2021 **AMR Preparedness Index**

Global Coalition on Aging

IDSA
Infectious Diseases Society of America

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Introductory Letter

As the world attempts to learn lessons from the ongoing COVID-19 pandemic, national policymakers must address another public health crisis that already kills an estimated 700,000 people each year[1]: the growth of antimicrobial resistance (AMR). If governments fail to combat this growing threat, the consequences could be catastrophic. One study projects that drug-resistant infections could claim 10 million lives annually by 2050.[2]

As resistance grows, our arsenal of antibiotics becomes less and less effective, undermining the foundation of our entire medical system. Without effective antibiotics, C-sections, organ transplants, chemotherapy, and even routine outpatient procedures become potentially life-threatening events. More broadly, the longevity revolution that has helped millions of people worldwide live longer, healthier, more productive lives is at risk. As the UN and WHO Decade of Healthy Ageing brings greater attention and energy to our remarkable demographic achievement, we must fully acknowledge the threat that AMR poses to the very prospect of human longevity. Without true action to effectively address AMR, millions of lives – both young and old – will be cut short.

Despite the urgency of the threat, policymakers have not shifted commitments to action on AMR. The AMR challenge requires a concerted effort from cross-governmental stakeholders to effectively tackle the myriad factors that contribute to the AMR crisis. There needs to be a focus on harmonizing these efforts: policymakers developing national strategies, public health authorities seeking to raise awareness and increase prevention efforts, regulatory officials and research funders attempting to spur innovations, decisionmakers working to improve access, clinicians striving to reduce misuse and overuse, environmental agencies aiming to limit antimicrobials in the environment, and the multitude of actors endeavoring to foster global collaboration and cooperation.

National governments must develop and implement national strategies holistically to address the multiple factors driving the crisis. This includes ensuring that the public becomes more aware and knowledgeable about AMR and their role in bringing it under control. Further, governments and health systems must strengthen surveillance to track and monitor AMR and to inform outbreak control and prevention.

To actively slow the continued growth of resistance and promote optimal patient outcomes, appropriate antimicrobials must be made reliably accessible to those who need them in parallel with sufficiently resourced stewardship programs in all healthcare settings

to guide their appropriate use and preserve their effectiveness. Measures to better control antimicrobials in environmental settings – including for manufacturing, use in livestock, and the disposal of antimicrobials – are another critical strategy.

Though initiatives in these areas are necessary to slow the growth of resistance, a robust pipeline of new therapies and tools – including antibiotics, antifungals, new technologies, diagnostics, and vaccines – is another essential part of the solution. Unfortunately, that pipeline has been in decline for decades. According to the Pew Trust 2021 tracker, only 43 new antibiotics are under development worldwide, and only one in four of these are classified as novel.[3] Yet, many governments are failing to follow through on previous commitments to adopt the innovative incentive programs widely recognized as central to addressing AMR.[4]

The world's slow start against COVID-19 teaches us – or at least should teach us – that delays in responding to an urgent public health crisis have deadly consequences. The cost for AMR initiatives pales in comparison to the cost of inaction. The World Bank estimates that on its current trajectory, AMR could drag down annual global GDP by 1.1% to 3.8% by 2050.[5] Should AMR go unchecked, the potential annual economic damage would likely exceed the 2008 financial crisis.[6] The World Bank also estimates that investing $200 billion in AMR containment measures through 2050 could avoid this $10 trillion to $27 trillion projected expense.[7] However, most countries have yet to dedicate adequate resources to successfully prepare for and address AMR.

Through G7 and G20 commitments, all of the countries in this Index have publicly articulated the need for action to address AMR and meaningful progress through these platforms will hopefully continue. This report assesses the implementation of these and other proposed initiatives, highlighting a global misalignment between stated commitments at the high level and tangible actions within countries.

To help countries drive progress, we are proud to share this *AMR Preparedness Index*, a first-of-its-kind examination of national level commitments to address AMR. Our research team examined 11 of the largest economies in the world to create a benchmark for measuring progress across seven areas crucial to combating AMR. In creating this Index, we set forth four main goals:

1 **IDENTIFY BEST PRACTICES**

2 **CREATE A FRAMEWORK FOR ACCOUNTABILITY AND EVALUATION**

3 **DRIVE POLICY CHANGE**

4 **STIMULATE ACTION AND COLLABORATION**

Our assessment is based on insights and perspectives gathered from surveys and one-on-one interviews with cross-sector and multidisciplinary experts, coupled with our extensive analysis of publicly available AMR data and research at the country level.

We hope you will use the *AMR Preparedness Index* as a tool to support ongoing research and to advocate for the policies that will help us work together to avert catastrophe and solve this urgent public health crisis. Over the coming years, we will continue to monitor progress in the evaluated countries to help policymakers successfully meet the growing challenge of AMR. We look forward to further collaborating with AMR stakeholders globally to promote innovative solutions to accelerate progress in combatting AMR and achieving healthy longevity for all.

Michael Hodin, PhD
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List of Definitions

AMR
Antimicrobial resistance

APIs
Active pharmaceutical ingredients

BARDA
Biomedical Advanced Research and Development Authority

CARB-X
Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator

CDC
Centers for Disease Control and Prevention, US

DDD
Defined Daily Dose

FAO
Food and Agriculture Organization

GDP
Gross domestic product

GLASS
Global antimicrobial resistance and use surveillance system

GMPs
Good manufacturing practices

GPs
General practitioners

HAI
Hospital-acquired infection or healthcare-associated infection

HCPs
Healthcare professionals

HICs
High-income countries

HTA
Health technology assessment

IAPO
International Alliance of Patient Organizations

IDSA
Infectious Diseases Society of America

IMI
Innovative Medicines Initiative

IPC
Infection prevention and control

JPIAMR
Joint Programming Initiative on Antimicrobial Resistance

LMICs
Low- and middle-income countries

NAPs
National action plans

NHSN AUR Module
National Healthcare Safety Network Antibiotic Use and Resistance Module, US

NIAID
National Institute of Allergy and Infectious Diseases, US

NIH
National Institutes of Health, US

Novel antimicrobials
Either novel class drugs, which have a chemical structure not used previously in human antibacterial contexts, or novel target drugs, which target new bacterial structures in human contexts

OIE
World Organization for Animal Health

One Health approach
An approach that recognizes the connections between the health of people, animals, and the environment and that uses cross-sectoral engagement and communication for the design and implementation of policies to improve public health outcomes[8]

OTC
Over-the-counter

PNECs
Predicted no-effect concentrations

Pull incentives
Financial incentives that reward drug development[9]

Push incentives
Financial incentives that lower the cost of drug development[10]

SPIDAAR
Surveillance Partnership to Improve Data for Action on Antimicrobial Resistance

WASH
Water, sanitation, and hygiene

WHO
World Health Organization

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Executive Summary

Antimicrobial resistance (AMR) is a growing public health crisis and represents one of the most urgent challenges facing national governments. AMR is a result of bacteria, fungi, viruses, and parasites adapting to existing antimicrobials – antibiotics, antifungals, antivirals, and antiparasitics. Over time, this process renders the drugs in our arsenal ineffective, leading to greater spread of infection, more severe infections, and fewer treatment options.[11] If countries do not adequately prepare for and address AMR, the very foundation of modern healthcare will fall away, taking with it the great achievement of human longevity. Yet, government action to date has failed to match the severity of the crisis.

To ensure AMR receives the attention and action it demands, the Global Coalition on Aging (GCOA), in partnership with the Infectious Disease Society of America (IDSA) and with support from the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA), has developed the *AMR Preparedness Index*, a first-of-its-kind examination of country-level progress in areas critical to combating AMR. The Index is intended to drive awareness, stimulate high-level discussions, and spur governments to implement policies needed to address this serious threat.

The *AMR Preparedness Index* builds on previous calls for collective action on AMR, including the need to expand access to antimicrobials, curb inappropriate use, facilitate new drug development, and enforce stronger manufacturing and disposal standards.[12]

In this Index, we assessed how 11 countries[13] are performing across seven distinct, yet interconnected categories that contribute to the AMR challenge.

In our findings, we define these categories and the metrics used to evaluate progress within them. For each category, we identify key insights and put forward concrete calls to action. Below, we summarize the top-level priorities and opportunities for impactful government action, based on the research.

Strengthen and fully implement national AMR strategies

The massive threat posed by AMR has yet to generate the political will needed to fund adequate solutions, including budgetary allocations for stronger surveillance networks, incentives for drug development, equitable access to drugs and diagnostics, stewardship programs, and environmental management initiatives. Without proper funding, national strategies cannot be implemented effectively. National governments must bolster AMR national action plans (NAPs) and create accountability for robust implementation and funding.

Raise awareness of AMR and its consequences, while targeting prevention opportunities

Patients and prescribers lack sufficient awareness about the AMR threat and their role in reducing it, which leads to antibiotic misuse and overuse. Governments must commit to national, regional, and segment-specific awareness campaigns to discourage overuse by patients and to curb inappropriate prescribing by providers. To help prevent the growth and spread of resistant infections, while also reducing future antimicrobial use, governments should strive to increase the uptake of and access to AMR-relevant vaccines.[14]

Bolster surveillance and leverage data across AMR efforts

Though great disparities exist in the quality and sophistication of the AMR surveillance networks, it remains critical to other efforts that all are strengthened. Investments in surveillance have myriad returns, helping to direct infection prevention and control efforts, inform stewardship programs, increase understanding of AMR's impacts, and guide R&D investments towards the most critical needs. In these ways, surveillance infrastructure is foundational in the fight against AMR. Yet, in some countries these programs are underfunded, and in other countries levels of reporting and sophistication remain alarmingly low. Further, there is increasing evidence that surveillance networks stopped collecting data during COVID-19, demonstrating the fragility of these systems, and hindering global understanding of how AMR developed across the pandemic.

Enable a restructured antimicrobial marketplace to stimulate innovation

To facilitate a robust innovation pipeline and to ensure access to effective medicines, the antimicrobial marketplace must be fundamentally restructured in three ways: First, governments must decouple the return on investment for antimicrobials from volume of sales. Second, governments must adopt new models that better reflect the full value of antimicrobials. Third, governments can spur private sector innovation by implementing incentives and improving access to new antimicrobials through reimbursement reform.

Promote responsible and appropriate use of antibiotics

Public demand, lack of healthcare provider training, lack of access to diagnostic tools, and inadequate stewardship lead to over-prescription and misuse of antimicrobials. Governments can do more to enhance sanitation infrastructure, accelerate vaccination programs, and strengthen surveillance and monitoring, all of which will reduce AMR. Most healthcare settings, especially outpatient facilities, lack the stringent stewardship regimes needed to improve monitoring and decrease misuse and over-prescription. Governments must improve stewardship by funding the training, expert personnel, and IT infrastructure needed to implement evidence-based stewardship programs, tailored to the needs of individual sites. Further, to reduce and ultimately eliminate over-the-counter sales of antibiotics, governments must strengthen systems and ensure equitable access to appropriate healthcare.

Enable reliable and consistent access to needed and novel antimicrobials

In high-income countries, many patients lack timely access to novel antimicrobials, while in many low- and moderate-income countries, access to antimicrobials generally is not guaranteed. Regulatory inefficiencies inhibit access to new antimicrobials in some countries, and global supply-chain frailty threatens access to needed pharmaceutical ingredients and drugs in all countries. Governments must address regulatory bottlenecks while working to shore up supply-chain networks and infrastructure.

More effectively integrate the One Health approach, including environmental considerations, into national strategies

The One Health approach language is being integrated into most national action plans and national-level policies, yet greater funding and broader implementation is needed. Though not AMR-specific, most countries have general legislation and policies for pharmaceutical manufacturing environments and pollutants, but the degree of enforcement and efficacy of these policies vary. Likewise, the role of AMR in agriculture and animals must be further investigated, and policies to reduce the use of antimicrobials in these settings must be further developed. Finally, private and third-party investments in the fight against AMR are often not integrated into a holistic One Health approach, leading to isolated and fragmented interventions.

Better engage with other governments, third-party organizations, and advocacy groups

Current levels of government engagement are not realizing the full potential of collaborative efforts in innovation, research, environmental and manufacturing standards, and surveillance and monitoring. Governments should establish, engage with, and promote cross-sectoral and public-private partnerships, which can leverage efforts to combat AMR from governments, NGOs, advocacy groups, and the private sector.

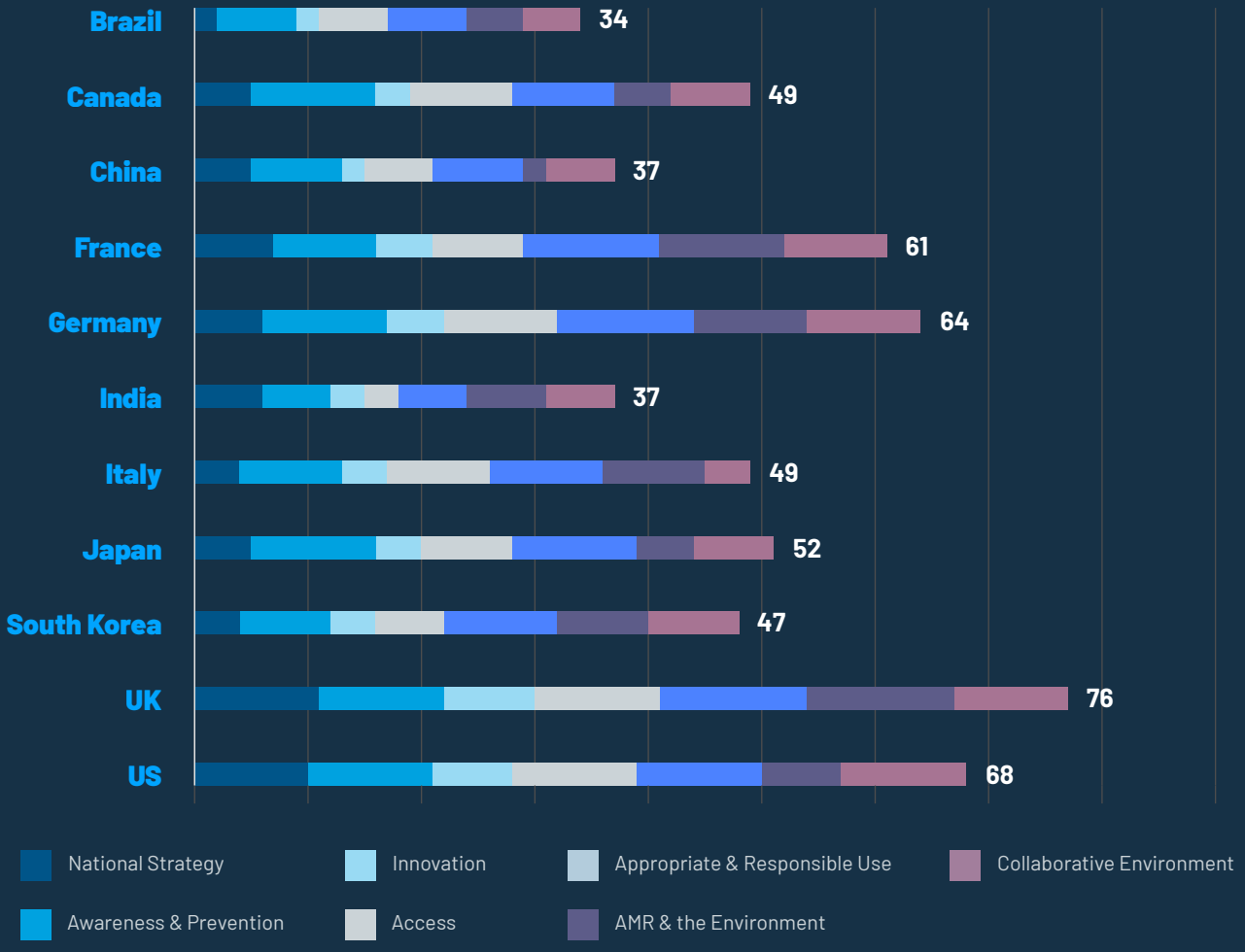
These recommendations are discussed in more detail throughout the report. Our hope is that the Index's findings and calls to action will inspire policymakers to take action to address AMR in their own countries and enable coordinated action across countries.

Overall Scores

The graph below provides a holistic view of each country's scores. It highlights categories where countries have the most opportunity for improvement and areas where countries are demonstrating best or "better" practices. Further scoring visuals for specific categories are provided throughout the Index.

The category scores have been equally weighted – with a maximum of approximately 14% per category – to construct an overall Index score on a 100-point scale. For all countries, there is clearly much room for improvement, though some trends have emerged: most countries (bar the UK and US who fare slightly better) perform especially poorly in the National Strategy, Innovation, and Collaborative Engagement categories, with scores in the Innovation category being the lowest overall; all countries perform insufficiently in the Awareness & Prevention and Access categories, with India lagging behind; and more developed countries tended to fare better in the Appropriate & Responsible Use category.

Overall Scores with Category Contributions



Methodology

The 2021 *AMR Preparedness Index* was developed using primary and secondary data sources collected and analyzed by GCOA. The primary data consist of interviews and surveys of global key opinion leaders and subject matter experts, including advocates, researchers, clinicians, and business leaders who are directly involved in combatting AMR.

The secondary data consist of existing research gathered from global authorities, including the Organisation for Economic Cooperation and Development (OECD) and the World Health Organization (WHO), as well as reports from national governments, nonprofit organizations, and other publicly available sources. Data sources, key secondary metrics, and the scoring framework are detailed in the report's appendices. The countries chosen for this Index include Group of 7 members (Canada, France, Germany, Italy, Japan, the UK and US) and key G20 economies (Brazil, China, India, and South Korea), which all must fully commit to the global AMR fight.

Framework

The Index is designed to evaluate the level of attention governments give to AMR and assess their performance. The results serve as a benchmark against which future progress can be measured. To understand how national governments are performing today, we asked the following questions:

- How robust are countries' national action plans, and how are they being implemented?
- What is being done to improve awareness and training?
- What is the status of the broader ecosystem for antimicrobial development?
- How are countries working to improve antimicrobial access, particularly to novel antimicrobials?
- What is being done to curb abuse, misuse, and overuse of antibiotics?
- What are countries doing to build better infrastructure to curb AMR?
- What types of pull incentives are being considered and adopted to facilitate the development and availability of novel antimicrobials and other innovations?

Categories and Indicators

To evaluate performance, we developed seven categories to cover a broad range of issues related to AMR.

National Strategy: Evaluates the high-level policies, commitments, and investments that national governments have undertaken to combat AMR.

Awareness & Prevention: Assesses the level of commitment within countries to fund and facilitate efforts to increase awareness among stakeholder groups and improve mechanisms that can prevent and monitor AMR.

Innovation: Quantifies government commitments to foster and support AMR innovation, especially in areas of greatest opportunity, including novel valuation and pull mechanisms.

Access: Measures patient access to both older and novel antimicrobials.

Appropriate & Responsible Use: Assesses governments' efforts to reduce misuse and overuse of antimicrobials and promote rational diagnosis.

AMR & the Environment: Examines how national governments are attempting to manage antimicrobials throughout their life cycle: production, procurement, usage across sectors (including non-human applications), and disposal.

Collaborative Engagement: Captures how effectively national governments are facilitating collaborative engagement to address AMR.

These categories are based on an assessment of the current AMR landscape and insights gleaned from other reports, such as the AMR Industry Alliance *Progress Report*,[15] Drive AB's *Revitalizing the antibiotic pipeline report*,[16] Charles Clift's *Review of Progress on Antimicrobial Resistance*,[17] WHO *Global Action Plan*,[18] and the Food and Agriculture Organization's (FAO) *Action Plan on Antimicrobial Resistance 2016-2020*.[19]

Scoring

Countries were scored on a 100-point scale, with final scores reflecting a composite of both qualitative and quantitative data across seven equally weighted categories, 25 component areas, and more than 100 metrics. The full list of metrics, indicators, evaluation criteria, and specific metric scores can be found in the appendices.

Individual metric scores were determined through a variety of methods, including direct numerical conversations to a 100-point scale, the assignment of relative scores based on assessed distance from highest achievable condition, and binary and qualitative conversions to a scale or banded scale. Wherever relevant, quantitative data were adjusted for substantial differences in population size and gross domestic product (GDP). For some metrics, expert judgment directly informed scoring. The purpose of employing this mixed methodology was to derive both useful and meaningful insights from complex and sometimes irregular data.

Individual metrics were then grouped into component areas and weighted to create a 100-point score for each. In turn, the component areas that comprise each category were weighted to produce a total category score, on a 100-point scale. Finally, these category scores were weighted equally and compiled to produce the overall Index composite score, again on a 100-point scale.

Component area and metric scores were weighted with the goal of more accurately reflecting country performance and impact within categories. The weights aimed to decrease the scoring influence of self-reported data while increasing the scoring influence

of externally validated data and data deemed most impactful to AMR preparedness by the experts and the literature consulted. Where all else was equal, weights were not applied. The research team iteratively adjusted and validated the weights in consultation with the expert contributors to the report.

Additional details on scoring methodology can be found in the appendices.

Assumptions and Limitations

While AMR is a global crisis, the scope of this report is limited to the 11 countries identified and the framework articulated within this section. The data cited and expert input evaluated do not fully reflect the breadth and scale of the AMR challenge; rather, they aim to highlight key strengths and opportunities within each country.

It should be noted that this Index is not an exhaustive compilation of all AMR data, rather it represents a distinct effort to collect accessible, "apples to apples" data to present a high-level representative overview of countries' performance across set categories, with a focus on human health. Lack of data accessibility, recency, and comparability posed limitations. Further, the complexity of the dynamics impacting AMR and the need for more research means that some AMR impacts and drivers are still not fully understood and remain difficult to capture. Still others fell outside the scope of this report.

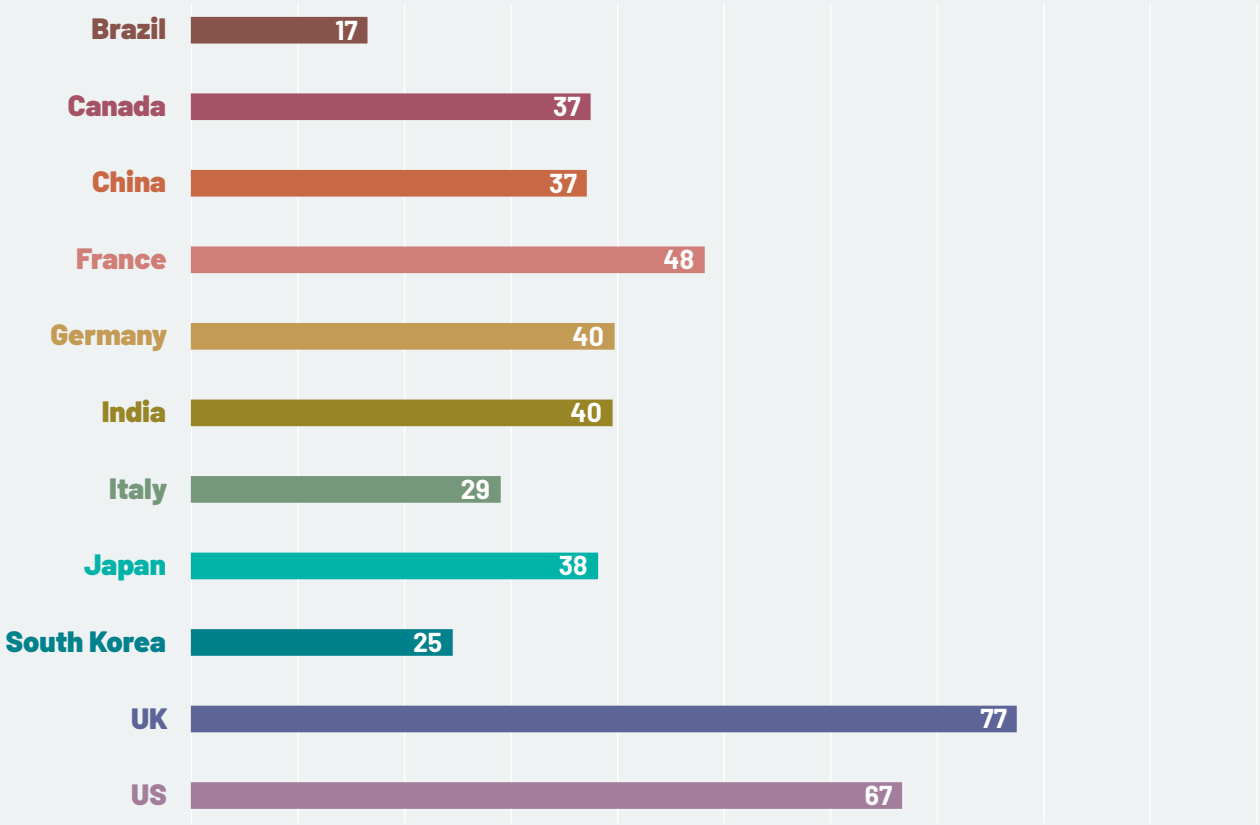
The majority of countries evaluated are classified as high income by the World Bank. Though high-income countries did not score higher in every category, the economic circumstances of a country did contribute to overall scores, particularly in the categories of Innovation, Access, Awareness & Prevention, and AMR & the Environment. In some instances, we have controlled for factors like GDP or population size in an effort to create a more level playing field on which to evaluate country-level progress, but this is an imperfect approximation.

The survey was available only in English and performed online. Interviews were conducted in English. All surveys and interviews were completed from September 2020 through June 2021. As a result, the research inputs and expertise available to the research team were limited by both time and access.

National Strategy

Evaluates the high-level policies, commitments, and investments that national governments have undertaken to combat AMR.

National Strategy Country Comparison



Key Findings

Countries are not making adequate investments to combat the AMR threat

Most countries examined in this report are simply not spending enough to address AMR. In analysis of national level expenditures, only the US and UK have committed material investments to address AMR, and experts in these countries agree that the resources available are still far from sufficient.[20] Even controlling for GDP, China, Brazil, Italy, and India have paltry allocations, and the borderless nature of AMR means that this lack of commitment is felt globally. When looking at total public AMR research funding, an area in which middle-income countries may look to close the gap, huge disparities remain.

National programs to increase public and HCP awareness are also falling short. AMR is one of the largest public health crises in which the general public and clinicians play a key role. Despite being one of the top five global health challenges cited by the WHO,[21] a large majority of the public remains uninformed and unaware of their role. More robust national campaigns are needed to raise awareness. Likewise, many HCPs continue to unknowingly contribute to the problem. National efforts to target and train these professionals require further investment.

National initiatives for surveillance and monitoring remain insufficient to address AMR. Though the WHO's Global antimicrobial resistance and use surveillance system (GLASS) 2020 report did mention political will to improve surveillance efforts in LMICs, greater investments must be made to track and assess AMR threats and drivers and to inform infection outbreak control and prevention efforts.[22]

Greater support and collaboration is necessary to increase capacity in many LMICs, while HICs must collect and provide more complete data to increase the robustness of international, regional, and domestic efforts.[23]

Even countries identified as leaders on multiple AMR metrics have yet to adequately support antimicrobial development. In the UK, experts described an inadequate innovation pipeline, with fewer than 20 biotech firms and 150 researchers working on developing novel antimicrobials,[24] compared to over 200 commercial clinical trials a year for cancer.[25] In India, which has no shortage of scientists and innovators, the government does not actively support and fund critical research efforts. One expert reported that most funding for promising startups in the country came from foreign or external sources.[26,27]

Beyond a lack of direct funding to support AMR innovation, governments have also failed to adopt policy reforms to improve market conditions. EU experts told us that while pan-European reforms are an important factor in jumpstarting the antimicrobial pipeline, national policy reforms could play a much bigger role in promoting change.[28]

In most countries examined in the Index, efforts to implement pull incentives were not robust enough to address failures within the antimicrobial market. In France, Germany, Italy, Brazil, India, China, Japan, and South Korea, governments have shown little commitment to these innovation-catalyzing programs.

Despite a clear need to improve access to novel antimicrobials and first- and second-line antimicrobials in LMICs, governments have not implemented the policies needed to ensure these drugs are available and affordable to

patients. Governments have yet to implement regulatory and reimbursement improvements to enhance access to these new antimicrobials. Globally, governments have not funded or otherwise addressed the required supply chain improvements necessary to ensure stable access to older drugs and APIs necessary to produce these drugs, as has been shown by disruptions during the COVID-19 pandemic.

All countries recognize rampant overuse and misuse and have paid lip service to the issue in national plans. Yet, stewardship programs to reduce improper usage have not been implemented widely or sufficiently funded.

Though many governments have championed the One Health approach and erected bans or policies to limit the use of antimicrobials in animals, there have been few efforts to actually address environmental effluents that contribute to AMR, such as from manufacturing processes. Programs to specifically combat AMR in the environment remain vastly underfunded, preventing the full integration of a One Health approach across all sectors.

As a global threat requiring global action, AMR also needs greater investment in international and regional programs that promote cooperation and collaboration to protect the common good – a fact national governments must recognize and prioritize.

National actions plans and their implementation must be bolstered

While almost every country examined has modeled their NAPs on the recommendations of the WHO and other leading organizations, experts agree these plans either lack substance or little is being done to properly implement NAP goals and commitments.[29]

Many experts believe the details of the NAPs are overly broad and lack actionable items that could be implemented and measured at the country level. Experts also felt that many countries were not sufficiently committed to building a robust surveillance and monitoring infrastructure.[30] Many suggested specific issue areas are not being fully funded or financed,[31] while others felt that NAPs fail to frame the issue for a wider range of stakeholders.[32] This is particularly worrying given the importance placed on surveillance, especially monitoring of healthcare-associated infections, in WHO minimum guidelines for infection prevention and control.[33]

AMR is not a political priority in most countries

Across the board, there is a gross disparity between the scale of the AMR crisis and the level of attention from governments.[34] Experts noted the low awareness of the problem among policymakers.[35] Many policymakers do not fully understand the large incentive proposals recognized by experts as necessary to restore the antibiotic innovation pipeline; the collective, long-term, and devastating costs associated with inaction; and the long runway that is required to develop the needed antimicrobials.

NGOs, advocacy groups, and patient organizations are often missing from national conversations

Interviews and research revealed that third-party organizations and interest groups are not being fully involved in AMR efforts. The patient community could be more fully engaged as a partner that supports both developing national AMR policies and communicating key messages to the broader public.[36] The AMR Patient Alliance, run by the IAPO-P4PS Observatory (International Alliance of Patient Organizations),

brings together many voices for patient-led efforts against AMR,[37] providing a platform for policymakers seeking to better engage patient groups in domestic AMR discussions. Additionally, only a few organizations, including Sepsis Alliance, Peggy Lillis Foundation and Cystic Fibrosis Foundation, are actively working to educate policymakers about AMR and its impact on patients. Yet, given the tremendous impact of AMR on patients, particularly those with compromised immune systems, patient advocacy on AMR remains a relatively underleveraged opportunity within countries.

The global nature of antimicrobial resistance (AMR) has discouraged countries from taking bold, unilateral actions

Experts nearly universally agree that policymakers in their countries understand that unilateral action alone cannot adequately address the AMR challenge. Experts also acknowledged that decisionmakers know that cross-sectoral multilateral initiatives are the most effective paths to progress. Yet, many countries are playing a high-stakes game of "chicken," experts observed, waiting for other nations to initiate programs and policies.[38,39]

Many countries are insufficiently engaged with the global AMR community

Research also found that many governments are not fully engaged with international organizations working to combat AMR. This lack of engagement risks depriving stakeholders of critical tools, assets, best practices, and knowledge that can be applied locally. Given the global nature of this challenge, participation in formal and informal organizations can help facilitate key exchanges, which can ultimately help strengthen domestic plans. Equally, in many LMIC contexts the global AMR community must better engage with governments. As AMR remains largely unintegrated within the framework of the Sustainable Development Goals, the threat can be left unaddressed by LMICs. So, when this is the case the global AMR community and fellow governments should seek to engage with the relevant domestic policymakers to ensure that AMR is properly prioritized and assistance can be provided.

Despite the generally lackluster state of participation, some are leading the way. For example, the EU's Joint Programming Initiative on AMR (JPIAMR) represents a multi-faceted collaborative effort to combat AMR. The program provides a platform for 28 countries over five continents to engage on the issue of AMR, developing a Strategic Research and Innovation Agenda (SRIA) in 2018 to promote and fund innovation.[40]

Like most aspects of AMR, environmental challenges are completely borderless. Thus, collaboration across national borders is essential to effectively addressing antimicrobials that pollute our environment and contribute to AMR. The Antimicrobial Resistance Summit Asia in 2019, held in Singapore, demonstrated a great regional effort.[41] Likewise, South Korea's hosting of the 7th Session of the Ad Hoc Codex Intergovernmental Task Force on Antimicrobial Resistance in 2019 also demonstrates a commitment to collaborate on environment facets of AMR, including the development of risk management guidelines that address the role of veterinary applications, plant protection and food processing on AMR, based on FAO and WHO recommendations.[42] Additionally, the Codex Alimentarius Commission (CAC), has produced guidelines and codes on how to best

minimize and contain AMR in animal husbandry, veterinary drugs, and food.[43]

COVID-19 has virtually halted implementation of national AMR strategies

The COVID-19 pandemic has caused a large reallocation of resources, which in turn has slowed implementation of national AMR plans; delayed renewals of plans; and diverted staff, tools, and resources away from AMR efforts.[44] Pre-COVID AMR challenges are also being exacerbated by a rise in healthcare-associated infections and decreased oversight on the use of prescription antibiotics.

The pandemic has indefinitely delayed the possibility of political action on AMR in many settings. New incentives, pilots, and projects have been sidelined.[45] Diverted funding has, in some cases, impeded antimicrobial research and development. While this is not surprising given the severity of the COVID-19 threat, as governments move past the initial phases of the pandemic, AMR must become a key priority for policymakers.

Calls to Action

Governments must make bolder financial investments to tackle AMR

As countries wait for others to act, many decisionmakers are also waiting for constituent pressure to advance solutions for AMR. However, as we learned from the slow COVID-19 response, a public health crisis requires governments to lead rather than wait for public consensus. To start, governments must build support for innovative, aggressive policy action now to prevent greater suffering in the long term through the full implementation of NAPs and adoption of new commercial models.

Governments should better engage NGOs, advocacy groups, and the patient community in developing and implementing NAPs and other AMR initiatives

Effective, long-term policies require the support of a diverse group of stakeholders. Yet, even in countries where some policy efforts are underway, nations like the US and UK both lack the incorporation of patient groups, which could help bolster future efforts.

NGOs and especially the patient community can be a critical partner to government and also play an essential role in keeping policymakers well informed about emerging AMR issues. Most policymakers lack a strong understanding of AMR – especially the severity of the threat and the market failure that inhibits the development of new antimicrobials. As long as this continues, policymakers are unlikely to prioritize AMR or champion the needed policy solutions. Increasing the level of policymaker awareness and understanding is critical to advancing AMR policy priorities.

Governments should develop more ambitious NAPs and provide sufficient funding to achieve goals

While governments have crafted NAPs based on guidelines developed by the WHO, many plans do not go beyond minimum standards. It is also difficult to determine whether plans are being effectively implemented or funded, due to a lack of evaluation studies.

Governments should lean into AMR initiatives and actions now

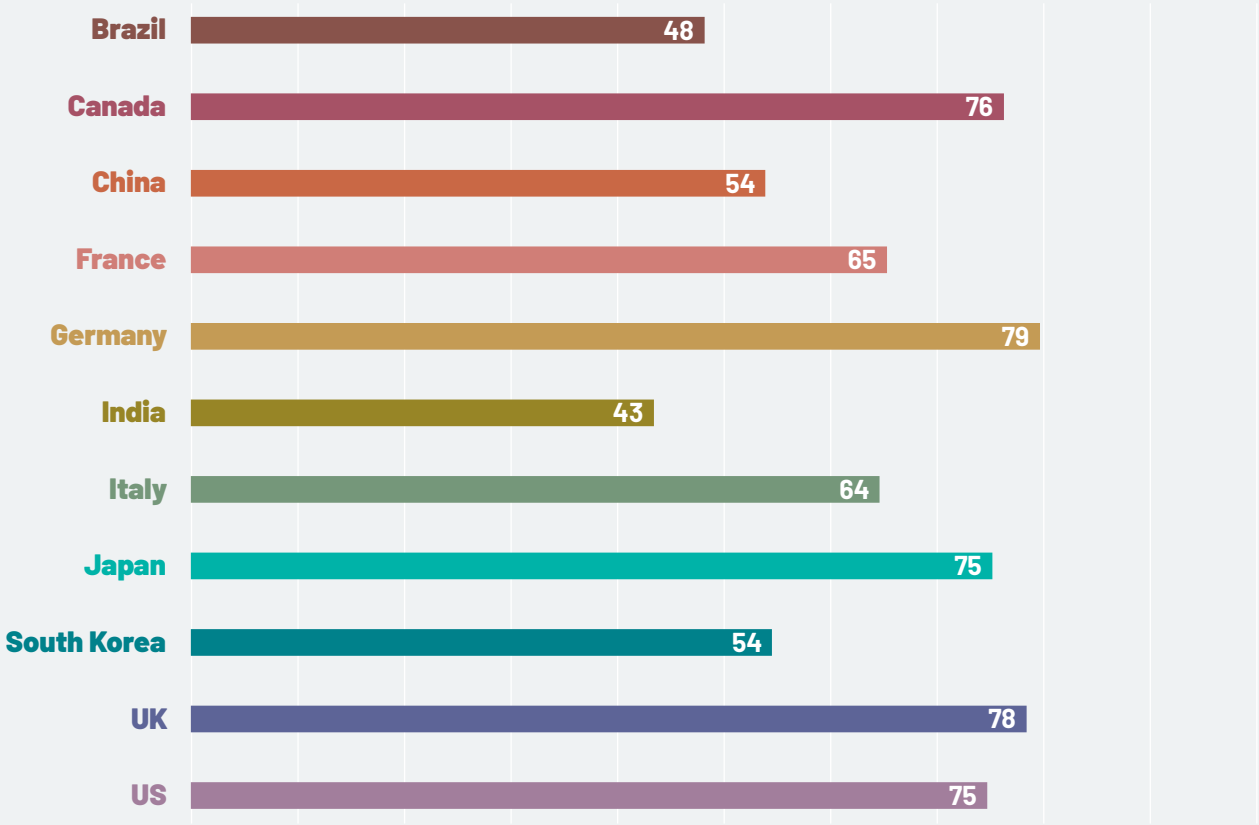
Experts in most countries report government reluctance to be a "first mover" on AMR initiatives. This wait-and-see approach delays progress and inhibits a collective approach against AMR. National strategies must not only implement the commitments in NAPs; new programs must be developed and piloted.

Waiting for new advancements in surveillance and monitoring programs further endangers populations. Implementing pilots for pull incentives, novel valuation models, and reformed reimbursement can help broaden the antimicrobial pipeline. To allow for equal access, governments must adopt policies that bring new drugs to patients and shore up supply chains for older drugs. Broader, more intensive stewardship programs are needed to help reduce the misuse and overuse of antimicrobials. Finally, piloting more well-integrated One Health approaches is necessary to combat AMR in the environment.

Awareness & Prevention

Assesses the level of commitment within countries to fund and facilitate efforts to increase awareness among stakeholder groups and improve mechanisms that can prevent and monitor AMR.

Awareness & Prevention Country Comparison



Key Findings

Public awareness across most countries remains low, driving overuse

Most people are unaware of the AMR threat, with little understanding of the link between antibiotic usage and consequences of AMR. Based on recent survey data, only 46% in Brazil, 51% in the US, 63% in China, and 68% in India recognize AMR as a term.[46] In Canada, one survey indicated that 57% believed antibiotics can be used to treat viral infections. In other countries, such as Germany, the public had greater awareness of AMR due to extensive media coverage of AMR-related deaths.

Low patient and prescriber awareness drives the misuse and overuse of antimicrobials, increasing the prevalence of AMR.[47] Over the past two decades, misuse of broad-spectrum and last-resort antimicrobials, in particular, has risen in LMICs, and misuse persists in HICs, despite awareness campaigns.[48]

Since not all forms of awareness generate behavior change, more work must be done to identify the most effective methods to communicate the dangers of AMR and the role of patients and providers in combating it.[49] Higher levels of awareness in Germany suggest that increased media coverage is a key factor. Greater investment to promote public understanding is critical; in fact, it is the first strategic objective of the WHO Global Action Plan to increase understanding of AMR across stakeholder groups.[50]

Countries' vaccination programs are not being fully leveraged

Adequately vaccinating populations against infections such as pneumococcal pneumonia, diphtheria, and tuberculosis, or even viruses like influenza and the novel coronavirus is a critical step to combating AMR. Yet, many countries we examined are failing in this area. In some countries, vaccine administration is disjointed and decentralized. In others, such as the US, there is no national-level vaccination mandate,[51] while many European countries require vaccines.[52] Canada's regionalized system for healthcare delivery can complicate efforts to vaccinate the population. Jurisdictional issues also undermine efforts in countries like Italy, where several regions decided to abolish vaccine requirements in 2005, leading to an alarming drop in immunization rates. Some governments, like South Korea, do not fully cover vaccination costs, which impedes access and reduces uptake. A few countries are failing to adequately invest in national vaccination programs: our analysis showed that China and India substantially lag behind other countries in per capita spending. Additionally, lapses in adult coverage remains worrisome, as vaccinating older adults is a key contributor to healthy aging as well as the fight against AMR.[53]

Despite these challenges, most countries are working to improve vaccination rates, such as Brazil and Italy who have worked to integrate vaccination programs into efforts to combat AMR. There are also many examples of national campaigns critical to reducing vaccine hesitancy. In Germany, the Robert Koch Institute runs vaccine awareness programs to reduce skepticism and increase uptake, and to improve vaccination rates in veterinary contexts the French Department of Agriculture ran two successful initiatives, "Immunization, Health Investment for Your Flock" and "Nourished, Housed, Vaccinated."

Most countries have also integrated vaccine policies into national AMR plans; however, this effort is often poorly implemented or underleveraged. Despite the obvious benefits, governments are not utilizing vaccine advisory committees to reduce the threat of AMR. Further, countries have not sought to describe how vaccines can combat AMR, monitor the effect of vaccination efforts on AMR development, track the implementation of vaccine initiatives, or effectively promote vaccine R&D, while also failing to set clear targets for vaccines more generally.

Weak, insufficient healthcare systems and inadequate public health infrastructure are major barriers

In countries where hospital settings lack sanitation standards or fail to enforce them, the rates of healthcare-associated infections (HAIs) rise dramatically. At a community level, poor sanitation increases the number of bacterial infections and directly contributes to increased antibiotic usage and AMR. Some countries are still failing to reduce HAIs and WASH-attributable deaths. Both India and Brazil scored poorly in this area.

In settings with a low doctor-to-patient ratio, general practitioners (GPs) are more pressed for time, reducing their ability to accurately diagnose patients. GPs in most countries also lack access to diagnostic tools needed to reduce unnecessary prescriptions of antibiotics. Stewardship practices and programs used in HICs may need to be adjusted for other contexts, given stark differences in access to resources, technologies, and expertise as well as greater need for antimicrobials.[54] Many have championed the adoption of "smart regulation" in LMICs to help address AMR, emphasizing cross-sectoral coordination and stakeholder engagement in the design of regulatory processes.[55]

Without these programs, countries can experience worse health outcomes and poor antimicrobial management. An American study on neonatal sepsis found that point-of-care diagnostics, more timely processing, and improved laboratory techniques were necessary to improve the screening and treatment of these cases.[56] In other words, a lack of proper healthcare infrastructure was limiting access to needed antimicrobials and, in cases of inappropriate prescription, worsening health outcomes.[57]

Even in countries with highly developed healthcare systems, a lack of infectious diseases specialists, who have expertise in managing patients with multidrug resistant infections and leading antimicrobial stewardship and infection prevention and control programs, is impeding national responses to AMR. In the US, infectious disease is one of the lowest compensated specialties, which hampers recruitment to the field.[58]

Most countries have dedicated surveillance and monitoring systems, but the degree of sophistication and transparency varies

In recent years, several countries have implemented systems to surveil and monitor antimicrobial resistance, with varying effectiveness. Since 2016, South Korea has implemented several systems, including Kor-GLASS, a GLASS-compatible national surveillance system for AMR,[59] a One Health-based research project to monitor surveillance of drug usage and disease transmission in human-animal environments, and a system to measure and compare antibiotic usage rates in hospitals.

In Canada, an intergovernmental taskforce is seeking to establish more rigid surveillance guidelines for the Canadian Antimicrobial Surveillance System (CARSS). Brazil's improvements in surveillance and monitoring have been used to inform patient safety and now contribute data to GLASS. In 2014, China also established a new surveillance system to replace older infrastructure, yet still has refused to participate in international efforts. Several European nations, including Germany, Italy, and France, have surveillance efforts that emphasize laboratory networks, reference libraries, and integration within NAPs.

Despite these initiatives, several countries are struggling with lower quality surveillance programs. Research for this Index found that the surveillance programs in Brazil, India, and South Korea were fundamentally less robust, despite initial efforts. In many cases, this is due to lack of program oversight and a simple inability to access the laboratory facilities and reference libraries necessary to administer a complex surveillance system. Further, China's unwillingness to participate in the WHO's GLASS demonstrates a lack of commitment to high-quality international surveillance efforts.

In many countries, data collected in monitoring systems are inadequate and do not drive decision making

While many countries are developing, maintaining, and growing surveillance and monitoring systems, the data being collected are not being optimized. Experts mentioned that collected data were not necessarily used to respond to spikes in resistance nor to inform decisions about how and where to allocate and deploy resources. Additionally, GLASS and national systems should leverage the collective data from industry to bolster existing databases.

AMR training for medical professionals is available but needs strengthening

In the UK, medical schools offer training on AMR, however, these curricula are not standardized throughout the country. The Society for AMR Chemotherapy is currently seeking to rectify this problem by formally incorporating AMR into all pre-service training, while in-service training is also provided. In Brazil, healthcare provider training (pre- and in-service) on AMR is outlined in the NAP. Training is also provided in India, including for veterinary-related professions, where AMR is formally incorporated into pre-service training and relevant human health groups handle in-service or continuing professional development nationwide.

Further, there needs to be a larger commitment by governments to ensure that the future generations of HCPs are able to actively contribute to reducing antimicrobial overuse and misuse, enabling stewardship from a bottom-up approach. IDSA has developed a curriculum for medical students on antimicrobial stewardship and began offering it to all medical students free of charge in April 2020. To date, over 200 medical students have participated. This curriculum allows medical students to model stewardship best practices in inpatient and outpatients settings, speak with patients and clinicians about appropriate antibiotic use, and utilize behavioral psychology techniques to talk with other prescribes to help effect change in antimicrobial prescribing.

Despite ongoing challenges, many governments and NGOs have successfully implemented awareness campaigns

Recognizing the critical role of public awareness in the fight against AMR, many governments and NGOs have implemented campaigns to reduce overuse and misuse.

Saudi Arabia

With research suggesting a rise in resistance rates throughout the country, Saudi Arabia has taken proactive measures to align with global and regional standards for AMR stewardship.

In 2016, the *Saudi Medical Journal* outlined a two decade-long acceleration in the prevalence of antimicrobial-resistant bacteria throughout the country. The paper reported that resistance rates among gram-negative bacteria (GNB) and extended spectrum beta-lactamase (ESBL) had increased dramatically since the 1990s, with mortality from outbreaks reaching as high as 40%. The paper further identified the first sightings of pan-drug resistant GNB in Saudi Arabia, posing an alarming risk to its healthcare system. Out of 200 tested health workers, 18% were found to be carrying a drug-resistant strain of S.aureus. The review determined that these trends would worsen without intervention, citing irresponsible antimicrobial use and prescriptions, high international travel rates (particularly within the country's vital pilgrimage industry), and lack of hygiene awareness as the chief contributors.

To combat the dangers of antimicrobial resistance, Saudi Arabia has begun an aggressive national response. The 2017 Saudi National Action Plan outlines a comprehensive initiative to strengthen the country's AMR infrastructure. Strategic objectives include developing AMR and hygiene awareness and training programs, a national surveillance network, laboratories, governmental structure, and stewardship guidelines. Saudi Arabia has pledged to uphold the WHO 2015 Global Action Plan, and as a member of the Gulf Cooperation Council Center for Infection Control (GCC-IC), co-released a regional AMR Action Plan in 2016. With these efforts, Saudi Arabia has taken clear steps to reverse the emergence of new drug-resistant bacteria.

Canada, France, the UK, and US[60] all run annual awareness weeks, alongside general campaigns. Likewise, Brazil, India, Germany, and recently Italy have run national campaigns on AMR. In South Korea, however, experts cited only small-scale brochure campaigns for the general public.

Stakeholder groups, including healthcare providers, are also being targeted by campaigns to raise awareness. Following provider-focused campaigns in 2011, hospital usage of antibiotics was substantially reduced in China. Experts also referenced "Antibiotic Awareness Week" directed at HCPs in South Korea and larger German campaigns aimed at improving responsible prescribing. The Public Health Agency of Canada (PHAC) provides HCP-directed awareness campaigns, while directing awareness efforts to the public and policymakers. Throughout the past decade, South Korea's government has led initiatives targeting key stakeholders, though recent AMR campaigns have been described as limited. In the US, the CDC targets providers through their AWaRe campaign, while the US Department of Agriculture participates in a non-human AB campaign for World Antibiotics Awareness Week.

Widespread antimicrobial stewardship guidelines and programs are not yet available in Italy. More targeted campaigns are working to fill this gap. For example, "Obiettivo Antibiotico" (Antibiotic Aim) has sought to raise

both public and provider awareness of prudent antibiotic usage in Sicily, while the "Targeting Zero" campaign, also in Sicily, aligns AMR surveillance and stewardship with broader infection control and protection activities.

Calls to Action

Governments should strengthen efforts to improve patient awareness

Governments must commit resources to public awareness campaigns to improve AMR awareness and ensure patients and providers understand the dangers of antimicrobial overuse and misuse. NGOs and patient organizations will play a key role in helping to educate and inform the public, though governments must ensure sufficient funding for mass media campaigns, including television ads and efforts targeted at specific groups, such as seniors. Raising overall awareness will also help GPs push back against pressure to prescribe. Additionally, governments must acknowledge that interventions will be necessary in order to force behavioral changes, as greater awareness will not necessarily guarantee more appropriate attitudes and behaviors.

Governments should bolster training requirements and program funding for medical professionals and medical trainees for IPC and beyond

Greater efforts to integrate and standardize healthcare professional training can also help improve awareness and prevention efforts. While AMR is included in most medical curricula, these programs need to be strengthened, and continuing medical education requirements vary. Countries must do more to require strong AMR curriculums in medical training, formal follow-up training, improve access to these programs, and ensure a greater range of medical professionals are participating. These programs should also seek to include specific education on infection prevention and control (IPC), so that trained HCPs can help guide hospital-level IPC programs along WHO guidelines.[61] Governments should consider working with stakeholders to make these trainings more affordable or publicly funded. Further, these trained HCPs need to be embedded within hospitals and other medical settings, as often stewardship programs are not sufficiently staffed with those needed to ensure appropriate and responsible use. Additionally, other professionals with the ability to prescribe and dispense, like pharmacists and veterinarians, need to be included in AMR training and stewardship programs.

Governments should redouble vaccination efforts

Expanding vaccine programs in AMR-relevant diseases can help prevent increasing resistance and infection rates, while also curbing healthcare-associated infections (HAIs). Unfortunately, several countries lack robust vaccine requirements and the infrastructure needed to accelerate uptake in the near term. Governments should build on learnings from COVID to enhance vaccine accessibility and improve public literacy on vaccine safety and benefits, with a particular focus on older adults. Some concrete steps governments can take include consolidating vaccine oversight and administration and integrating vaccine data into regional or national registries. Vaccines must generally be viewed as a more important part of AMR efforts, as currently most governments are undervaluing their utility. Sadly, national immunization committees are more reluctant

to consider vaccines as a key aspect of the AMR challenge, largely because data is simply limited. Unfortunately, this type of data is exceedingly difficult to collect, and few investments have been made to do so. Ergo, governments should be willing to accept more predictive and modelled data to ensure vaccines are more strongly integrated into NAPs.

Governments should improve sanitation in healthcare systems and public health infrastructure along WHO IPC guidelines

Most countries could benefit from improving their healthcare sanitation infrastructure and optimizing it to fight AMR. Governments should ensure funding is allocated to upgrade this infrastructure. Given the alarming rate of healthcare-associated infections (HAIs) and WASH-related challenges in several countries examined, basic sanitation guidelines need to be stringently followed and improvements implemented to reduce HAI rates and slow growing resistance profiles.

As is outlined in WHO IPC guidelines, WASH and acute care facility standards must be bolstered in most lower-resource healthcare settings in order to effectively implement IPC programs.[62] These programs are intrinsically linked to WASH efforts: IPC programs can help enforce WASH standards and WASH standards are necessary for IPC program success.[63] Without improved sanitation policies in healthcare settings (and better IPC training) infection prevention and control efforts become less effective, enabling HAIs to wreak more havoc on healthcare systems and resistance profiles to grow more rapidly. Therefore, governments must fully adopt WHO IPC guidelines to improve WASH standards and also the necessary IPC training and surveillance which can help enforce sanitation protocols and reduce HAI prevalence.[64]

Countries can also do more to improve overall public sanitation. In the Clift review of the O'Neill report, many GPs in LMICs expressed a wariness not to prescribe antibiotics because of poor sanitary conditions in patient homes.

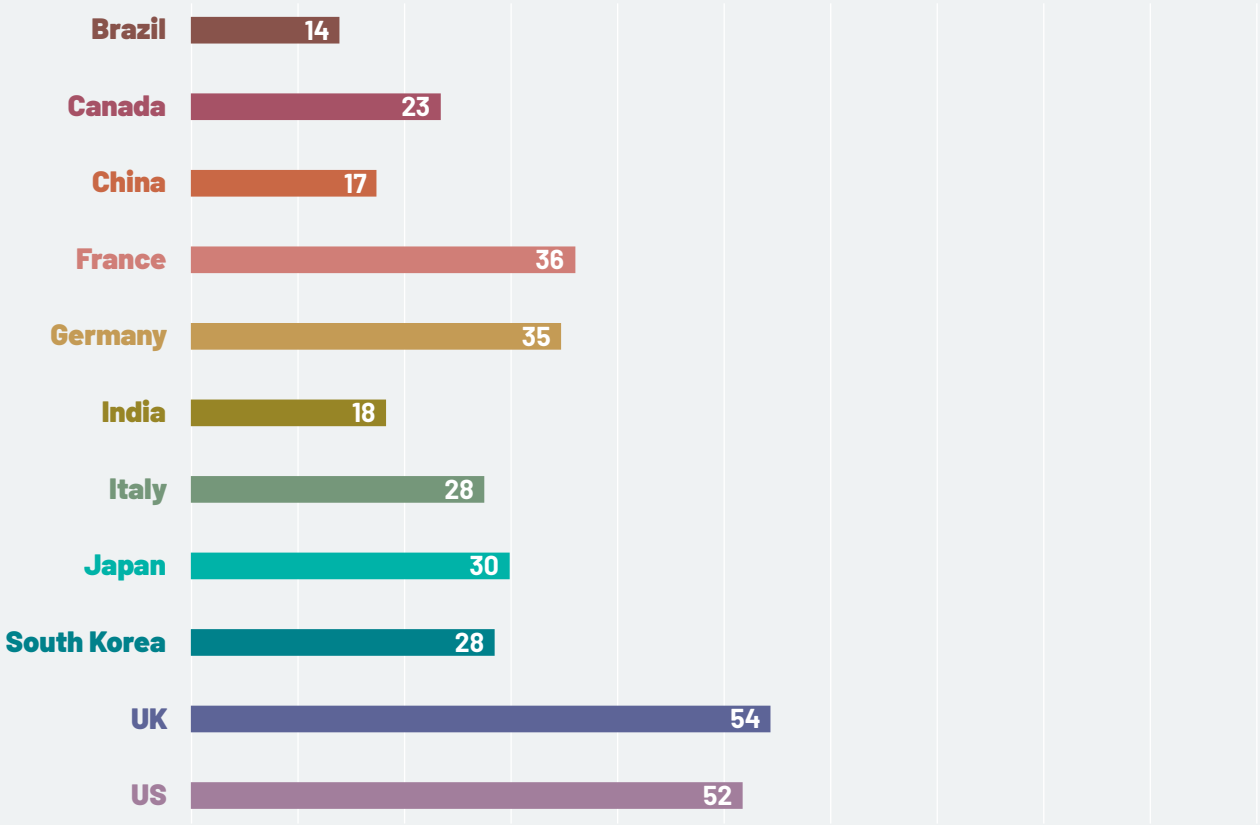
Governments should increase surveillance and monitoring commitments

While these efforts demonstrate a willingness and ability to establish a surveillance infrastructure, these networks need to be strengthened. Promoting increased participation in country-wide monitoring efforts and assisting laboratories and medical facilities can help improve national surveillance infrastructure. These improved surveillance systems are also critical in informing hospital and national level IPC programs. Further, governments should develop partnerships with private sector surveillance programs, in order to leverage this data to augment government led initiatives. Countries should also commit to greater levels of data transparency as collection improves so global surveillance efforts can be raised alongside national efforts.[65]

Innovation

Quantifies governments' commitments to foster and support AMR innovation, especially in areas of greatest opportunity, including novel valuation and pull mechanisms.

Innovation Country Comparison



Key Findings

There is a consensus that antimicrobials are not fairly valued in most countries and that reforms are needed

The lack of new and novel antimicrobials is acutely felt by hundreds of thousands of patients in need, yet the antimicrobial pipeline remains narrow due to a distinctive market failure. Experts in every country consistently raised improper valuation of antimicrobials as a central challenge. Although AMR experts have reached a consensus on several ways to improve the valuation of antimicrobials, country-by-country research found little evidence these methods have been implemented.[66]

Valuation discussions are taking place in a handful of countries. The UK has addressed health technology assessment (HTA) changes in their pilot program, and the US has considered legislation to improve the way antimicrobials are valued. Yet, these efforts are only preliminary and do not go far enough. Valuation can help segment new antimicrobials from older generic drugs, but this still does not decouple revenue from sales volume, a key factor in effective reform. Valuation reform must work in tandem with other incentives to ensure innovation in the antimicrobial pipeline. Though unable to unilaterally pass the needed measures to reform valuation, the EU has assisted by developing financing approaches through multilateral partnerships, such as InnovFin: EU Finance for Innovators and the New Drugs for Bad Bugs program.[67]

No countries have effective pull incentives

Experts and advocates alike largely agree the depleted antimicrobial pipeline represents a true market failure and that pull incentive programs will be essential to jumpstarting innovation. However, recent country-level efforts have been almost nonexistent, despite previous commitments to these programs. Only two countries in this Index - the UK and the US have even attempted to implement a pull incentive, and no country has done so successfully, as of the writing of this report.

The UK's program, in which volume and revenue are decoupled, is the furthest along in progress. Under this approach, the UK Department of Health and Social Care will pay two drug developers up front for their anticipated antibiotics based on the expected value to society. The UK is betting the new drugs will fight drug-resistant infections, making subscription payments to ensure developers can recoup their investment in a drug that should not be sold in high volumes. AMR decisionmakers worldwide should follow suit and consider the UK pilot as a potential model for pull incentive programs in their own countries.

In the US, the PASTEUR Act has been proposed with bipartisan support and expert endorsements. If passed, the PASTEUR Act would implement decoupled subscription payments for new antimicrobials, allowing the federal government to enter into contracts with developers of novel antibiotics and pay for the value of those antibiotics rather than the volume used, providing a predictable return on investment.[68] This novel pull incentive could revitalize the antibiotic pipeline and pave the way for sustainable antibiotic research and development. In addition to novel pull incentives, reimbursement reform proposals would give hospitals with antimicrobial

stewardship programs better reimbursement for antimicrobial drugs through federally sponsored Medicare.[69] This approach could also boost support for antimicrobial development.

Most countries have stalled on high-level discussions

While progress in the US and UK is commendable, most countries have yet to move beyond high-level discussions. Research found numerous policy proposals demonstrating a clear understanding of the problem and the key steps needed to address core challenges. Despite this level of clarity, experts lamented the lack of action by governments worldwide.

In Japan, cross-sectoral proposals affirm the need for a pull incentive framework, but no concrete steps have been put in place.[70] Experts in Italy report that "productive discussions" have taken place between AMR stakeholders and the Ministry of Health, but no specific programs were proposed.

In the EU, experts believe anticipated policies from the European Medicines Agency (EMA) will include language regarding pull incentives. Currently, it is not financially viable for antibiotic developers to distribute to the EU,[71] so recognition of the need for pull incentives by the EMA may be a transformative development. The European Commission's Pharmaceutical Strategy for Europe also addresses the implications of AMR and the lack of sustainable incentives to ensure new drug development, citing the need for pull incentives.[72]

Very few countries have erected the research infrastructure necessary to support the development of AMR diagnostics, surveillance technologies, and new antimicrobials

Only a few countries examined have implemented the infrastructure needed to support AMR research and the development of new antimicrobials. China, Brazil, and India all lack intellectual property protection systems, disincentivizing the development of new drugs. Apart from the UK, US, South Korea, and Germany, no country has more than 10 sources of AMR research funding. The UK, US, and Japan lead in terms of AMR-focused research projects, with more than a 1,000 each, yet experts resoundingly agree that even in those countries, insufficient resources have been dedicated to AMR research. The US National Action Plan includes objectives related to the development of a clinical trials network for AMR and the training of new AMR investigators, but increased resources are needed for implementation. Germany and Canada host 412 and 398 projects respectively, while all other countries trail much further behind. The table below highlights the massive disparities in public funding for AMR research.[73]

Research infrastructure is lacking and funding in all countries remains too low, even among the best performers. These shortcomings inhibit the development of newer, faster, and more accurate diagnostic tools that could help ensure more appropriate use and equitable treatment. Further, the pandemic has underscored the worthiness of investments in more intelligent technologies for surveillance, but their development in the AMR context is mixed. Finally, research programs that could develop new drugs to protect populations from AMR have not been financially prioritized by governments.

Total Public AMR Funding ($, millions)	
China	7.64
Brazil	1.49
Italy	0.35
UK	206.08
France	9.89
Germany	47.33
US	389.47
Canada	19.39
South Korea	0.68
India	3.19
Japan	5.71

Most countries have made measurable progress implementing push incentives

Most countries examined have not implemented the pull incentives experts believe hold the most promise for stimulating needed antimicrobial development. Yet, these countries have had relatively greater success developing push incentive programs, such as tax credits, subsidies, and country-level risk sharing.

The multilateral Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) provides funding to push the development of preclinical and Phase 1 antimicrobials, while also lending expertise and business support to increase chances of success.[74] CARB-X is partially funded by the US Biomedical Advanced Research and Development Authority (BARDA), and CARB-X awardees are also provided preclinical drug development and technical support from the US National Institute of Allergy and Infectious Diseases (NIAID).[75]

The EU has funded push mechanism projects through the Innovative Medicines Initiative (IMI) and JPIAMR, though not enough to generate sufficient returns on antibiotics. Currently, about 90% of the EU's AMR budget is directed toward the IMI.

Germany offers subsidies valued at up to 25% of R&D activities for new product development. An additional country-level risk sharing program covers 25%-75% of eligible costs, while DZIF, the German Center for Infection Research, runs a cost-sharing program for clinical trials.

France has implemented a 30% tax credit for eligible expenses related to new product development, established AMR R&D grants, developed cost-sharing clinical trial programs, and has established programs to aid start-up drug developers.[76]

Italy introduced a patent box program, which offers a 50% exemption from corporate and local tax on income derived from the licensing or direct exploitation of qualifying intellectual property, such as a novel antimicrobial. The government also provides a tax credit worth up to 50% of the annual increase of average R&D expenses. The maximum grant value the government provides to private companies is €150,000.

Brazil provides "super deductions" of 160% to 200% of eligible expenses for new products, and the Ministry of Science, Technology, and Innovations (CNPq) offers grants covering up to 90% of project costs. India offers a "super deduction" of up to 200% on R&D, pending

Australia

Recognizing the dire threat posed by AMR, Australia has engaged a coalition of nonprofit, public policy, and industry leaders to tackle a range of issues head on.

Over the past decade, Australia has rapidly established itself as an energetic, committed participant in the fight against AMR. The country has advanced pharmaceutical innovation for over a century, starting with Australian Sir Howard Florey's contribution to the development of penicillin, the first antibiotic. Australia understands the immense personal, economic, and healthcare-based costs of AMR. Nearly 300 Australians die every year from antimicrobial-resistant bacteria; as many as 20,000 lives are forecasted to be at risk by 2050. In 2015, the first Australian Antimicrobial Resistance Strategy was released. An updated action plan was released in March 2020, a 20-year vision program compared to its 5-year long predecessor.

MTPConnect, Australia's nonprofit wing dedicated to accelerating pharmaceutical growth and medical innovation, has worked tirelessly to build an AMR coalition across the public and private sectors. The organization has outlined steps to correct overuse by encouraging prudent antimicrobial stewardship, improved surveillance, and greater public awareness. To streamline the supply of drugs, MTPConnect has conducted workshops focusing on improved valuation methods, product development gaps, and stronger push and pull incentives. Alongside MTPConnect, Australia has vastly expanded its reach into AMR innovation through the Australian Strategic and Technical Advisory Group on AMR (ASTAG), the Pharmaceutical Benefits Scheme (PBS), and NPS MedicineWise.

government approval of the drug; risk-sharing loans for projects of national importance, at 5% interest, which cover up to 50% of the project cost; and a technology development program offering money for equity, equal to up to 25% of project funding. Japan has taken a different approach, seeking to revalue antibiotics by aligning pricing more closely with development costs.

Calls to Action

Governments should implement pull incentive programs within the next three years

With the 10-year anniversary of the WHO Global Action Plan on AMR in 2025,[77] the AMR Action Fund's 2030 developmental goals,[78] and national plan expirations all approaching, countries must dramatically accelerate progress in the AMR fight. Boosting the antimicrobial pipeline remains central to addressing AMR, and without new incentives to spur drug development, we face a looming antimicrobial catastrophe where we can longer treat certain infections.

For many countries, pursuing a pull program does not represent an entirely new effort, but simply a fulfillment of previous commitments. Pull incentives are widely recognized by experts as the most promising approach to broadening the antimicrobial pipeline by rewarding innovation, and first movers in this area have been applauded for their efforts, as has been seen with the UK's pilot program. Yet, the commitment from policymakers globally is not enough to drive needed drug development. Governments that have failed to honor past commitments must follow through now.

Governments should increase investments in AMR innovations for surveillance and diagnostics

AMR innovation clearly needs stronger government support. To promote stewardship practices and rational usage, national health systems continue to need new diagnostic tools and surveillance mechanisms, innovations which now receive less funding than needed to combat AMR effectively. Diagnostic tools that provide faster, more accurate results and digital technologies that that can leverage data to improve surveillance and monitoring efforts remain critical components to the fight against AMR.

Governments should ensure pricing reflects the full value of novel antimicrobials.

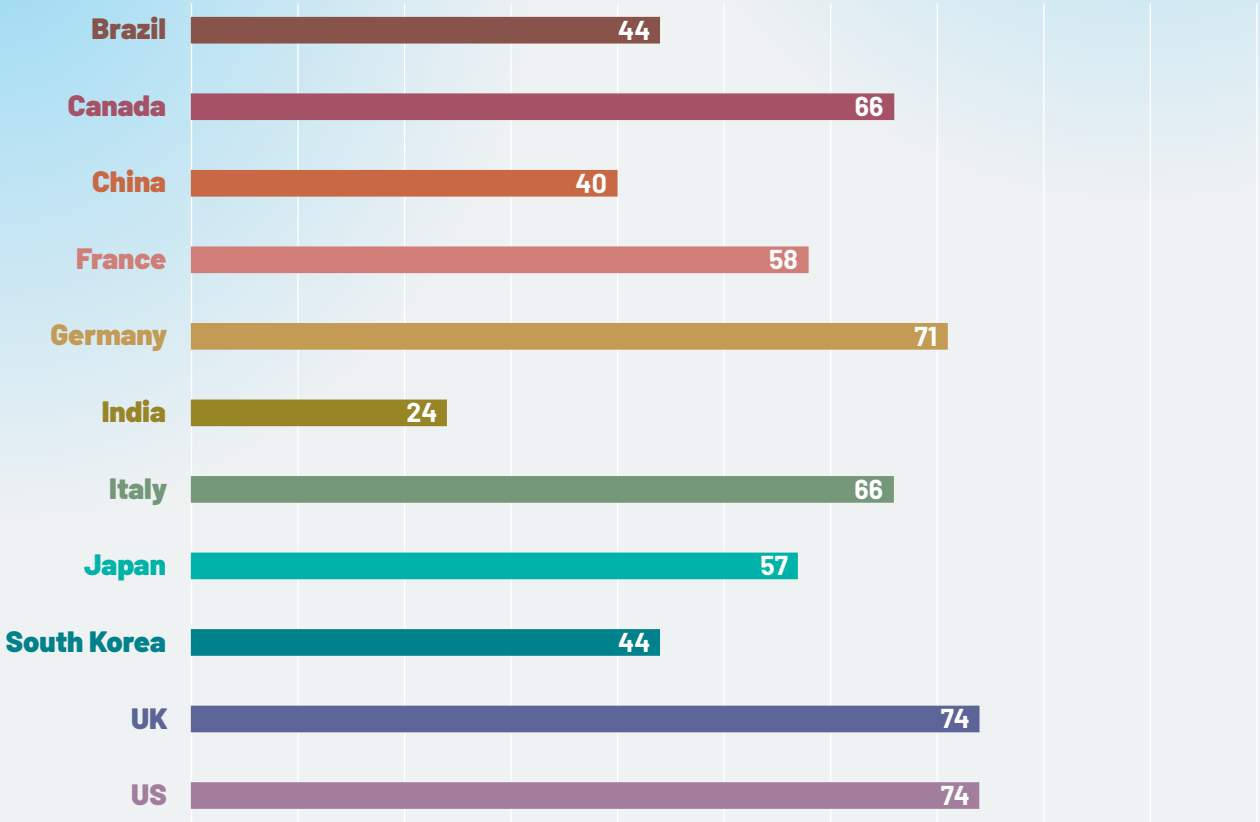
Current valuation models fail to capture the full range of benefits provided by novel antimicrobials and do not price these drugs commensurate to their value to society. Drug development is costly and time-intensive in any event, but developing antimicrobials is particularly risky. By using research-validated value models, governments can more accurately and fairly price new antimicrobials to reflect their full value.

New models can help decisionmakers create a more attractive market for antimicrobials.[79] While opinions about these models vary, experts generally agree that governments should take into account the following factors to determine the value of antimicrobials: spread of infection, developmental cost, cost of inaction, losses associated with continued spread (economic and human), and societal value (patients, community, etc.).

Access

Measures the level of access that persons within countries have to both older and novel antimicrobials.

Access Country Comparison



Key Findings

Access to novel antimicrobials is limited in all but a few countries

Even patients in HICs face difficulties accessing newly launched products, as high costs often mean hospitals forego procuring them.[80] Lengthy regulatory approval and reimbursement processes can make markets unfeasible for new antimicrobials and block patient access to these needed drugs. Some countries have worked to streamline these processes, highlighting best practices. In Germany, a new 2020 regulation treats reserve antibiotics (active against multi-resistant bacteria) as orphan drugs, automatically assuming benefit, thereby encouraging the marketing and development of these drugs.

The Ministry of Health in Brazil has likewise adopted new criteria for introducing vaccines, promising an efficient and timely integration within the country's pre-existing immunization program. In practice, however, approval times take much longer than limits mandated by the Brazilian government, inhibiting patient access. In general, traditional models undervalue antimicrobials, which reduces the incentives for innovation and decreases accessibility. In Italy, the reference pricing model limits the entry of novel antimicrobials,[81] unfairly tying revenue, and thereby commercial viability, to the volume of sales.[82]

Patients continue to struggle accessing older (non-novel) antimicrobials

Although antibiotics are widely available to much of the world, an estimated 5.7 million

Approval and Reimbursement Status for 3 Novel Antimicrobials[83]

	Lefamulin	Meropenem + Vaborbactam	Ceftazidime + Avibactam
Brazil	No approval	No approval	Approved
Canada	Approved	No approval	No approval
China	No approval	No approval	Approved
France	Approved	Reimbursed	Reimbursed
Germany	Approved	Approved	Reimbursed
India	No approval	No approval	Approved
Italy	Approved	Reimbursed	Reimbursed
Japan	No approval	No approval	No approval
South Korea	No approval	No approval	No approval
US	Reimbursed	Reimbursed	Reimbursed
UK	Approved	Reimbursed	Reimbursed

people die each year due to lack of access to these drugs.[84] Access is most limited in LMICs that have higher burdens of infectious diseases and generally weaker healthcare systems, where fragile supply chains, counterfeit drugs, and out-of-pocket costs can prevent access to even first- and second-line antibiotics.[85]

Research indicated many countries struggle to provide access not just to novel therapies, but to older, non-novel antimicrobials as well. Research on 15 antibiotics launched between 2010 and 2020 revealed that in two countries none of the drugs are available and in three other countries fewer than five of the drugs are available.

Experts we interviewed also flagged significant access disparities between urban and rural areas. For example, in rural western areas of China, affordability posed a significant barrier to access, leading some patients to seek alternative medicines in lieu of antimicrobials. This, however, is not only an issue in less developed settings, and can occur wherever inequities exist. In the US, for example, one study found that black patients were much likely to succumb to septicemia,[86] while other studies have shown that white patients receive twice at the antimicrobial prescriptions per capita compared to non-white patients.[87]

Government delays in moving drugs to a reimbursement list can also stymie access

Reimbursement designation is an important step to ensure that novel antimicrobials are not only prescribed, but also made available to patients at an affordable price. Unfortunately, many countries have not taken steps to ensure that approved drugs are reimbursed at a level aligned with patient behavior and expectations. This misalignment is particularly pronounced for antimicrobials, which patients expect to be inexpensive.

Research on the availability of three recently approved novel antimicrobials: Lefamulin (approved 2019), Meropenem + Vaborbactam (2017), and Ceftazidime + Avibactam (2015), showed that access was limited to a handful of countries, in part due to reimbursement status. So-called "reimbursement list lag," the time between market launch and placement on a reimbursement list, exceeded 400 days for countries where the three novel drugs mentioned earlier have been launched. In Italy, Ceftazidime + Avibactam was approved and launched, but took another 600 days to make it to the reimbursement list. Most countries set maximum wait times for drugs to be included, but these mandated time limits are usually unenforced. The table on page 36 highlights where three novel antimicrobials are included on reimbursement lists and thereby affordable to patients. It should be noted that some countries did not recognize these new drugs as "innovative;" however, in Italy, Meropenem + Vaborbactam was the first to receive such a designation.

Calls to Action

Governments should expedite access by reducing regulatory hurdles and accelerating government adoption

Even when valuable antimicrobials are developed, regulatory barriers and slow decision-making can inhibit access and discourage companies from pursuing additional development projects. Ceftazidime + Avibactam, the oldest of the three drugs we examined, was first approved

in 2015, yet it is only available and reimbursed in Italy, France, Germany, the UK and the US. Over five years later, the drug has still not been approved in South Korea, Canada, and Japan. In over half of the countries examined, none of the three drugs are reimbursed. As resistance profiles continue to grow, these drugs will only become more urgently needed, making it imperative for governments to shorten the timeline for approval.

While certain regulatory policies are better suited for LMICs than HICs and vice versa, regional or cooperative regulatory models can provide the most efficient means of addressing approval hurdles.[88] For instance, the Japanese Pharmaceuticals and Medical Devices Agency (PMDA) has initiated conversations with the FDA and EMA to harmonize clinical guidelines for antimicrobials in an effort to potentially lower developmental costs and reduce wait times for approval.[89,90]

Affordability can be improved by faster adoption of newly launched drugs onto national reimbursement lists, reducing the economic barriers to access. The bureaucratic lag between market approval and reimbursement decision for new antibiotics in many countries discourages the development and market entry of novel antimicrobials altogether. Regardless of whether this lag is intentional or simply administrative in nature, the net effect can limit drug availability, affordability, and access for patients and therefore warrants serious attention by government leaders.[91]

Governments should make the availability of novel antimicrobials a national priority

Access to novel antimicrobials remains difficult for patients in many of the countries examined in the Index. Without access to these last

Sweden

Sweden's PHAS (Public Health Agency Service) is piloting a new Reimbursement Program from 2018-2022 that will establish clear benchmarks for access and antimicrobial stewardship initiatives.

Under the pilot program, the Swedish government mandates pharmaceutical companies to produce a set total of antibiotics in exchange for a guaranteed minimum annual revenue. The initiative, partly financed by Vinnova (the Swedish Innovation Agency), aims to ensure the supply and continuous availability of existing low volume antibiotics and novel antibiotics to improve availability.

Typically, Sweden's national reimbursement programs are run through the Dental and Pharmaceutical Benefits Agency (TLV), which sets national pricing and coverage under the Pharmaceutical Benefit Scheme. Although not in collaboration with the TLV, PHAS released a report on developing new models for identifying targeted antibiotics and providing for economic compensation, storage and distribution, and rational usage. The two government agencies have been commissioned to assess a new business model for stewarding access to new antibiotics by the Swedish Association of the Pharmaceutical Industry (LIF). The new lump-sum model will attempt to incentivize stewardship from the Swedish Pharmaceutical Industry, prioritizing the value of a drug to the healthcare system over volume production. A successful pilot could also encourage exploration of a fully decoupled model between drug pricing and quantity, prioritizing both responsible AMR production and innovation in the industry.

lines of defense, many are put at unnecessary risk of infection and death. COVID-19 has demonstrated the importance of national stockpiles of needed drugs and consideration for antimicrobials as well. Stringent stewardship mechanisms should remain in place to protect the utility and value of novel antimicrobials even as they are stockpiled. Following WHO recommendations for usage of Watch and Reserve antibiotics, as well as developing country-specific measures, can ensure that governments appropriately provide access to much-needed novel antimicrobials.

Governments should establish or support sustainable systems for manufacturing and dispensing antimicrobials across the supply chain

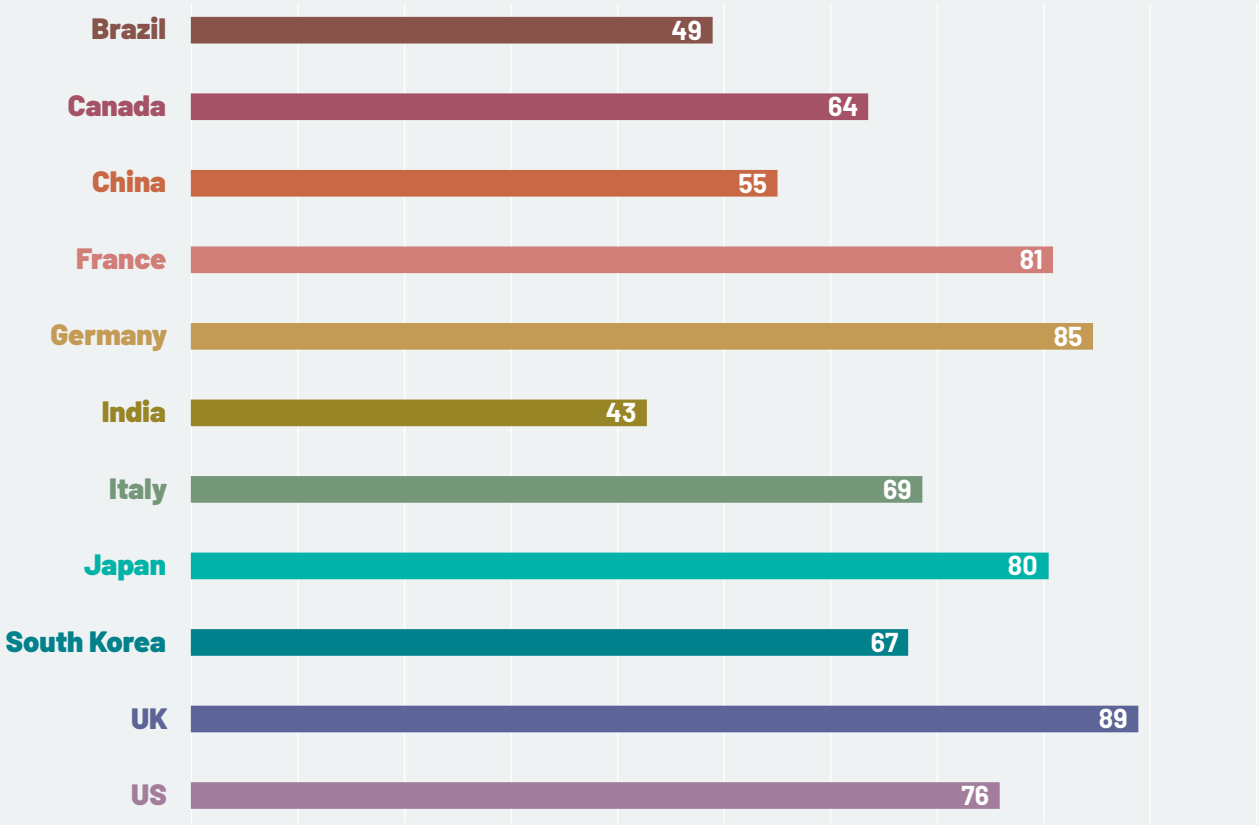
In many LMICs, weaker supply chains continue to threaten stable access to older and generic antimicrobials for patients, which also fuels the sale of counterfeit and subpar-quality drugs. The WHO estimates that about 10% of medical products in LMICs are either counterfeited or of substandard quality.[92] These stockouts and substandard drugs undercut the effective treatment of infections, serving only to further fuel AMR risk.[93]

A recent WHO survey revealed that 36% of antiretroviral therapy clinics in 35 countries had at least one antiretroviral drug out of stock in the previous 12 months.[94] COVID-19 has placed greater stress on these already frail structures and has demonstrated the need for countries to invest in infrastructure to support more resilient supply chains. COVID has also made clear that countries need to establish new methods and systems to encourage better resource allocation and unfettered access for those in need. USAID, GAVI, and the Global Fund have all made massive investments to improve the robustness of supply chains in LMICs, after identifying them as key threats to efforts against AMR.[95] National governments must follow suit to ensure that supply chains are able to aid in AMR efforts, rather than hindering access and contributing to growing resistance profiles. Further, all governments must recognize, assess, and address the fragilities within their supply chains which have been uncovered due to the current crisis.

Appropriate & Responsible Use

Assesses governments' efforts to reduce misuse and overuse of antimicrobials and promote rational diagnosis.

Appropriate & Responsible Use Country Comparison



Key Findings

Over-the-counter availability compounds AMR challenges

In several countries examined in the Index, common antimicrobials are available for over-the-counter (OTC) purchase, which can undermine efforts to effectively limit overuse. A recent Indian study revealed that pharmacies dispense antibiotics at the highest rate when directly interacting with patients, rather than referring them to another healthcare provider.[96] In many communities, OTC antimicrobials are dispensed without a proper medical evaluation. In China, experts noted that access to OTC antibiotics has increased unnecessary usage.[97] In countries that lack strong healthcare systems and equitable access to care, pharmacies and OTC antimicrobials may be the only available sources of care for many vulnerable individuals, heightening the need to increase healthcare access in order to reduce OTC antimicrobial use. Most countries have penalties and restrictions to prevent the sale of OTC antibiotics, but enforcement varies greatly.

For drugs that require a prescription, overprescribing is a problem

While most countries we examined require a prescription to access antibiotics, prescriptions are not a failproof safeguard against overuse. Overprescribing poses a serious challenge. Too many healthcare providers are empowered to prescribe antibiotics, often without the training to do so safely and effectively. In the UK, despite some success in curbing overprescription, antibiotics are still prescribed at double the rate of comparable countries. In China, where prescriptions are legally required to access antibiotics, 84% of pharmacies still provide the drugs without prescriptions. The CDC in the US also estimates gross overuse, stating that at least 30% of antibiotics prescribed in an outpatient setting are unnecessarily prescribed.[98] Outside urban environments in India, some traditional medicine and other informal healthcare providers prescribe antibiotics freely despite restrictions.

General practitioners lack tools and resources needed for proper diagnosis

In some countries, a lack of time and resources contributes to antibiotic overuse. In India, the ratio of healthcare professionals to population varies greatly between urban and rural settings. Rural providers often lack time, resources, and diagnostic tools, resulting in higher prescription rates of antibiotics. In the UK, many GPs rely on a symptoms-based approach to prescribing antibiotics, despite access to more advanced diagnostic technology. During the pandemic, where telemedicine has become much more common, GPs and HCPs have had greater difficulty in appropriately prescribing antimicrobials to patients, compounding COVID-19 related stewardship challenges, and further contributing to HCP overprescription and inappropriate prescribing.

Patients clamor for antimicrobials

Patients play a major role in the overuse of antibiotics. Despite efforts to reduce usage, Canada's antimicrobial purchasing rate increased by 30% between 2014 and 2018. In South Korea, the total prescribed antibiotic Defined Daily Dose (DDD) rose approximately 50% between 2002 and 2013, with 72% of 2013 prescriptions distributed at clinics. In France, healthcare providers prescribe 50% more antibiotics than the European average. In some cases, patients clamor for drugs, driven by a

Kenya

Despite considerable infrastructure and regulatory challenges, Kenya is implementing a bold antimicrobial stewardship program.

To meet the many AMR challenges facing the country, including the need for increased AMR surveillance, lack of funding for programs, and under-regulation, Kenya has put forward a highly structured and aggressive response to ensure responsible antimicrobial use. Kenya's first National Action Plan to combat AMR, first introduced in 2017, will expire in 2022. At the highest level, Kenya's National Antimicrobial Stewardship Interagency Committee (NASIC) was formed to direct AMR policy from the Ministries of Health and Agriculture, Livestock, and Fisheries.

The County Antimicrobial Stewardship Interagency Committee (CASIC) mirrors NASIC's policy function at the local level, and works to build a coordinated approach across all levels of government. Kenya's National Action Plan and AMR Containment Policy stress surveillance expansion, drug innovation, and legislative review to promote strong stewardship. Initiatives include more strenuous clinical examinations, stewardship guidelines, hospital-wide AMS programs, national stewardship awareness programs, and rapid diagnostic tool development. Several studies have been conducted evaluating the current stewardship practices of Kenya's health system. The findings are promising. Although only one hospital has defined stewardship protocols, doctors surveyed possessed a strong understanding of antimicrobial use in their practices. The studies found adequate antimicrobial knowledge, structures, and resources in most Kenyan hospitals, which, combined with national policy, could yield a highly effective stewardship program.

lack of awareness of AMR and other cultural factors. A recent Canadian study revealed that doctors prescribe antibiotics 53% more when they sense that patients expect them. Italy's national insurance covers generic antibiotics, putting immense pressure by patients on GPs to prescribe them.

Some patients use antibiotics prescribed to others, finish courses from previous prescriptions, and buy antibiotics illegally, all of which can contribute to the growth of AMR.[99] Patients who are in circumstances with limited healthcare provisions, poor availability of diagnostic services, poor accessibility, and the inability to pay for treatment are often driven to the above routes to secure some sort of treatment. Additionally, some studies have shown statistical linkages between poor general education, healthcare dissatisfaction, and inappropriate usage, suggesting these factors are prime indicators of patients lilkelihood of misusing antimicrobials.[100] Likewise, the prevalence of informal providers in areas with poor healthcare access leads to untrained and even unlicensed persons inappropriately prescribing or dispensing antimicrobials to patients.

Governments fall short on monitoring and oversight

Many countries have inadequate systems to track, manage, and monitor antibiotic prescriptions. In the US, data on antibiotic sales and use are almost entirely private; even the government must license data from private market research firms. Further, the CDC's monitoring and stewardship tool, the National Healthcare Safety

Network Antibiotic Use and Resistance Module (NHSN AUR Module) only receives data from 27% of acute care hospitals.[101] Siloed data not integrated with the national database hampers efforts to track antibiotics in Japan. Similarly, fragmentation and a lack of coordination has harmed the efficacy of NHS initiatives in the UK. Italy suffers from decentralized standards and data collection, with no consistent sources for data.

While South Korea implemented an AMR stewardship program in 2016, the number of general hospitals receiving a grade 4 or 5 for antibiotic prescriptions in excess has stagnated at 2,200 of 3,200 (68.75%), calling the program's effectiveness into question.[102] The national Health Insurance Review and Assessment Service (HIRA) called on the government to strengthen the current stewardship program, citing inadequate personnel and funding. The goal is to calculate and deliver customized information for each medical institution, allowing an active stewardship program to be embedded within each hospital.

In the EU, monitoring issues persist, with the EU CDC finding it difficult to compile comparable data across the region. Most EU countries maintain their own stewardship policies due to differences in products and resistance levels. The European Prescribing Guidelines act only at a high level, while the EU CDC serves as a common surveillance function. In many EU countries, monitoring efforts are weak and fragmented, leading to greater selling and use of counterfeit drugs. Lack of oversight hinders restrictions on antimicrobial prescriptions in France, a major reason why the country's antibiotic usage rates are 50% higher than the European average. In China, despite intensive government action within hospital settings, pharmacies remain largely unregulated.

Hospitals outperform outpatient settings, but stewardship efforts are generally still inadequate in many countries

Many initiatives taken by countries focus on hospital environments. As a result, experts in many countries highlight the success of hospital systems in tracking AMR and promoting responsible use. For example, while outpatient antimicrobials in China only declined about 7% between 2010 and 2016, inpatient antimicrobials declined almost 25%. In the US, Medicare began requiring hospitals to implement antibiotic stewardship programs in 2019, but experts report that most hospitals lack the resources needed for full implementation. The COVID-19 pandemic exacerbated these challenges, as stewardship staff were often redirected to pandemic response duties.

Some countries are taking additional action to curb overprescription

Many countries have introduced policies to address rampant overuse and misuse of antimicrobials. South Korea has implemented a national policy that prohibits doctors from dispensing drugs, which a study found can reduce inappropriate antibiotic prescribing.[103] In India, the Integrated Management of Neonatal and Childhood Illness (IMNCI) features guidelines for appropriate use in diarrheal diseases and respiratory infections, though not for other diseases of public health importance like enteric fever. In 2010, Brazil implemented policies to enforce existing laws restricting consumption of antibiotics to patients presenting a prescription. The Chinese government has introduced limits on antibiotic

usage in the past five years to those with severe symptoms and who have the requisite bloodwork.

Calls to Action

Governments should provide better access to diagnostic tools for general practitioners

Improving access to diagnostic tools can help healthcare providers make more informed decisions when prescribing antibiotics. These tools not only enable HCPs to determine when antibiotics are needed, but also which antibiotics can provide the most effective treatment.[104] A German pilot program to enable GPs to make informed prescription decisions demonstrates an effective attempt to ensure decisions are made with stewardship and patient outcomes in mind. Support for patient outcome studies that demonstrate the positive impacts of tests are critical to inform appropriate reimbursement and clinical uptake.

Even in HICs, poorly resourced facilities struggle to implement and support stewardship programs to combat misuse and overuse. In a recent US study on sepsis patient outcomes, a lack of diagnostic tools for resistant pathogens testing led to unnecessary and inappropriate prescription of antibiotics, leading to worse health outcomes.[105] A 2019 CDC report found some areas lack the resources to run diagnostic testing programs to aid stewardship, especially in settings such as nursing homes and long-term care facilities.[106]

Governments should improve enforcement and administration of existing mechanisms

Better regulation and enforcement can reduce the overuse of antibiotics. In South Korea, improvements to the regulation of non-prescribed antimicrobial use seem to have positively affected resistance profiles. And the policy to prohibit doctors from dispensing has had several positives outcomes, including decreased antibiotic prescriptions for viral illnesses, a reduction in the number of different antibiotics prescribed, and lower prescribing overall, both of antibiotics and other drugs. However, in Brazil, policies aimed at preventing antibiotic purchases without a prescription lack strong enforcement and oversight,[107] making this regulation largely ineffective.[108] A 2017 European Commission report revealed that rampant OTC consumption persisted despite policies intended to stop non-prescribed use, leading to a calls for governments to better enforce these measures.[109]

Governments should provide guidance and funding to strengthen stewardship in inpatient settings and to implement stewardship in outpatient settings

As described above, many of the greatest strides in stewardship and prudent usage are being made in the hospital environment. While the successes in hospital settings demonstrate the promise and potential of stewardship efforts, gaps remain and the same level of oversight and commitment to antimicrobial stewardship must be applied to other settings (i.e., clinics, pharmacies, and in the home). Furthermore, it should be noted that many cases of misuse and overuse could be avoided through improved accessibility to these settings, as presently affordability and geography are key barriers in some contexts.

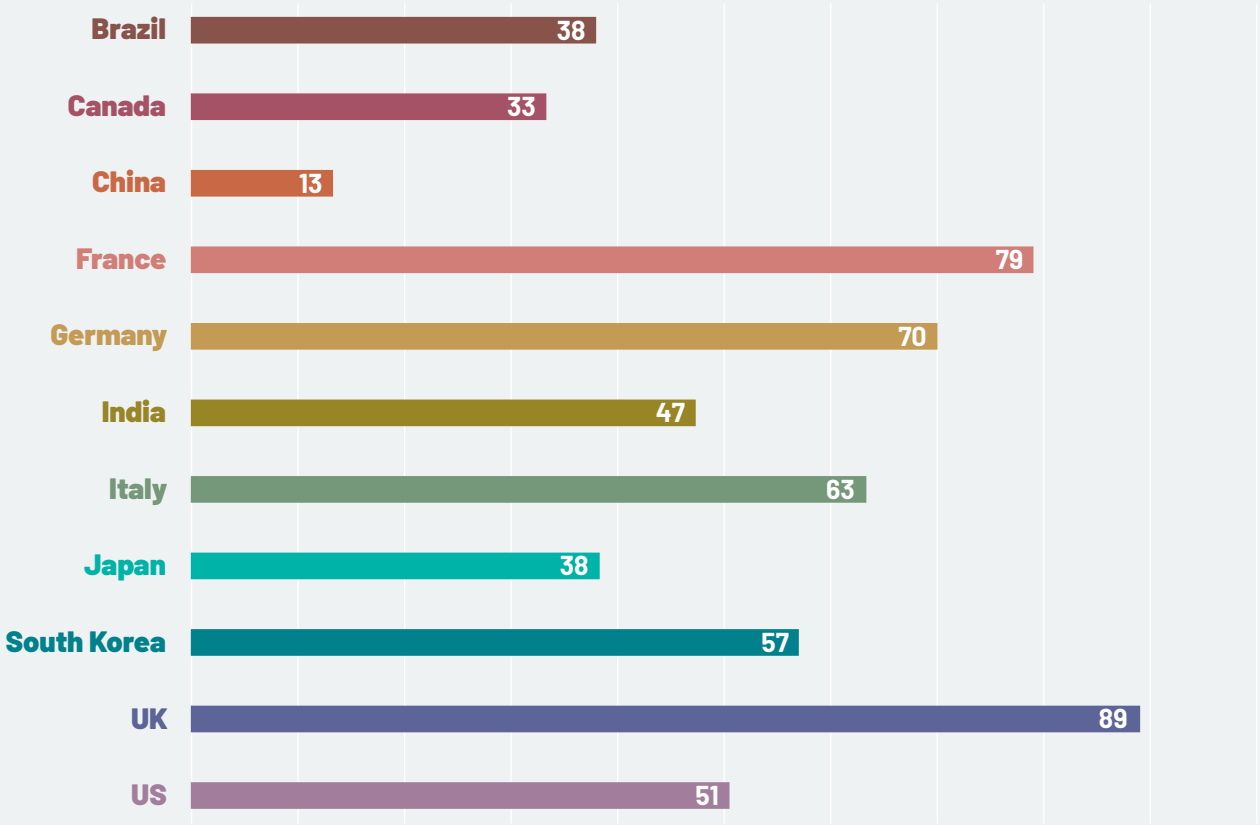
Governments should support the expansion and training of the medical workforce necessary to promote appropriate antibiotic use

Though it is necessary for AMR training and awareness to be bolstered more generally, policymakers must also consider broadening the scope of those in the medical workforce who are required and able to undergo such training, including pharmacists and veterinarians. In many countries there are numerous HCPs with the ability to prescribe, dispense, and recommend antimicrobials, many of which are not required or captured by AMR training held for more traditional or formal medical professionals. Several studies have established that healthcare students and HCPs generally have poorer access to AMR training than would be expected.[110] Therefore, to fulfill goals in many national plans and to improve HCP practices and habits, national and international bodies must promote increased accreditation in continued medical education and license renewals, set curricula for pre-service HCPs, and support libraries for the sharing of research.[111] These steps will help to incentivize training, ensuring all HCPs enter service with AMR knowledge, and disseminate best practices globally so as to create a workforce more prepared and better suited to combat AMR. Governments must also ensure that healthcare facilities have access to and utilize personnel who have been fully educated on AMR and stewardship practices.

AMR & the Environment

Examines how national governments are attempting to manage antimicrobials throughout their life cycle: production, procurement, usage across sectors (including non-human applications), and disposal.

AMR & the Environment Country Comparison



Constraints and Limitations

While almost all areas examined in this report would benefit from more robust data being available, nowhere was this need more evident than in AMR & the Environment. In many cases, meaningful data were simply unavailable for many or all countries. In others, the available data were self-reported, or the environmental data did not relate directly to antimicrobials.

After an extensive review of the available literature and consultation with environmental AMR experts, the data included in this category were reduced to just a few metrics identified as most relevant, important, and informative. The scores and rankings that result provide important insight and are worthy of discussion, but these few metrics can only provide a partial picture. The gaps and limitations – the data that are not here – are equally important to note. These gaps include antimicrobial-specific data on pharmaceutical levels in the environment and research on the concentrations of antimicrobials or antibiotic-resistant bacteria or genes that can be considered safe, data showing the relationship between antimicrobials in the environment and drug-resistant infections, and data demonstrating which environmental sources are the biggest drivers of resistance and therefore deserving of the most attention, among many others.

The network of interactions that need to be researched are endlessly complex. Pharmaceutical manufacturing and hospital wastewater, antibiotic-treated patient and livestock excretion, the consumption of foods containing antimicrobials, and the improper disposal of medicines all result in more antimicrobials in our water, soil, and environment more generally. With more antimicrobials in the environment, there are greater chances for the development of resistant genes and microorganisms that may directly impact human health.

This chapter highlights the need for further evidence gathering by governments and calls out several areas as particular priorities. Though all countries in this report have acknowledged that environmental factors are one driver of AMR, there has not been a commensurate investment to gather the data necessary to better understand the impact on human health of antimicrobials in the environment. This relationship is comprised of a much overlooked, complex, and intertwined series of interactions and flows, which – if better understood – could help inform effective policymaking to slow and reduce the threat of AMR.

Key Findings

The principles of the One Health approach continue to gain traction worldwide and are being acknowledged in environmental policies and private sector actions

Most governments have referenced the One Health approach in their NAP and AMR initiatives, yet many need to go beyond simply labeling efforts as such and ensure that these efforts are well integrated and implemented with actionable objectives and dedicated funding. Some NAPs, such as the Canadian national strategy, have outlined significant efforts to regulate and improve oversight of veterinary, livestock, and aquaculture antimicrobial use, though the implementations

of these environmental frameworks are varied. Several countries have made strong commitments to reducing antibiotic use in agriculture and animals. After the Chinese government banned several agricultural growth promoters due to AMR, antimicrobial use in Chinese agriculture fell 57% between 2014 and 2018. Though the progress in China is promising, widespread use of antimicrobials continues throughout the agricultural sector.

In countries where WASH remains a significant challenge, it is difficult to envisage effectively addressing AMR fully through regulatory policy. While all countries do need to target antimicrobial pollutants from homes and hospitals, agriculture, and where antimicrobial manufacturing takes place, improving wastewater management and sanitation must be a top priority as it is foundational to reducing the risk of spread of infectious disease, including resistant infections.

More AMR environmental research is required, and non-human uses remain critical

Though some countries have placed bans on antibiotic use in livestock, animal, and agricultural use, these contexts remain responsible for the majority of antimicrobials in the environment. Further, even where bans do exist, many countries lack the appropriate accountability mechanisms and evaluation measures to effectively enforce non-human usage and track progress. Additionally, despite the size of the impact, research on the relationship between antimicrobials in the environment and human health remains underprioritized.

Policies and implementation are limited, but some stakeholders are taking action

Most HICs have strong systems in place to monitor antimicrobial manufacturing for quality, but they lack the guidelines to better control disposal of antimicrobial containing wastes. Though all countries in the Index mention the environment in their NAPs, only the UK specifically outlines an approach to promote responsible manufacturing domestically and abroad.[112]

Though other environmental areas (e.g., aquaculture and hospital discharge limits) have not been addressed by policymakers, the EU Pharmaceutical Strategy 2020 has made it a priority to assess how better manufacturing policies could limit antimicrobial emissions in the environment, while committing to internationally raising awareness on AMR environmental concerns, sharing best practices, and working to develop and establish guidelines for manufacturing.[113] The European Commission has also been pursuing measures to reduce the unsafe disposal of pharmaceuticals, including antimicrobials.[114] Yet, these initiatives are only a first step. Others have called for a greater investment in incentives and disincentives to help reduce AMR-related emissions from manufacturers, and generally more open discussions between industry and governments to develop further guidelines and regulations.

The AMR Industry Alliance has developed and published a common antibiotic manufacturing framework and a table of antibiotic predicted no-effect concentrations,[115] which member companies are using to minimize and manage antibiotic emissions from manufacturing sites across their global supply chains.[116] Additionally, the WHO has released documents outlining how environmental requirements within existing Good Manufacturing Practices (GMPs), may be

used to help combat AMR and are currently conducting a pilot evaluation. The results of the WHO pilot are expected at some point during 2021 and will help inform further developments of AMR-relevant GMPs. In the meantime, the WHO is calling upon member governments to establish their own national guidelines and implement stringent inspection measures.[117] Collaborative engagement between stakeholders, including industries both up- and downstream that play an important role in AMR, can help lead to more robust solutions.

Calls to Action

Governments should better integrate environmental controls in their National Actions Plans

Environmental controls for antimicrobials in aquaculture, agriculture, and livestock; manufacturing, hospital, and general wastewater; and medicine disposal are lacking in NAPs. These measures need to be appropriately tailored to national contexts and implemented. A robust institutional infrastructure is then needed to ensure these environmental controls are monitored and enforceable.

On manufacturing, the recently released targets on predicted no-effect concentrations (PNECs) for antimicrobials by the AMR Industry Alliance provide strong, science-driven, and risk-sensitive parameters that should be adopted more broadly by stakeholders to align with effective environmental protections from AMR.[118] In connection with the pending results from the WHO GMP pilot, consideration should be given to supporting its development to enable further roll out including to other countries. The organizational capacity and knowledge to effectively communicate and enforce AMR-relevant environmental requirements through a quality management system should be better understood before widespread adoption, as should any possible barrier to the inspectorate fulfilling quality obligations. Collaboration between all stakeholders will be essential to achieving effective solutions and maintaining a sustainable antimicrobial ecosystem.

Governments should continue to integrate the One Health approach and give equal weight to environmental components

To effectively reduce antimicrobials in the environment, governments should fully integrate the One Health approach into policymaking and country-level environmental standards, while broadly bolstering key areas of environmental management directly connected to the AMR threat. One Health can guide countries to appropriately advance or support development of controls (including necessary standards, regulation, or guidance) in areas such as livestock and agriculture, aquaculture, and pharmaceuticals in the environment (PIE).

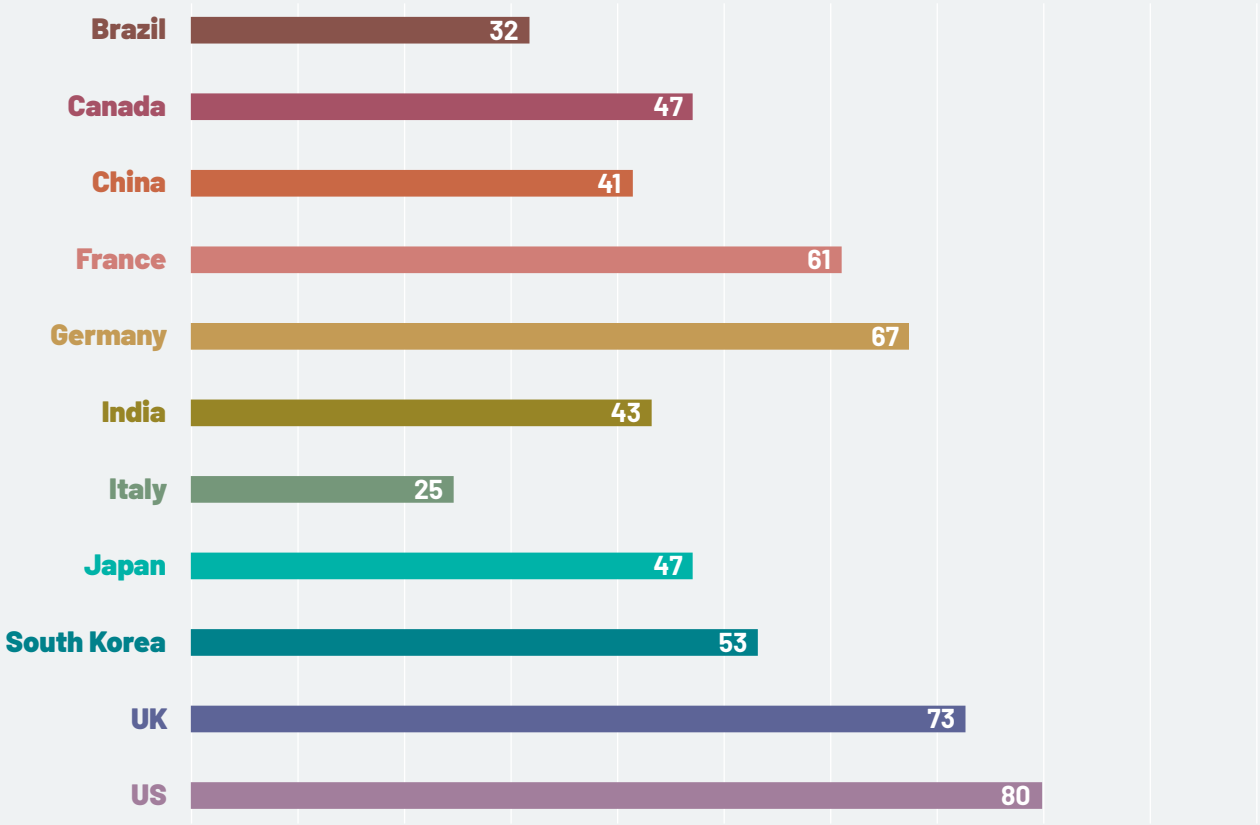
Governments should support enhanced data collection to improve global understanding of the impact of antimicrobials in the environment

In order to develop and enact more effective policies to diminish the environmental contribution to AMR, governments must pursue and prioritize rigorous evidence-generating programs. Though there have been efforts to reduce the use of antimicrobials for growth promotion and isolated all out bans on their use in animals, there needs to be a greater investment in studying how AMR grows in environmental contexts, such as in livestock and agriculture, to support more evidence-driven policymaking that will curb the spread of resistant infections, preserve antimicrobial effectiveness, and ultimately protect human health.

Collaborative Engagement

Captures how effectively national governments are facilitating collaborative engagement to address AMR.

Collaborative Engagement Country Comparison



Key Findings

Country-level NGOs, advocacy groups, and patient organizations play a critical role in advancing AMR initiatives in four core areas: innovation, research, surveillance, and monitoring and awareness

Innovation

Research identified numerous projects to further the development of antimicrobials and harmonize global research efforts. In 2017, the Japanese Pharmaceutical Manufacturers Association (JPMA) called on the Ministry of Health, Labour and Welfare to fund a public-private consortium aimed at advancing antimicrobial development. In 2019, the JPMA specifically called for introducing pull-type incentives.[119] Many pharmaceutical firms have signed the 2016 Davos Declaration and expressed the need for global harmonization of research and increased R&D incentives.[120] Many firms also have also joined the AMR Action Fund, a consortium of companies that seeks to invest in smaller biotech firms developing antimicrobials,[121] with a goal of bringing two to four new antibiotics to patients by 2030.

Research

Countries examined for this report are engaged in a variety of research programs. France's Inserm (along with ANR, the French National Research Agency) is a member of JPIAMR and coordinated the AMR Programme Prioritaire de Recherche (PPR) in 2019, which guides collaboration between research partners to ensure a One Health approach.[122] In Brazil, the National Research Institute for Antimicrobial Resistance (INPRA) introduced specific funding to encourage collaborative research, training efforts and capacity building to manage antimicrobial resistance.[123] While in the UK the Global AMR Innovation Fund (GAMRIF) supports research worldwide to reduce the AMR threat in LMICs.[124]

Nevertheless, there is a stark disparity between the number of AMR research organizations across countries. Germany, the UK, the US, and Japan all have over 150 of these organizations, while the majority of remaining countries have fewer than 50.

Surveillance and Monitoring

Like R&D and environmental protections, surveillance requires a global network to ensure that all stakeholders can effectively track, monitor, and predict antimicrobial resistance patterns. Ergo, it is once more imperative that collaboration remains a central tenet for erecting, funding, improving, and submitting data to monitoring systems. Some actors have assumed a leading global role, such as the UK's Fleming Fund, who have worked to finance the surveillance capacity in LMICs.[125]

Awareness Campaigns

Awareness campaigns by NGOs, advocacy groups, and patient organizations play an important role in advancing the AMR conversation and prompting policymaker action. In the US, the *Stand up to Superbugs* initiative from the Pew Charitable Trust uses personal narratives to highlight the importance of AMR. Organizations like Research!America and the Partnership for Fighting Infectious Disease (PFID) are furthering the conversation by coordinating campaigns to increase awareness about the causes and effects of AMR. Comparable German organizations, including the German Society for Infectious Diseases and the German Society for Hygiene

and Microbiology, have also brought national attention to AMR.

While the Infectious Diseases Society of America published *The Faces of AMR*, a series of stories about patients impacted by AMR, the inclusion of patients in awareness efforts is in its nascent stages. Engagement needs to be expanded to include other patient groups impacted by drug resistant infections, such as those in oncology, hematology, immunology, cardiology, pulmonology, and others.

The Wellcome Trust (UK) has demonstrated an enormous commitment to AMR awareness, while also dedicating resources to expanding the antimicrobial pipeline.[126] Wellcome has worked with key not-for-profit and

Russia

Russia has formed strong partnerships to develop multi-national solutions to the AMR crisis.

The issue of antimicrobial resistance has become one of the foremost concerns in Russian healthcare policy over the past three decades. According to a 2018 report, the country has seen substantial increases in gram-negative bacteria across healthcare-associated infections, with carbapenem-resistant bacteria forming the leading cause of Russia's nosocomial infections. Furthermore, surveillance studies of Russian hospitals conducted by the IAC and IACMAC found multiple-drug resistance in over 50% of nosocomial P.aeruginosa and over 60% of nosocomial A. baumanii and enterobacteriales.

Russia's lack of regulations on OTC prescription use, scarce laboratory services, and weak prescription monitoring programs are key barriers to proper antimicrobial stewardship. To address the growing threat, Russia launched a series of partnerships to strengthen international collaboration and further a multi-pronged approach to AMR innovation. In 1997, The Interregional Association for Clinical Microbiology and Antimicrobial Chemotherapy (IACMAC) established The Alliance for Prudent Use of Antibiotics (APUA), whose Russian chapter has expanded to 1,300 members across all 48 regions of Russia.

The chapter has developed significant ties across Europe (European Society for Clinical Microbiology and Infectious Diseases, British Society for Antimicrobial Chemotherapy), the United States (American Society for Microbiology), and Asia (Western Pacific Society of Chemotherapy). In 2017, the British AMR Centre (AMRC) reached a formal agreement with Russia's Skolkovo Foundation to identify joint-funding opportunities to advance mutual research. AMRC will offer research assistance and funding opportunities through their partner CARB-X, furthering Russia's integration within the international research community. Russia has developed a similar joint effort with the Finnish Institute for Health and Welfare, creating the Nordic-Russia Antimicrobial Cooperation project. The cooperative program seeks to bolster awareness and training for antimicrobial use in Russia among both healthcare professionals and the public.

private partners to develop and coordinate campaigns to reduce misuse and overuse, while also investing in countries to increase AMR knowledge and spur national action by policymakers. Additionally, through the Surveillance Partnership to Improve Data for Action on Antimicrobial Resistance (SPIDAAR), the Trust has collaborated with the national governments of Ghana, Kenya, Malawi, and Uganda and industry to initiate surveillance programs these countries.[127] It is difficult to overstate the contributions made by the Wellcome Trust to slow resistance profiles through public action and to encourage policymakers to pursue real change.

Calls to Action

Governments should provide more direct support for research institutions and working groups, including establishing and growing clinical trial networks

To fully leverage research and collaborative capabilities, governments must commit greater direct support to these efforts. While there are many examples of governments interacting with research institutions and working groups, these entities need greater funding support to fully embed them within national and international AMR strategies.

Governments should partner with NGOs, advocacy groups, and patient organizations on pilot programs

Contributions to the fight against AMR should not be solely limited to governments. NGOs, advocacy groups, and patient organizations can provide knowledge and expertise that cannot be found within government, especially through the creation and implementation of innovative pilot programs.

Countries should invest in training the next generation of AMR researchers and clinicians to support clinical trials

In order to ensure that there are continued personnel resources to commit to further broadening the AMR developmental pipeline, governments should continue to invest in training programs and clinical trial infrastructure for the future. As resistance profiles continue to grow and the antimicrobial pipeline remains narrow, decision makers must set-up following generations for their role in combating AMR through innovation. The UN Interagency Coordination Group (IACG) on AMR has expressed the need for inquiry into how best organizations can ensure that there is a strong pipeline of researchers to thereby protect and grow R&D for the field.[128]

Many have called for research prioritization mechanisms to ensure that work on AMR is continually funded at an appropriate level and researchers can properly access said funding.[129] Calls have also been made to ensure that research is pursued in an open fashion, allowing more access for those in the field and for a more pooled and compounding knowledge base.[130] Along these lines, JPIAMR has attracted researchers to the field through greater transnational collaboration and the leveraging of country-level funding, with additional investments in projects, mobility, and training for researchers.[131] Through specifically sponsored government research training programs nations can ensure that they will have the requisite workforce to develop the new and novel antimicrobials needed to preserve the antimicrobial pipeline and save lives.

Conclusion

The AMR crisis is here, and national governments must step up now to address existing threats

The world has reached a key inflection point. There is widespread recognition that countries must do more to aggressively combat AMR. But few governments have translated their commitments and statements of intention into real investment and concrete action. Despite the growing threat, AMR remains a low priority for policymakers. This must change.

The COVID-19 pandemic has demonstrated the importance of responding proactively and immediately to a public health crisis

COVID-19 has demonstrated the capacity for infectious disease to wreak havoc in today's world and highlighted gaps throughout our healthcare systems. The enormous supply chain challenges that hampered the global pandemic response have rightly raised concerns regarding drug development, access, and the breadth of the antimicrobial pipeline. Moving forward, efforts to bring the COVID-19 pandemic under control must be closely linked to AMR.

If countries fail to take needed action, the AMR crisis will become a full-blown humanitarian catastrophe, threatening the miracle of human longevity

Continued inaction on AMR collectively borrows from the future, foreclosing our children's access to lifesaving drugs, while threatening the promise of our own longevity. Without action in each of the areas examined in this report, AMR may grow too large for policymakers, health systems, or the private sector to combat effectively. The AMR crisis poses a dire threat to tens of millions of lives, the efficacy of modern medicine, and global economic prosperity. The world is dependent on national policymakers to steer us away from this imminent catastrophe.

With concerted action, progress can made

Although the multi-faceted nature of AMR makes it a challenging problem for stakeholders to manage, it is clear that each of the areas examined in this report can be effectively addressed through leadership, political will, and research-informed policy actions. From improved hygiene standards in rural hospitals to innovative initiatives to broaden the antimicrobial pipeline, all efforts in the fight against AMR contribute towards a solution that benefits us all. The recent success in rapidly developing COVID-19 vaccines and the ever-increasing pace of distribution demonstrates that cross-sector stakeholders have the willingness and capacity to come together and tackle seemingly insurmountable public heath challenges. Building on this success and aligned to the momentum of the UN/WHO Decade of Healthy Ageing, countries, advocates, and the international community have a clear mandate and an opportunity: We cannot wait. The time for AMR action is now.

Appendix A

Country Profiles

BRAZIL

Brazilian commitments to national strategy and innovation for AMR are severely lacking. Although efforts to improve awareness, access, and usage are underway, the effects of these initiatives have not yet been realized.

National Strategy

Enacted in 2018, Brazil's NAP (PAN-BR) is set to run through 2022. The plan is detailed and has mechanisms in place for self-evaluations and modifications as needed, however, experts have also acknowledged that the plan's adoption has been constrained by the government's failure to dedicate funding for implementation.[132] Government financed research on AMR is equally poor.[133]

Awareness & Prevention

In 2009, Brazil established the Technical Chamber of Antimicrobial Resistance in Health Services (CATREM) to support the efforts of both ANVISA (the National Health Surveillance Agency) and the Technical Committee of Rational Antimicrobial Use and Antimicrobial Resistance (CURAREM).[134] CATREM is tasked with creating regulations related to AMR monitoring, controlling, and prevention.[135] However, government efforts to raise AMR awareness through HCP-targeted and usage campaigns are almost entirely absent. Further, healthcare infrastructure to prevent hospital-acquired infections and the spread of AMR is lacking, as demonstrated by high rates of sanitation-related deaths[136] and hospital-acquired MRSA infections.[137]

Innovation

Poor intellectual property policies[138] and lengthy patent processes[139] make Brazil an unfavorable environment for innovation, resulting in few pharmaceutical patents. Currently, there are no antimicrobials in development,[140] and no new antibiotics have been developed since 1999.[141] Brazil has extraordinarily few AMR research funders, organizations, and projects.[142] Further, there have been no efforts to implement pull incentives or develop new valuation models to encourage the development of new antimicrobials.

Access

While Brazil provides good reimbursement for drugs, including antimicrobials,[143] general healthcare system access and quality is poor.[144] The availability of antimicrobials also remains worrisome, with only one of the three novel antimicrobials studied (Lefamulin, Meropenem + Vaborbactam, and Ceftazidime + Avibactam) approved and none of the 15 other recently developed antibiotics launched.

COUNTRY RANK
11

Overall Score
34

National Strategy
17

Awareness & Prevention
48

Innovation
14

Access
44

Appropriate & Responsible Use
49

AMR & the Environment
38

Collaborative Engagement
32

Appropriate & Responsible Use

Brazil has not banned the unprescribed use of medically important antibiotics,[145] and antibiotic usage rates have increased by over 160% in recent decades.[146] The pandemic has also substantially impacted the Brazilian AMR landscape.[147] In recent months, antibiotic usage overall has skyrocketed, leading many experts to fear increased antimicrobial resistance, and Brazil lacks antimicrobial stewardship interventions to address this global trend.[148]

AMR & the Environment

Though there are references to the environment in the NAP, there are no direct references to the implications of AMR emissions and pharmaceutical manufacturing on the environment.[149] In fact, Brazilian national legislation does not regulate the concentration of pharmaceuticals in drinking water or the environment more broadly.[150] Indicative of Brazil's lackluster commitment to environmental concerns, there are no bans on using antibiotics for growth promotion in livestock.[151]

Collaborative Engagement

The Alliance for the Prudent Use of Antibiotics (APUA-Brazil), established in 2001 by a group of healthcare providers, is the main external organization working on AMR initiatives in the country. APUA-Brazil has sought to promote the rational use of antibiotics through research and educational activities for both human and veterinary medicine.[152] Brazil is also engaged at the international level. The BR-GLASS program is hoping to expand their efforts to about 100 hospitals across all five regions of the country over the next five years.[153] Brazil also participates in the South American Working Together to Fight AMR project, which has evaluated implementation efforts for AMR NAPs, providing a National Landscape Analysis.[154] The Analysis will provide a baseline for AMR governance and track progress on a regional level.

CANADA

Though Canada has demonstrated strong implementation of training, awareness, and healthcare infection prevention programs, investments in innovation and commitments to national strategy are lacking.

National Strategy

Canada released its National Action Plan in 2015, with full implementation promised by 2020. However, as of mid-2021, many of the programs and initiatives outlined in the plan have yet to be fully implemented. Further, the pan-Canadian Action Plan on Antimicrobial Resistance, which aims to better integrate and coordinate efforts through a One Health approach,[155] was originally due for release in the autumn of 2019, but remains delayed as of mid-2021.[156] In 2019, after the Canadian Minister of Health announced AMR as a key priority, the government began working to coalesce various AMR stakeholders to work collectively to address challenges. In this vein, Project: AMR Network, an initiative spearheaded by the Public Health Agency of Canada, has worked to engage key partners from across stakeholder groups to "unsilo" current efforts against AMR.[157]

Awareness & Prevention

There are targeted awareness campaigns and AMR training for HCPs in Canada, though training could be more comprehensive. Further, while the vaccine program in Canada is moderately strong,[158] it has not been fully leveraged in the fight against AMR. Though Canada already has a robust GLASS-compatible program,[159] the CODEX Intergovernmental Taskforce is seeking to establish more rigid surveillance guidelines through its Canadian Antibacterial Resistance Surveillance System (CARSS) program.[160]

Innovation

Though there are few AMR research organizations and projects,[161] the Canadian Antimicrobial Innovation Coalition has facilitated a partnership between Infection Prevention and Control Canada and government representatives to help identify opportunities for faster development, commercialization, and adoption of AMR-related innovations.[162] Additionally, the Canadian Institutes of Health Research (CIHR) has demonstrated a strong commitment to supporting international research efforts, most notably leading the development of JPIAMR's Virtual Research Institution.[163] CIHR also has developed a very accessible online platform to help provide prospective grantees with detailed information on all Canadian AMR funding opportunities.[164] While the federal government has done very little in recent years to meaningfully stimulate and jump-start the antimicrobial development pipeline, there seems to be renewed interest in discussing possible incentives models. This lack of progress comes against the backdrop of a report released by the Council of Canadian Academies (CCA), which found that in 2018 over 25% of bacterial infections were resistant to first-line antibiotics.[165]

Access

General healthcare accessibility and quality are strong in Canada, and few Canadians are pushed to spend beyond 10% of their income on healthcare.[166] Though there is good reimbursement for antibiotics,[167] based on three novel drugs (Lefamulin, Meropenem + Vaborbactam, and Ceftazidime + Avibactam) and 15 other new antibiotics, Canada's new antimicrobial availability is mixed.

Appropriate & Responsible Use

Though it is clear that COVID-19 has affected the country's stewardship efforts, the specific impacts have yet to be quantified. Looking ahead, some AMR researchers have suggested that the COVID-19 pandemic creates unique opportunities for the federal government to take action against AMR while promoting the One Health approach.[168] On a provincial level, British Columbia's Centre for Disease Control has developed a community stewardship program to address unnecessary usage in the community setting, where 90% of usage occurs.[169] This multipronged effort features community outreach through the Antibiotic Wise campaign, public education through Do Bugs Need Drugs, professional education through dissemination of British Columbia's guidelines on usage, and monitoring in partnership with the Ministry of Health and the private sector.[170]

AMR & the Environment

While Canada's AMR strategy does include the environment,[171] most environmental protections derive from the 1999 Canadian Environmental Protection Act (CEPA), which have not been updated to specifically address AMR.[172] Recent legislation banned non-prescription uses of medically important antibiotics in animals,[173] but use of antibiotics for growth promotion in livestock continues.[174]

Collaborative Engagement

The AMR One Health Consortium, a collaborative multisectoral initiative based in Alberta, supports research programs in three areas: Treatment Optimization, Surveillance, and the Prevention of Transmission. The organization hopes that by leveraging the cross-disciplinary expertise of its researchers, useful programs can be scaled nationwide.[175] NGO-driven research centers (e.g., the National Collaborating Centre for Infectious Disease[176]) and country-level product-development partnerships (e.g., Find Diagnosis for All [177]) have also fostered moderate levels of collaboration.

COUNTRY RANK
6

Overall Score
50

National Strategy
37

Awareness & Prevention
76

Innovation
23

Access
66

Appropriate & Responsible Use
64

AMR & the Environment
33

Collaborative Engagement
47

CHINA

While there have been isolated improvements, Chinese research investment, vaccine utilization, and surveillance efforts are insufficient, while usage rates and the environment for innovation remain concerns.

National Strategy

In response to the WHO Global Action Plan on AMR, an inter-ministerial team developed the NAP (2016-2020) ahead of the G20 Summit. However, the Chinese NAP was assessed as one of the least aligned with the WHO's GAP.[178] In 2020, the Notice on Continuous Doing Well in the Management of Clinical Use of Antimicrobial Drugs was released as the NAP ended, providing greater training, antimicrobial usage restrictions, and management processes for pharmacists.[179]

Awareness & Prevention

AMR poses considerable challenges in China. A 2021 study estimated the total societal economic cost incurred by inpatients due to AMR alone to be more than $77 billion - or 0.37% of China's 2017 GDP.[180] Yet, per capita expenditures on vaccines, which could limit AMR, remain low, at less than $0.40.[181] Despite a 2019 study indicating generally fair levels of AMR awareness among patients, much more work is needed to educate key segments, namely older adults and those living in rural areas.[182] Further, a recent review of Chinese AMR surveillance efforts revealed that most data is collected in the southeastern region and not generalizable at a national level.[183] In response, the researchers stressed the need for greater inclusion of hospitals (primary- and secondary-care settings) and further investments into surveillance infrastructure.[184]

Innovation

China's low number of AMR research funders, organizations, and projects,[185] is matched with a very poor intellectual property[186] and patent process environment.[187] Additionally, there have been no public discussions on the implementation of incentives or new valuation models to encourage antimicrobial development.

Access

Low GP to patient ratios[188] and high out-of-pocket healthcare costs,[189] coupled with an acute rural-urban divide make access to healthcare extremely variable in China. Though reimbursement is available for some antimicrobials,[190] there are extremely long delays for drugs to gain reimbursement status, highlighting the need for regulatory reform.[191] These glacial approval and reimbursement processes could also explain why all 15 of the new antibiotics reviewed are unavailable in China.

COUNTRY RANK
9

Overall Score
37

National Strategy
37

Awareness & Prevention
54

Innovation
17

Access
40

Appropriate & Responsible Use
55

AMR & the Environment
13

Collaborative Engagement
41

Appropriate & Responsible Use

In line with the goals of the Healthy China 2030 directive, the government aims to further improve the scientific use of antibiotics and better manage overuse. These efforts have had uneven success. In recent years, the government has enacted strict limitations and regulations to curb inappropriate use. There are still high levels of last-line antibiotic usage. In 2012, the Administrative Regulations on the Clinical Application of Antimicrobial Agents categorized antimicrobials into three groups: nonrestricted, restricted, and controlled, with intensive administrative hurdles and penalties regarding prescribing applied to controlled drugs especially.[192] Stewardship programs can now track which doctors are appropriately diagnosing and prescribing antibiotics, though these measures apply almost exclusively to public hospitals, and patients can also access antibiotics through pharmacies. In general, doctors in pharmacies prescribe with much less oversight than their counterparts in hospital settings. Even enforcement in hospital settings, is imbalanced, with tier 1 and 2 city hospitals enforcing more robust regulations and controls than their rural counterparts.

AMR & the Environment

Though the Chinese NAP has references to the environment and AMR emissions,[193] antimicrobial consumption in livestock is extraordinarily high[194] and there are still no bans on usage for growth production.[195] Further, China has high concentrations of antibiotic-resistant genes across environmental settings: in water, soil, city smog, animal waste, sewage plant effluents, and clinical settings.[196] The government has faced pressure to introduce environmental policy solutions to address AMR, but there is no evidence that any action has been taken.[197]

Collaborative Engagement

Programs from the R&D-based Pharmaceutical Association Committee[198] and PPD in Greater China[199] respectively represent NGO-led and product-development partnership efforts. There is also Chinese support for public-private partnerships.[200] However, China's unwillingness to participate in the WHO's GLASS program represents a significant failure in international collaboration.[201]

FRANCE

France does well in many areas but is stymied by poor government research investment and a lack of models and incentives to encourage antimicrobial development. The overuse of antibiotics by humans is high but improving.

National Strategy

The government's record on combating AMR is mixed. While AMR governance in France is more organized than in most countries, with a top-down structure that ensures better alignment between national and regional initiatives, several areas need improvement. French decisionmakers have struggled to draft and implement clear national plans. Between 2001 and 2016, France had three different NAPs. The most current NAP, the Interministerial Roadmap for Controlling Antimicrobial Resistance, has also recently released the 2020 update on the implementation of several new efforts to combat AMR (e.g., the Innobio2 investment fund, which could potentially help fund antimicrobial development).[202]

Awareness & Prevention

France has largely been at the forefront of awareness efforts, developing and providing access to educational tools for students (eBug) and materials (One Health, One Planet) for the general public and professionals to better understand AMR and France's One Health approach.[203] Similarly, France's vaccination programs are well funded[204] and the country manages a strong database to aid in AMR prevention.[205] The GLASS-compatible, national surveillance program has also been well integrated into NAPs[206] and is considered robust and sophisticated.

Innovation

In 2015, then Minister of Health Marisol Touraine established the Task Force for Antibiotic Preservation to combat rising rates of antibiotic consumption nationwide. This task force recommended the creation of an inter-ministerial committee to promote the development of new antimicrobials and diagnostic tools by streamlining the regulation processes and lowering R&D costs.[207] The task force's recommendations also led to the establishment of a five-year national research program, which was first implemented in 2016.[208] Despite favorable intellectual property legislation[209] and reference drug program policies, there have only been high-level discussions on changing how antimicrobials are valued to encourage development.[210] Likewise, there have not been discussions to implement pull incentives to encourage the development of new antimicrobials.

Access

The underlying healthcare infrastructure in France is both very accessible and of the highest quality,[211] with very low general out-of-pocket costs.[212] Reimbursement policies for antimicrobials are also good.[213] However, looking at two of the most recently developed novel antimicrobials (Meropenem + Vaborbactam and Ceftazidime + Avibactam) suggests large lags between market

approval and market launch and between market launch and adoption on government reimbursement lists. These lags may suggest the need for further regulatory streamlining and reforms to improve timely access to new antimicrobials. Additionally, the country's supply chain remains fragile, as has been demonstrated by COVID-19, leading to the government to call for manufacturers to domestically produce APIs.[214]

Appropriate & Responsible Use

France has national "Pay for Performance" incentives that reward general practitioners who reduce antibiotic prescriptions,[215] and antibiotic usage has decreased in recent years, a commendable achievement compared to peers. However, despite improvements, usage rates remain about 30% higher than the mean in Europe.[216] Experts noted that French patients are more likely to pressure GPs to prescribe than in some comparable European nations, perhaps suggesting the need for greater interventions and efforts to change patient expectations. Further, despite national requirements, a 2019 study revealed that stewardship programs were not fully implemented across the country due to a lack of institutional support and investment.[217]

AMR & the Environment

Ecoantibio 2, the animal health plan for AMR, is set to run until 2021, and has sought to fully align itself with WHO, World Organization for Animal Health (OIE), and the UN Food and Agriculture Organization (FAO) recommendations.[218] Additionally, RESAPATH, a surveillance network for animal health, has also been integrated within the One Health-modeled NAP.[219] Further, the third national plan on environmental health (2015-2019) has called for increased monitoring and data sharing regarding antibiotics in the water supply,[220] though the extent to which this has been acted on is unclear.

Collaborative Engagement

Institut Pasteur, a key third party organization, has specific AMR initiatives to improve modeling of the spread of resistant antibacterial strains, identify new therapies and drugs to treat AMR infections, and analyze the molecular mechanisms of microbial development.[221] Institut Pasteur also collaborates with partner institutions and Institut sites worldwide, engaging 40 multidisciplinary teams from their network in ongoing AMR research efforts. France is also generally well-engaged internationally, with commitments to several global collaborative projects and an expressed desire to lead Europe in combatting AMR.

COUNTRY RANK
4

Overall Score
61

National Strategy
48

Awareness & Prevention
65

Innovation
36

Access
58

Appropriate & Responsible Use
81

AMR & the Environment
79

Collaborative Engagement
61

GERMANY

German national strategy, surveillance, and international collaborative initiatives are robust, though there remains more work to be done to encourage antimicrobial development.

National Strategy

The German government has taken a more active role in efforts to combat AMR in recent years. As part of the last NAP (DART), which ran from 2015 to 2020, the government was able to leverage a strong healthcare system to better surveil, monitor, and track AMR.[222]

Awareness & Prevention

The Protection Against Infection Act (IfSG) established a national-level surveillance and monitoring program, with support from the Robert Koch Institute.[223] This GLASS-compatible program has several robust features and is more sophisticated than many other systems. Certain states, such as Lower Saxony and Bavaria, have additional sub-national surveillance systems in place.[224] Vaccination is also acknowledged in the NAP as an important AMR-prevention tool, and German per capita vaccine spending is already among the highest in Europe.[225] Despite a relatively low rate of healthcare-associated infections[226] and low number of AMR-related deaths, high-profile news coverage on AMR, alongside campaigns focused on prescription reduction, have raised overall public awareness of the issue. Likewise, a recent study underscored the high levels of GP knowledge on and awareness on AMR issues.[227]

Innovation

Though Germany has not proposed or implemented any dedicated pull incentives, there are a number of programs available to antimicrobial developers, including tax incentives (up to 25% of cost up to €500,000), country-level risk sharing programs (25% to 75% of cost), and clinical trial cost-sharing programs run by DZIF. Equally, German legislation has taken a step in the right direction, adding antimicrobial resistance as an evaluation factor for the clinical benefit of new drugs and working to streamline market-entry requirements to ensure more timely access.[228] However, this valuation model needs further strengthening to truly encourage antimicrobial development.

Access

Germany boasts a high quality and accessible healthcare system,[229] with good reimbursement policies for antimicrobials.[230] The legislation discussed above has also helped improve patient access by making reimbursement list additions for new drugs timelier and using better-defined clinical benefits to ensure the reimbursement of necessary antimicrobials.[231]

COUNTRY RANK

3

Appropriate & Responsible Use

Family doctors also understand the threat well, and federal programs are currently working to educate HCPs in diagnostic practices for prescribing antibiotics. In 2011, Germany passed legislation to adjust the processes for the detection and reporting of high-risk bacterial infections in hospital and some outpatient settings, introducing certain patient isolation polices and more stringent monitoring of particular antimicrobials.[232]

AMR & the Environment

German efforts to monitor pharmaceuticals in the environment (PIE) are centered around commitments to the European Water Directive, with additional national and state-level monitoring programs to augment these commitments.[233] Experts noted that German PIE surveillance is some of the strongest globally. Germany also has food-producing animal and veterinary surveillance systems in place, GERM-VET and ZOMO, which provide annual reports and analysis on trends within these areas.[234] The Federal Office for Consumer Protection and Food Safety has also established the GERMAP working group, which has regularly sought to highlight the risk of current and developing AMR in animals.[235]

Collaborative Engagement

German officials have also helped elevate the issue of AMR on the global stage, with President Merkel delivering a speech on AMR to G7 and G20 member countries at the 2018 World Health Summit and Grand Challenges Meeting in Berlin.[236] During the German G7 presidency (2014 to 2015), the government also helped secure firmer political commitments to finance AMR initiatives.[237] As part of the Berlin Declaration on Antimicrobial Resistance, a pledge made by all G7 Health Ministers to investigate mechanisms to encourage and support the development of new drugs and therapies,[238] Germany itself committed to spending €500 million on AMR over ten years. Part of these commitments helped launch the Global AMR R&D Hub, a voluntary data repository started in 2018 to help isolate and then target R&D opportunities for high-level policymakers, facilitate better resource allocation, and to encourage greater investment.[239]

Overall Score

64

National Strategy

40

Awareness & Prevention

79

Innovation

35

Access

71

Appropriate & Responsible Use

85

AMR & the Environment

70

Collaborative Engagement

67

INDIA

India has been unable to effectively manage and tackle the AMR threat, with poor healthcare and sanitation infrastructure and rampant antimicrobial misuse and overuse.

National Strategy

India's 2017 to 2021 NAP is large in scope and is mirrored by state action plans, though the implementation of this plan has been severely limited due to lack of financing.[240] Further, the decentralized nature of the plans oversight and funding has hampered implementation.[241] To be successful, the NAP must seek greater stakeholder engagement and drum up the political will necessary to reform the plan's management structure.[242]

Awareness & Prevention

Culturally, patients are accustomed to overuse of antibiotics, with many seeking the drugs for a wide range of illnesses. This behavior is more prominent in populations less aware of the problems that can stem from overuse. To its credit, the government has engaged in several initiatives to increase overall awareness. The Medicines with the Red Line Campaign (2016), an awareness initiative run by the government and WHO,[243] aimed to decrease over-the-counter usage, curb self-prescription, and encourage course completion.[244] The Swachh Bharat Abhiyan and Kayakalp initiatives have attempted to improve general and clinical setting sanitation,[245] however, sanitation-related deaths[246] and rates of hospital-acquired infections[247] remain high.

Innovation

Despite a rapidly growing economy and a growing pipeline of researchers, the Indian government has invested next to nothing in AMR research and development.[248] There are too few research organizations, funders, and projects,[249] and only one antimicrobial in development.[250] Additionally, pull incentive and valuation discussions are notably absent.

Access

In India, healthcare quality and access are generally poor,[251] and out-of-pocket costs for healthcare remain high.[252] The healthcare system is stretched thin, with high patient-to-GP and patient-to-bed ratios contributing to a growing threat domestically.[253] An urban-rural divide has led to huge disparities in access to treatment and diagnostics. Smaller hospitals in rural or semi-urban settings often lack access to laboratories or a full-time microbiologist to enable accurate diagnostics and have less oversight regarding antimicrobial stewardship. Further, due to poor healthcare access, informal providers fill the care gap for many. Without proper training (or even licensing), informal providers can contribute to patient misuse and overuse of antimicrobials.

Appropriate & Responsible Use

A key plank of the current NAP also calls for the establishment of registries at pharmacies to help limit over-the-counter purchasing, a key driver of resistance. Recently, the Public Health Foundation of India has worked with professional organizations and private partners to establish training modules to build a large cohort of HCPs trained in stewardship practices and able to change poor practices in various healthcare settings.[254] Unfortunately, COVID-19 has driven attention away from AMR and stewardship. Antibiotics are being prescribed widely to COVID-19 patients, and the much-needed focus on stewardship programs have been lost.[255] Though the Indian Council of Medical Research (ICMR) has established the AMR-stewardship program (AMSP), much work remains to implement and sustain robust stewardship and surveillance programs.[256] This will require an investment in diagnostic tools in low-resource settings, where diagnosis is largely empirical, and countrywide COVID-19-specific AMR interventions.[257]

AMR & the Environment

Though the Centre for Science and the Environment (CSE) has been an integral part of the NAP development process, India lags far behind its peers in addressing AMR in the environment. WASH remains a significant challenge, particularly in rural areas, and meaningful action on AMR and the environment will be challenging without first prioritizing improvements to water and sanitation infrastructure. In January 2020, the Government of India issued draft legislation to better manage and place limits on antimicrobial residues released into the environment by drug manufacturers,[258] but these limits have been omitted from later iterations of the drafted legislation. Massive amounts pharmaceutical manufacturing waste have been directly tied to rising levels of antibiotic concentrations, and it has been reported that complaints by affected communities have been quieted by local police.[259] Further, a study by the Indian Institute of Technology revealed antibiotic concentration in one river to be over 1,000 times higher than those in rivers of more advanced economies countries.[260]

Collaborative Engagement

There are few AMR-focused NGOs active in India, so research organizations are leading the push for more stewardship and public awareness efforts. Progress is also being made on developing more public-private partnerships.

COUNTRY RANK
10

Overall Score
37

National Strategy
40

Awareness & Prevention
43

Innovation
18

Access
24

Appropriate & Responsible Use
43

AMR & the Environment
47

Collaborative Engagement
43

ITALY

AMR is a serious challenge for the Italian government, with over 10,000 people dying each year due to drug-resistant infections and an annual cost for the health system alone of $393 million,[261] yet commitments to national strategy, innovation, testing infrastructure, and appropriate usage are low.

National Strategy

Italy had a national plan which ran from 2017 to 2020. A new plan was reportedly being finalized at time of publication, but experts have expressed concern over the lack of clarity on funding allocations and measures for implementation.

Awareness & Prevention

Patient expectations regarding prescriptions remain a particularly acute challenge in Italy. Not only do patients demand antibiotics, but GPs have also been observed to be more pliant to their requests than in other countries,[262] indicating a clear need for intensive awareness campaigns and targeted interventions in prescription settings. All laboratories in Italy that perform antimicrobial sensitivity testing are integrated in the national AMR surveillance system, through a national network coordinated by a National Reference Laboratory. However, there is homogeneous access to quick diagnostic and laboratory testing, due to the absence of a "hub and spoke" type model to coordinate resources between regional governments, hospitals, and GPs.

Innovation

Though the Italian medicines agency has given innovative recognition to new antimicrobials, this is not due to a full value approach that encapsulates the clinical benefits in light of AMR or the intense developmental costs. On the positive side, the Italian government appears to have begun efforts to reform the way antimicrobials are evaluated. As current reimbursement and pricing mechanisms largely ignore the cost of new antimicrobial development, the government's efforts to place an AMR specialist in the HTA system represents a step in the right direction. While there is some broad acknowledgement of the need for new antimicrobial valuation strategies, no specific incentives have been passed or proposed by the government to encourage the development of new antimicrobials.

Access

Though general healthcare system quality and access are good,[263] and tier 1 antibiotics are fully reimbursed, tier 2 drugs are paid completely out-of-pocket.[264] In terms of availability, Italian patients have similar access to new antibiotics as other European patients, but the lag between market approval and availability for patient use seems to be shorter in Italy than in other European countries.

COUNTRY RANK

7

Overall Score

49

National Strategy

29

Awareness & Prevention

64

Innovation

28

Access

66

Appropriate & Responsible Use

69

AMR & the Environment

63

Collaborative Engagement

25

Appropriate & Responsible Use

While COVID-19 has raised attention to the issue, the pandemic has also exacerbated AMR-specific challenges. A preliminary study from Milan revealed that two-thirds of COVID-19 patients received at least one course of antibiotics.[265] Further, it is clear that overuse of antibiotics grew, particularly of azithromycin and ceftriaxone, in part due to a reallocation of resources that left antimicrobial stewardship without the necessary personnel and infrastructure.[266]

AMR & the Environment

The former AMR NAP referenced the role of AMR in the environment and environmental emissions,[267] and a ban on antibiotics for growth promotion in livestock has been established.[268] However, Italy has one of highest rates of veterinary antibiotic use in Europe.[269] A recent study of coastline aquaculture revealed that over 90% of all samples contained at least one drug contaminant.[270] Though there have been isolated studies on pharmaceuticals in the environment, this area remains particularly under-researched in Italy.

Collaborative Engagement

Several NGOs, advocacy groups, and patient organizations are active in combating AMR in Italy. The Codex Alimentarius Commission (CAC) serves as an intergovernmental association (over 180 members) to protect public health and ensure best practices in the food industry. CAC has expressed specific interest in combating foodborne and veterinary AMR. Additionally, Farmindustria, the national trade association of pharmaceutical companies, has facilitated awareness campaigns and continued to work with key national and international stakeholders on the topic.

JAPAN

In 2017, two deadly drug-resistant bacteria strains ravaged Japan, causing an estimated 8,000 deaths. Although prevention efforts are strong, antimicrobial usage has remained fairly stable and calls to revive the antimicrobial pipeline have gone unanswered.

National Strategy

Japan's NAP was in its fifth and final year in 2020, with an updated version expected to be released by the end of 2021. The COVID-19 pandemic has already caused several delays to the revision process, which is currently underway. The Japanese AMR Alliance has proposed that this new plan establish appropriate outcomes, incentives to ensure sustainable antimicrobial R&D, and measures to solidify and protect the antimicrobial supply chain.

Awareness & Prevention

The AMR Clinical Reference Center has led many awareness raising efforts for the general public through traditional campaigns and media buys, while also providing online AMR education for both the general public and through targeted programs to HCPs.[271] Further, the country has strong vaccination funding. While the NAP has sought to integrate vaccination efforts into AMR prevention,[272] vaccination rates in general remain substantially lower in Japan than among peers. Japan's GLASS compatible surveillance network is also more robust than most and undergoing further improvements.[273]

Innovation

Despite admirable efforts to slow the pace of resistance, AMR does not receive much political attention in Japan, and there are very few high-level discussions on strengthening the innovation environment. Although the pharmaceutical industry has proposed the introduction of pull incentives to spur development, the dearth of domestic drug developers has led many to see their potential impact as small in relation to global efforts. Nonetheless, there are still small grants available to interested antimicrobial developers.[274]

Access

The Japanese healthcare system is both accessible and robust,[275] and out-of-pocket costs for patients remain low.[276] Further, reimbursement for antibiotics is strong, with most fully covered by national insurance and other drugs at least 70% reimbursed.[277] Japan's lag between market approval and reimbursement decision is remarkably low, suggesting an efficient regulatory process, which ensures timely access to new drugs for those who need them.[278]

COUNTRY RANK

5

Overall Score

52

National Strategy

38

Awareness & Prevention

75

Innovation

30

Access

57

Appropriate & Responsible Use

80

AMR & the Environment

38

Collaborative Engagement

47

Appropriate & Responsible Use

The Japanese government has erected robust standards for appropriate use, with the Ministry of Health, Labour and Welfare continuously making recommendations to enact premiums to discourage over- and misuse. Since 2006, all healthcare settings must establish infection control guidelines, infection control leadership, and training of infection control for all staff. Experts cautioned that retrospective data from the pandemic may reveal an uptick in the use of broad spectrum antibiotics, which were already high among some populations. A review of usage rates following the implementation of Japan's NAP (2016) has revealed immediate positive effects, and there is hope for further improvement following the adoption of an updated version.[279]

AMR & the Environment

Domestically, principles and standards for the use of antimicrobials set forth by the World Organization for Animal Health and Codex Alimentarius Commission have been implemented. The government also established its own guidelines for prudent use of veterinary antibiotics, including a ban on colistin for growth promotion in livestock.[280] Though the NAP cites the need for environmental monitoring for AMR,[281] there have been calls for the Japanese government to further increase testing and surveillance as current efforts are seen to be too narrow, while also reforming the structure and methodology of these processes to better capture environmental impacts.[282]

Collaborative Engagement

Japan has displayed moderate international engagement on AMR, notably through the e-Asia Joint Research Program.[283] 'NGOs like the Health and Global Policy Institute, which has helped direct attention and funding to the AMR challenge, are supporting work on this topic.[284] Likewise, AMR Alliance Japan has sought to actively engage in the development of effective policy by providing recommendations across several facets of AMR for the government to integrate into national efforts.

SOUTH KOREA

Though South Korea has prioritized surveillance infrastructure, there remains room for improvement in this and many other areas. South Korea's inadequate investment in research, poor implementation of training and awareness programs, weak vaccine programs, and relatively few efforts to stimulate antimicrobial development hamper progress.

National Strategy

Modeled off the WHO Global Action Plan, the South Korean NAP (2016-2020) focused on reducing the usage of antimicrobials and erecting the necessary surveillance mechanisms for AMR, relying heavily on an integrated stakeholder approach.[285] Though this plan has recently expired, preparations for the second phase plan have been ongoing since 2020,[286] which experts hope will build off the efforts of the first phase plan and continue implementation.

Awareness & Prevention

Though there have been efforts to raise awareness,[287] these efforts seem limited and smaller in scale than those of peer countries. Training on AMR remains inaccessible and narrow in focus.[288] Additionally, despite the inclusion of vaccines in the AMR NAP, vaccine spending per capita is less than that of Brazil, and vaccine costs are not fully covered by national insurance.[289] The Kor-GLASS system was established in 2016 as a national-level GLASS-compatible surveillance system for AMR.[290] Unlike some less sophisticated programs, the system was developed with harmonization and localization in mind, leading to greater system efficiency and utility.[291] However, the program still remains less robust than surveillance initiatives in other developed countries.

Innovation

The South Korean intellectual property[292] and patent[293] policy environments are generally favorable and should encourage innovation. However, there are comparatively few ongoing AMR research projects[294] and no antimicrobials in development.[295] Development is further inhibited by a lack of effort to capture the full value of new antimicrobials and to develop effective pull mechanisms.

Access

Though out-of-pocket costs are fairly low[296] and the healthcare system is of good quality,[297] incidence of catastrophic health spending is high.[298] Further, the lag between market approval and reimbursement decisions for drugs was over ten times longer than that of Japan, demonstrating poor access to new drugs.[299] Research showed that none of the three new novel antimicrobials examined (Lefamulin, Meropenem + Vaborbactam, and Ceftazidime + Avibactam) have yet been approved.[300]

COUNTRY RANK
8

Overall Score
47

National Strategy
25

Awareness & Prevention
54

Innovation
28

Access
44

Appropriate & Responsible Use
67

AMR & the Environment
57

Collaborative Engagement
53

Appropriate & Responsible Use

The government has made substantial improvements in limiting non-prescription antimicrobial use, a bright spot for South Korea, which seems to have favorably affected resistance profiles. As a result of a national policy prohibiting doctors from dispensing drugs, inappropriate antibiotic prescriptions for viral illness have decreased considerably, as have the number of antibiotics prescribed per episode. Supplementing these efforts, the KCDC also developed a system to better measure and compare antibiotic usage rates in hospitals in 2019. And the Korean Society of Infectious Diseases is currently working with the Health Insurance Review & Assessment Service (HIRA) to classify antibiotic usage more accurately in hospitals.

AMR & the Environment

In 2017, Korea Centers for Disease Control & Prevention (KCDC) launched a One Health-based research project to monitor surveillance of drug usage and disease transmission in human-animal environments. Additionally, several bans on antibiotic usage in animals over the past two decades have also contributed to varying levels of decreased resistance and consumption in livestock.[301]

Collaborative Engagement

The South Korean chapter of the Alliance for the Prudent Use of Antibiotics (APUA-South Korea), established in 2000, is a leader in this space. Having identified a lack of usage surveillance and acute respiratory infections (ARI) as the most worrisome aspects driving AMR in Korea, the organization has facilitated collaboration between the Korean Department of Health and FDA, academia, hospitals, pharmaceutical companies, and human and veterinary groups to monitor and promote appropriate antibiotics usage.[302] The International Vaccine Institute (IVI), hosted by South Korea, has partnered with the Technical University of Denmark in a joint effort to improve AMR surveillance data through the Strengthening External Quality Assurance for AMR in Asia (EQASIA) project.[303] Though third party organizations are engaged on AMR issues, international collaborative project and program engagement could be improved.

UK

The UK has shown a willingness to tackle AMR head on, by implementing a comprehensive national plan and by developing a first-of-its-kind, de-linked, subscription-based pull incentive program.

National Strategy

The UK's current NAP, Tackling Antimicrobial Resistance 2019-2024, focuses the government's attention on several important areas: expanding mandatory hospital reporting for all priority resistant pathogens, documenting deaths due to resistant pathogens, and exploring new data-gathering approaches to support the efficacy of new antibiotics. This second five-year NAP builds off the efforts of the previous plan and sits within a new "20-year vision for AMR" aimed at ensuring a fuller pipeline of antimicrobials by 2039. As in many countries, COVID-19 has diverted government attention away from AMR in the short term, with fundraising and loans for antimicrobial projects now delayed at least six to twelve months. Despite ongoing pandemic-related challenges, experts remain cautiously optimistic that the structural changes precipitated by the pandemic (a reversion to more centralized control over processes and policy) will provide a suitable environment for the further integration of AMR into broader public health policies.

Awareness & Prevention

Stakeholders continue to work to improve data collection efforts related to AMR, with the country's NAP explicitly calling for better data management for AMR surveillance and usage monitoring.[304] The national strategy also calls for raising awareness among the myriad stakeholders who must be engaged to effectively tackle this problem: students, pet owners, veterinarians, farmers, HCPs, and the general public.

Innovation

As part of its heralded subscription program, the UK will pay drug developers upfront for their "development service" in an effort to capture the public health value of novel antimicrobials and mitigate the economic risks of development.[305] However, the final valuation of these novel antimicrobials is still unclear, and the pilot program does include a reimbursement cap. Experts believe that for the program to be successful, the valuations must capture the full value of these drugs, including insurance value, and the pilot should be expanded through further investment. If the program is successful, it would help meaningfully advance global efforts to combat AMR by providing a template for other governments to help encourage and incentivize the development of new antimicrobials. The government plans to test the pilot for two drugs, with a goal of expanding to other antimicrobials if successful.

COUNTRY RANK

1

Access

The British healthcare system is both highly accessible and robust,[306] with low out-of-pocket costs[307] and strong reimbursement policies for antibiotics.[308] There is also strong availability of recently developed antibiotics, though the lags between market approval and reimbursement decisions could be shortened through process reforms.

Appropriate & Responsible Use

In addition to pull incentive schemes, the UK has also done relatively well in implementing initiatives to curb overprescription. Similar to France, the UK has established incentives programs to reward GPs who prescribe fewer antibiotics. GPs are also generally well trained on AMR-relevant issues, and the profession has a decades-long tradition of managing patients' expectations for antibiotics. Further, British hospitals have maintained strong regulation and auditing over the years. Crucial among these is the Care Quality Commission's antibiotic usage rating, which helps ensure that stewardship and appropriate use are a constant priority among hospital staff.

AMR & the Environment

Notably, through a G7 communiqué, the UK has demonstrated a strong commitment to improving the global understanding of and implementation of initiatives to address AMR in the environment.[309] The announcement has called for greater evidence gathering and surveillance, and, acknowledging the work done by the AMR Industry Alliance, has promised forthcoming standards on drug concentrations in the environment.[310]

Collaborative Engagement

The UK is also seen as a unique leader on the international stage. From the commissioning of the O'Neill report in 2014,[311] an effort by then PM David Cameron to raise the profile of the issue globally, to the Global AMR Innovation Fund (GAMRIF),[312] the UK has been heavily committed to ensuring global stakeholders remain committed to tackling this issue. Like its predecessor Germany, the UK has also made AMR a priority for its 2021 G7 presidency.[313]

Overall Score
76

National Strategy
77

Awareness & Prevention
78

Innovation
54

Access
74

Appropriate & Responsible Use
89

AMR & the Environment
89

Collaborative Engagement
73

US

PASTEUR presents a unique opportunity for the US, which has committed commendable resources to AMR national strategies and collaborative projects, though more investment in research in necessary.

National Strategy

Following a ten-month lapse at the expiration of the 2015-2020 NAP,[314] the US introduced the 2020-2025 Combating Antibiotic-Resistant Bacteria (CARB) NAP. This new NAP, developed by the Federal CARB Task Force with input from an external federal advisory group of multisectoral stakeholders, stresses the need for more public-private collaboration to effectively tackle this growing threat.[315] The new 2020 to 2025 plan now also includes clearer recommendations to implement infection control, prevention, and antibiotic stewardship programs.[316] Overall, the US has a stronger response to AMR than most countries, with better integration of the One Health approach in planning and more coordination across and cooperation among federal agencies with AMR portfolios.[317] CARB, which pulls together almost a dozen separate agencies, demonstrates the government's commitment to tackling the AMR issue.

Awareness & Prevention

The US also has strong efforts in areas outside the NAP. The CDC and USDA have both pursued campaigns on appropriate use and general AMR awareness, targeting human health and, critically, non-human elements.[318] Further, many experts hope that the COVID-19 crisis will help increase overall investment in public health infrastructure, funding which could help to bolster surveillance and monitoring efforts.

Innovation

Numerous pieces of legislation to implement pull incentives for antimicrobial development have been introduced in Congress over the past decade, though the recent reintroduction of the PASTEUR Act, currently under consideration by Congress, is the most serious effort to date, and would mark a global win for efforts to broaden the antimicrobial pipeline.[319,320] At this time, however, no votes have been scheduled in Congress. Proponents hope that if passed, the bill could – like the pilot in the UK – offer a template or framework for stimulating the development of antimicrobials both domestically and abroad.[321]

Access

The US leads in terms of availability of new and novel antimicrobials and antibiotics, with a shorter lag between market approval and a reimbursement decision than most.[322] Though the US healthcare system is regarded as strong,[323] reimbursement coverage is variable due to fragmented state-led policies.[324]

Appropriate & Responsible Use

One major area of concern for the US is the alarming increase in the use of antibiotics during the pandemic. A meta-analysis conducted in August 2020 by IDSA found that only 7% of all hospitalized COVID-19 patients suffered from a bacterial co-infection, yet over 70% received antibiotic courses.[325] Increased treatment of COVID-19 patients in hospital settings is likely to have correlated with increased usage of antibiotics, which experts anticipate has hastened resistance.

AMR & the Environment

The US Department of Agriculture has also committed itself to AMR, and its surveillance efforts on the food supply are integrated within the NAP.[326] However, a joint report co-authored by the CDC underscores the existence of research gaps regarding AMR and environmental implications.[327] Further, there is only a voluntary ban on the use of antibiotics for growth promotion in livestock,[328] and the US is estimated to have much higher general rates of antibiotic use in animals than elsewhere.[329]

Collaborative Engagement

The US has been a leader of international collaborative projects in many cases, with the CDC's AMR Challenge being a notable example.[330] Further, the US has engaged in multilateral partnerships to further AMR research through the Global Antibiotic R&D Partnership.[331] Equally, NGOs, such as the University of Minnesota's Center for Infectious Disease Research and Policy, have led impressive programs to expand AMR knowledge and promote innovation.[332]

COUNTRY RANK
2

Overall Score
68

National Strategy
67

Awareness & Prevention
74

Innovation
52

Access
74

Appropriate & Responsible Use
76

AMR & the Environment
51

Collaborative Engagement
80

Appendix B

Click here to view scoring breakdown

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Global Coalition on Aging

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