	All	1.00
SULFADIMETHOXINE	All	0.50
SULFADIMIDINE	All	4.00
SULFADIMIDINE + TRIMETHOPRIM	All	0.40
SULFADOXINE	All	0.50
SULFADOXINE	Enteral	0.60
SULFADOXINE	Parenteral	0.40
SULFAFURAZOLE	All	4.00
SULFALENE	All	0.10
SULFAMETHIZOLE + TRIMETHOPRIM	All	0.80
SULFAMETHOXAZOLE	All	2.00
SULFAMETHOXAZOLE + TRIMETHOPRIM	All	1.90
SULFAMETHOXYPYRIDAZINE	All	0.50
SULFAMETROLE + TRIMETHOPRIM	All	1.90
SULFAMOXOLE + TRIMETHOPRIM	All	1.00
SULFANILAMIDE	All	NA
SULFAPYRIDINE	All	1.00
SULFATHIAZOLE	All	NA
SULTAMICILLIN	All	1.50
TAZOBACTAM	All	NA
TEBIPENEM PIVOXIL	All	0.56
TEDIZOLID	All	0.20
TEICOPLANIN	All	0.40
TELAVANCIN	All	1.30
TELITHROMYCIN	All	0.80
TEMOCILLIN	All	4.00
TETRACYCLINE	All	1.00
THIAMPHENICOL	All	1.50
TICARCILLIN	All	15.00
TIGECYCLINE	All	0.10
TINIDAZOLE	All	1.50
TINIDAZOLE	Enteral	1.50
TINIDAZOLE	Parenteral	1.50
TOBRAMYCIN	All	0.22
TOSUFLOXACIN	All	0.45
TRIMETHOPRIM	All	0.40
TROLEANDOMYCIN	All	1.00
TROVAFLOXACIN	All	0.20
VANCOMYCIN	All	2.00