



Executive Summary

DRUG-RESISTANT INFECTIONS

A Threat to Our Economic Future

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Executive Summary

This report examines the economic and development consequences of antimicrobial resistance (AMR)—the capacity that disease-causing microorganisms acquire to resist the drugs we’ve created to fight them. The report uses World Bank Group economic simulation tools to put a price tag on AMR’s destructive impacts on the global economy from 2017 through 2050, if adequate measures aren’t taken to contain the AMR threat.

The report highlights actions low- and middle-income countries and their development partners can take to counter AMR, and estimates the investment required. It shows that putting resources into AMR containment now is one of the highest-yield investments countries can make.

What Is AMR?

Antimicrobials are drugs that destroy disease-causing microbes, also called pathogens, such as certain bacteria, viruses, parasites, and fungi. The most familiar and important antimicrobials are antibiotics, which treat bacterial infections. Other antimicrobials combat viral and parasitic diseases, such as AIDS and malaria. Since their use began some 70 years ago, antimicrobials have saved hundreds of millions of lives.

AMR occurs when pathogens undergo adaptive evolutionary changes that enable them to withstand antimicrobials. People or animals who encounter resistant pathogens may then suffer infections that can’t be treated. The pathogens survive, patients get sicker and may die, the cost of medical care rises, and disease continues to spread.

Every use of antimicrobials, even the most prudent, creates opportunities for AMR. However, rigorous management can limit the risks. In recent decades, though, overuse and misuse of antimicrobials have caused avoidable AMR emergence and spread. As a result, antimicrobial drugs are rapidly losing their effectiveness in both developing and developed countries. If this trend continues, humanity may face a reversal of the public-health gains of the past century, and the economic growth, development, and poverty reduction these gains enabled.

A Tragedy of the Commons

The loss of efficacy of antibiotics and other antimicrobials worldwide can be understood as a “tragedy of the commons.” A tragedy of the commons occurs when people in a community squander a limited, shared resource, as each actor pursues her own short-term self interest by exploiting the resource for private benefit. No one wants the common resource to be exhausted. Yet the group’s collective behavior leads to precisely this result. This concept has been applied, for example, to the collapse of fisheries due to overfishing. The overuse and misuse of antimicrobial drugs worldwide show a similar pattern.

Protecting a Global Public Good

As effective antimicrobial treatment is part of the global “commons,” containment of AMR is a global public good. All countries can enjoy the benefits of successful AMR containment. Conversely, all countries will be harmed if AMR is not kept in check. The status of AMR containment as a global public good underscores the critical responsibility of public authorities, especially national governments, in protecting this good.

This responsibility is all the more crucial, because victory over AMR is never final, since pathogens constantly evolve, and they eventually develop resistance to any medication we discover. However, with wise policies and careful stewardship, the life-saving power of antimicrobials can be greatly extended. The inherent fragility of this public good makes it even more important to defend it well.

To date, action on AMR has been dangerously inadequate. Policy and financing choices by governments and development partners have resulted in weak public-health systems across broad regions of the world, enabling the undetected spread of pathogens, including drug-resistant strains.

A Threat to the Global Economy

What can motivate countries to focus on AMR and deploy the comprehensive response this threat demands? Often, economic interest provides an impetus to political action. In this report, we have used World Bank economic simulation tools to quantify the losses that AMR may inflict on the global economy between now and 2050.

Our simulations included two scenarios, corresponding to low AMR impacts and high AMR impacts. AMR impacts were modeled as shocks to labor supply and livestock productivity—a conservative approach that underestimates AMR’s full economic effects.

In the optimistic case of low AMR impacts, the simulations found that, by 2050, annual global gross domestic product (GDP) would likely fall by 1.1 percent, relative to a base-case scenario with no AMR effects; the GDP shortfall would exceed \$1 trillion annually after 2030. In the high AMR-impact scenario, the world will lose 3.8 percent of its annual GDP by 2050, with an annual shortfall of \$3.4 trillion by 2030 (Figure ES1).

A Crisis That Won’t Quit

During much of the period through 2050, the annual reduction in global GDP caused by AMR could be as large as the losses provoked by the 2008–2009 global financial crisis, at their most severe (Figure ES2). However, the cost impacts of AMR on GDP would be worse than those of the financial crisis in two respects. First, they would be felt during the entire simulation period (through 2050), not just for a couple of very bad years, as was the case in the acute phase of the recent financial crisis.

Poorer Countries Will Suffer Most

Moreover, with AMR, low-income countries would experience larger drops in economic growth than wealthy countries, so economic inequality between countries would increase. The differential impacts on GDP result from higher infectious disease prevalence and greater dependence on labor incomes in countries with lower per capita incomes.

Impacts on International Trade, Livestock Production, and Health Care Costs

International trade may be heavily affected if AMR spreads unchecked. By 2050, the volume of global real exports may fall below base-case values by 1.1 percent in the low-AMR scenario and by 3.8 percent in the high-AMR scenario. Output and trade in livestock and livestock products are especially vulnerable to AMR impacts. Livestock production in low-income countries would decline the most, with a possible 11 percent loss by 2050 in the high AMR-impact scenario.

FIGURE ES1. Substantial and Protracted Shortfalls in Global Economic Output
World Real GDP

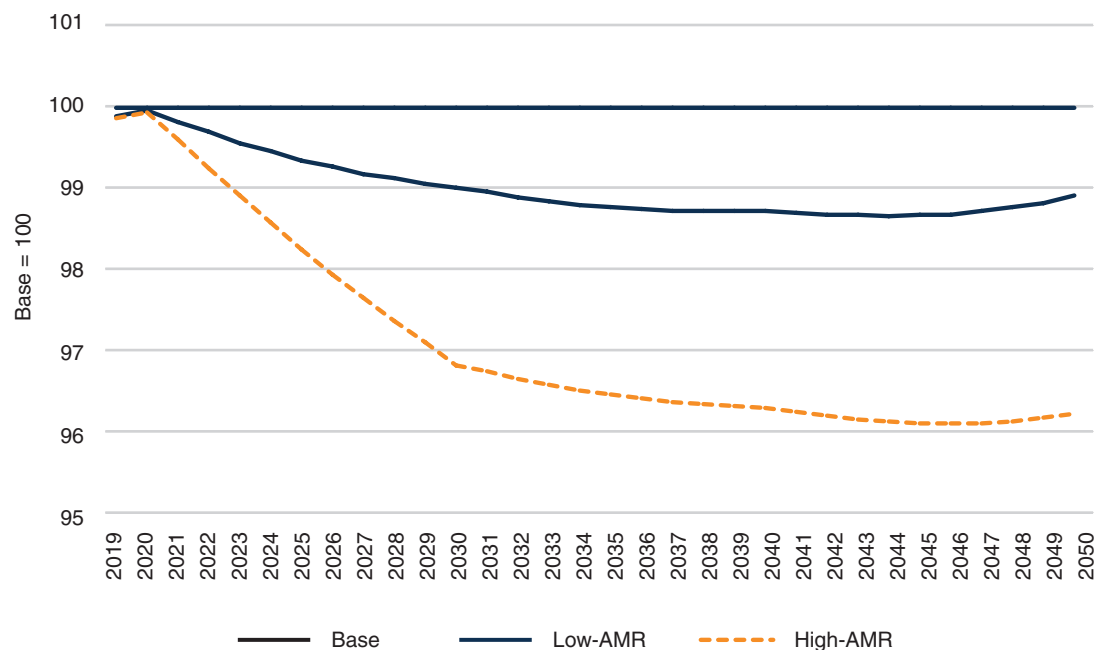
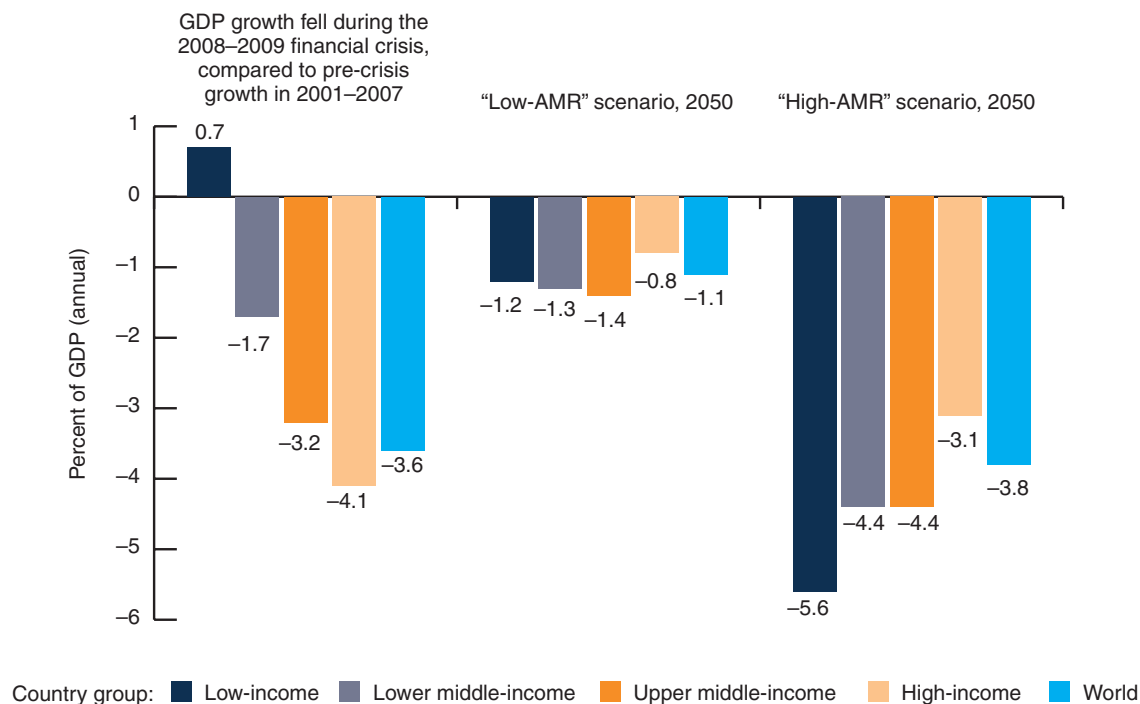


FIGURE ES2. Economic Costs of AMR May Be as Severe as During the Financial Crisis
AMR could reduce GDP substantially—but unlike in the recent financial crisis, the damage could last longer and affect low-income countries the most
(annual costs as % of GDP)



Meanwhile, as AMR spreads, health care expenditures, both public and private, will increase in step with the rising disease burden; by 2050 the annual costs may exceed the base-case level by some 25 percent in low-income countries, 15 percent in middle-income countries, and 6 percent in high-income countries.

Derailing Global Development Goals

Without AMR containment, the Sustainable Development Goals for 2030—such as ending poverty, ending hunger, ensuring healthy lives, reducing inequality, and revitalizing global development partnerships—are less likely to be achieved.

The impacts of AMR on poverty are particularly concerning. In the high AMR-impact scenario, an additional 24 million people would be forced into extreme poverty by 2030. Most of the increase would occur in low-income countries. As a result, the World Bank Group goal of eliminating poverty by 2030 would be harder to reach.

High-Yield Investments

Policy makers may be concerned that the cost of tackling AMR will be excessive. On the contrary, our analysis shows that action on AMR constitutes one of the highest-yield development investments available to countries today.

The cost of AMR containment measures is estimated at \$9 billion annually in low- and middle-income countries. About half of this amount is for investments in, and operation of, core veterinary and human public-health systems in 139 countries. The recommended investments in AMR containment are justified according to two key economic criteria.

The Net Present Value Test

First, the test of net present value (NPV) is unambiguously satisfied. This is the case not only globally, but also separately for high-income countries and upper middle-income countries. Assuming that just 50 percent of AMR costs will be avoided by vigorous AMR containment efforts, the expected cumulative global benefits from AMR containment in 2017–2050 range between \$10 trillion and \$27 trillion, far greater than the investment costs of \$0.2 trillion. The net present value is thus between \$9.8 trillion and \$26.8 trillion.

Different countries stand to benefit from AMR control in different ways. Low-income countries will see substantial economic payoffs, relative to the size of their economies. The largest absolute and per capita gains, however, will actually flow to upper middle-income and high-income countries. Assuming, very conservatively, that only 10 percent of the modeled costs were averted through AMR containment measures, high-income countries would still obtain benefits of \$0.9 trillion and \$2.7 trillion, in the low AMR-impact and high AMR-impact cases, respectively. This is four times and thirteen times more than the global investment cost of \$0.2 trillion (Figure ES3).

Remarkable Returns

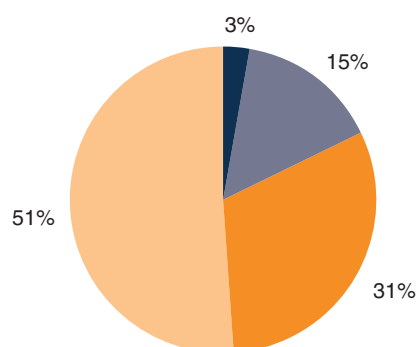
The second test of the investment case for AMR control considers the expected economic rate of return (ERR) on the \$9 billion annual investment. Assuming that investments would be made for seven years before any benefits materialize, the ERR ranges from 31 percent annually (if only 10 percent of AMR costs can be mitigated) up to 88 percent annually (if 75 percent of AMR costs are avoided). The chance to obtain returns of this magnitude constitutes an exceptional investment opportunity for countries.

FIGURE ES3. High-Income and Upper Middle-Income Economies Stand to Benefit the Most from AMR Containment, Both in Absolute and per Capita Terms

Proportion of global AMR containment benefits

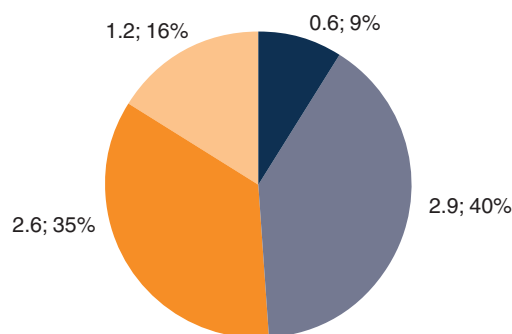
(based on present value of total benefits in 2017–2050)

Upper middle-income and high-income countries will obtain more than 80 percent of the benefits from AMR containment



Total world population: 7.3 billion

(population in billions; share of global total)



Country group:

- Low-income
- Lower middle-income
- Upper middle-income
- High-income

A Bold Agenda: Integrated Public-Health Protection in All Countries

We have argued that aggressive action to tackle AMR is needed now. But what exactly must be done?

Before we discuss specific recommendations for action on AMR, we need to emphasize a general principle. AMR cannot be managed in isolation. Drug-resistant infectious diseases are a subset of the broader range of microbial threats to human and animal health and welfare. From a public-health and policy-making standpoint, drug-resistant infections have practical similarities to all infectious diseases with pandemic potential. The surveillance, diagnostic, and control capacities needed to deal with AMR are closely related to those required to control diseases like Ebola and Zika. Instead of viewing AMR as a separate issue isolated from other health challenges, it will be more effective and less costly over time to build a common core of permanent capabilities in all countries for managing the full range of infectious threats.

As AMR control is part of a wider agenda of infectious disease management, so the response to infectious diseases in turn depends on the robustness of countries' broader health systems. Competencies for the AMR fight can't be built independently of the health system's durable core capacities. Effective AMR action depends, for example, on reliable health information systems, rational procurement and management of drugs, and the presence of a trained and motivated health workforce.

Building core human and veterinary public-health and infectious disease surveillance capacities in all countries is the critical step in confronting the AMR threat. Where these capacities exist, AMR can be detected and contained. Where they don't, it can't. This is the fundamental fact.

When discussing AMR policy measures, we describe them as "AMR-specific" or "AMR-sensitive." AMR-specific actions are those whose primary purpose is combating AMR (though they may bring other benefits, too). An example is tightening legislation and enforcement on the sale of antimicrobials without a prescription. AMR-sensitive measures are those whose main purpose is not actually AMR-related, but which can be designed and implemented in such a way that they contribute indirectly to AMR containment. Expanding access to clean water and sanitation, thus reducing the incidence of

infections, is an example. Both AMR-specific and AMR-sensitive measures are needed now to contain the spread of drug-resistant pathogens.

Options for Country Action

WHO's Global Action Plan on AMR (WHO 2015), developed in collaboration with the World Animal Health Organisation (OIE) and the United Nations Food and Agriculture Organization (FAO), defines five broad objectives for the AMR fight (Figure ES4). Building on the global plan, several recent landmark reports have provided additional guidance on national policies and implementation strategies to fight AMR. These publications include the final report from the U.K. Review on AMR (Review on Antimicrobial Resistance 2016) and global plans from OIE (2016) and FAO (2016). Together with the Global Action Plan, these sources have set forth a comprehensive high-level policy agenda for the AMR fight.

This also means that we don't need to "reinvent the wheel" here. Our recommendations concentrate on select areas where opportunities for important advances exist, and where World Bank knowledge, experience, and resources can add value to the country efforts we propose.

To implement the Global Action Plan and in particular to understand how it will be financed, it is useful to analyze country options through a sectoral lens. Accordingly, our recommendations for country AMR action are structured by sector, including: (a) health; (b) agriculture; and (c) water, sanitation, and hygiene.

Driving AMR Progress from the Health Sector

The health sector offers many entry points for AMR control. Our recommendations focus on three topics: (1) universal health coverage reforms as an enabling platform; (2) harnessing the International Health Regulations (IHRs) to accelerate AMR action; and (3) strengthening laboratory-based surveillance, including through regional networks.

1. Universal health coverage (UHC) provides the best enabling framework to tackle AMR. UHC models are diverse, but UHC efforts will generally strengthen AMR containment through the following mechanisms:

- ✱ *Expanded coverage.* By definition, UHC designs lead to greater breadth and depth in the population coverage of health services. This includes services like vaccination, preventative care, and hygiene measures that lower the need for antimicrobials and thus slow the spread of AMR. Covering the whole population with vaccinations shows one potent way UHC will reduce the incidence of infections, advancing a key objective of the Global Action Plan on AMR.
- ✱ *Better oversight and quality of care.* UHC models improve oversight in health care practice. Among other benefits, this helps ensure that antimicrobial use conforms to rational standards. UHC strategies promote rational, regulated access to antimicrobials for all patients under the guidance of trained health professionals. Thus, UHC provides a framework for simultaneously expanding the well-regulated use of antimicrobials where they have been lacking, and tackling the overuse and misuse that have accelerated AMR in other settings. UHC strengthens antibiotic stewardship in health facilities, reinforces the use of standard treatment protocols for infections, and can improve procurement, quality control, and other features of antimicrobial management—with the potential for major gains against AMR. These UHC features support another of the five Global Action Plan objectives: optimizing current antimicrobial use.
- ✱ *Smarter, fairer financing.* The expansion of health systems towards UHC promises more efficient and equitable financing. This will help close existing access gaps for treatable infections. Pooled, prepayment financing also encourages rational purchasing and prescription, supporting the optimization of antimicrobial use and protecting the efficacy of current drugs.

FIGURE ES4. Five Objectives of the Global Action Plan on AMR, 2015–19

Strengthen Knowledge and Evidence Base	Reduce the Incidence of Infection	Optimize Use of Antimicrobials	Improve Awareness and Understanding of AMR
<ul style="list-style-type: none"> * Develop an AMR surveillance system for: <ul style="list-style-type: none"> • health care facilities and community • animal husbandry and agriculture • using at least one reference lab * Share information internationally * Collect and share data on antimicrobial use (human/animal/agriculture) * Consider an AMR research agenda, including: <ul style="list-style-type: none"> • responsible use • infection prevention • development of novel agents 	<ul style="list-style-type: none"> * Implement and strengthen hygiene and infection prevention programs <ul style="list-style-type: none"> • make it part of health care and veterinary training • develop and implement standards of practice * Test and report susceptibility of hospital-acquired infections (HAI) * Implement prevention best practices in animal health and agriculture * Promote vaccination of food animals 	<ul style="list-style-type: none"> * Implement a comprehensive action plan with: <ul style="list-style-type: none"> • antibiotics access only through qualified individuals • only quality, safe and efficacious drugs authorized • reimbursement, promotion and treatment guidelines • laboratory capacity to guide optimal use • evidence-based stewardship programs • elimination of financial incentives to prescribe • effective and enforceable regulation • reduction/phasing out of non-therapeutic antibiotic use in agriculture 	<ul style="list-style-type: none"> * Public communication targeting human and animal health audiences as well as schools and public media * Establish AMR as element of professional education * Elevate AMR to priority agenda across government
			Make Economic Case for Investment <ul style="list-style-type: none"> * Secure required financing for implementation * Engage in international research collaboration—between developed and developing countries * Public-private partnership * New market models for investment and access

WHO Global Action Plan on Antimicrobial Resistance, adopted by the World Health Assembly in May 2015. See http://apps.who.int/iris/bitstream/10665/193736/1/9789241509763_eng.pdf?ua=1.

* *Better information.* UHC generally enables improved data collection and management within the health system, at the population, facility, and individual provider levels. By strengthening data systems, UHC approaches may better equip them to support AMR surveillance, monitoring, and response. These features support the Global Action Plan (GAP) objective to strengthen AMR knowledge and the evidence base.

* *Improved stewardship and governance.* A robust UHC approach builds systems-governance and coordination capacities that are critical for the AMR fight. Moreover, under UHC models, regulatory capacities tend to be enhanced. Health facility accreditation provides an example. Requirements for improved antimicrobial stewardship can be built into accreditation processes for hospitals and clinics to bolster AMR control at the facility level. AMR training can also be incorporated into the pre-service and in-service education of health providers, advancing the Global Action Plan objective to improve awareness and understanding of AMR.

2. Implementation of the International Health Regulations (IHR) can accelerate AMR action and focus global support.

Under the IHR, 196 countries have committed to work together to prevent, detect, report, and manage public health emergencies, such as infectious outbreaks. To meet their IHR implementation requirements, many countries are participating in systems-diagnostic and planning exercises, for example through the Joint External Evaluation (JEE) process, under the Global Health Security Agenda (GHSa). Systems-evaluation exercises provide opportunities for countries to assess their capacities and needs in areas like infectious-disease and AMR surveillance. Among other benefits, such efforts help lay foundations for the AMR Global Action Plan's five objectives, especially the first, strengthening knowledge and the AMR evidence base.

In order for these exercises to achieve full impact, it is important that each country designate institutions and individuals who will be accountable for following up on the evaluation results. The designated actors will lead a process to translate assessment recommendations into methodical action to build national capacity for surveillance and response. Because each country's implementation of IHR commitments benefits all other countries by improving detection and response to transborder threats, the international community has an interest in adequately financing this global good.

- 3. Countries at all levels of income can build laboratory capacities for AMR surveillance—and create synergistic regional laboratory networks.** Strengthening AMR surveillance capacities, including in low- and middle-income countries, is a cornerstone of AMR control, captured in the first objective of the Global Action Plan. The creation of a national AMR surveillance network is becoming technically feasible and affordable for an increasing number of countries. Kenya, for example, is in the process of launching its own national AMR surveillance network at an estimated annual cost of about \$160,000. (This figure represents the specific added expense of AMR surveillance, beyond the ongoing costs of operating the country's clinical laboratory network.)

A background study commissioned for this report examined the East Africa Public Health Laboratory Networking Project (EAPHLN), in which Kenya participates, along with Burundi, Rwanda, Tanzania, and Uganda. The study documented the benefits that can accrue when countries link their laboratory resources into a regional network structure. The EAPHLN has accelerated innovation and fostered new forms of learning and collaboration, including: (1) joint annual peer audits, in which countries assess each other's laboratories, and (2) cross-border disease surveillance, simulations, and investigations that have enabled swift regional responses to Ebola and Marburg outbreaks.

Agriculture: A Critical Frontier for AMR

The bulk of antimicrobial use in many countries occurs in the agriculture sector, particularly in livestock. Worldwide, in 2010, livestock consumed at least 63,200 tons of antibiotics and probably far more, exceeding total human consumption. The precise impacts of this heavy use of antimicrobials in animal production continue to spark debate, and data are scarce. However, recent research suggests that AMR is already common in agricultural systems in low- and middle-income countries.

- 1. All countries can progressively reduce the use of antibiotics in animal production.** Systematic reduction and eventual elimination of antibiotic use for livestock growth promotion is critical for long-term AMR control. This goal has drawn increasing consensus among scientific experts and many political leaders. European Union countries have banned the use of antimicrobials as growth promoters since 2006.

Countries' specific contexts must be taken into account in designing plans and establishing timelines. Countries that currently rely heavily on the use of antibiotic growth-promoters may require more time and support to adapt their production regimes. Some low-income countries may benefit from extensive technical support.

Experts, including the U.K. Review on AMR, have recommended the use of national numerical targets to drive reductions in the use of antibiotics in agriculture. We support this approach. The use of time-bound, quantitative targets can be a powerful motivator.

Solutions for the livestock sector should foster the adaptability of animal productions systems to reduced use of antimicrobials. Recommendations call for an integrated approach, with cycles of innovation and learning: First, developing policies, setting targets, and monitoring antimicrobial use in livestock production; then identifying gaps or problems in current production systems and methods to address them; and finally sharing knowledge on improved management.

We can protect farmers as antimicrobial practices change. Small farmers may be especially vulnerable as changes to established production methods are introduced. Governments and development partners have a fundamental responsibility to accompany small farmers in adapting their modes of animal production, as we act to save a global public good.

Policy action must also take account of global disparities in access to antimicrobials for livestock, mirroring those in human health. The same drugs that may be used excessively in livestock production in some parts of the world remain unavailable in others, where they could have legitimate applications and save lives and livelihoods.

- 2. An urgent effort is needed to strengthen country surveillance systems for tracking the use of antimicrobials and the spread of AMR in animals.** A consistent finding from country case studies commissioned for this report was a deficiency in data needed to analyze antimicrobial use in livestock, in terms of epidemiology and economic impacts.

Each country may commit to develop a system for collecting standard data on animal populations and animal production systems in its territory. Countries should be supported to build basic data collection

systems to track both the use of antimicrobials and AMR in animal production. OIE's current effort to develop a worldwide system for data collection on antimicrobial use in animals merits strong support.

3. **New partnerships can spur innovation for AMR control across agriculture, the environmental sciences, and health.** Scientists and policy makers increasingly recognize that integrated strategies are needed to tackle the drivers of AMR simultaneously in livestock production, environmental management, and human health. Today, research on integrated strategies and new technologies to fight AMR is slowly gathering momentum. Yet the field remains under-resourced and fragmented.

Evidence-based, consensus directions for priority research have yet to be defined. International coordination and stewardship of AMR knowledge production are urgently needed. In particular, there is a need to inform and incentivize the global innovation agenda to target the points of highest priority and greatest opportunity for the development of new AMR-management technologies. This would include not only new antibiotics, but also new vaccines (both animal and human), the rapid-diagnostics agenda, and policy innovation in areas like compensation or insurance mechanisms for farmers who cut antibiotic use. Targeted learning and innovation in a broad range of sectors, from pharmacology to development finance, must be nurtured simultaneously.

How might this be done? We can point to promising precedents: innovative models of collaboration that have proven effective for other complex, multi-sectorial challenges. One example is CGIAR, a global consortium of agricultural research centers supported by an extensive network of partners, including the World Bank. For some 50 years, CGIAR has generated creative and practice-relevant research on food security, rural poverty reduction, and sustainable resource management. Today, to jumpstart new investment in AMR research and technological innovation, we can learn from CGIAR and other network models for knowledge production.

A hybrid, networked research center might pursue learning and innovation simultaneously in agriculture, animal health, and human health. To our knowledge, no such hybrid research hub currently exists. However, its feasibility could be explored with existing CGIAR network centers, other research consortiums, countries, donors, and other stakeholders. Through such partnership models, countries will tap into networks of innovation to multiply the impact of their individual actions against AMR.

Water, Sanitation, and Hygiene: AMR-Sensitive Development Priorities

Historically, safe drinking water and sanitation facilities, along with basic hygiene practices such as hand washing with soap and water, were decisive in reducing the spread of infections, even before modern antimicrobials were invented. In the age of AMR, such infection-prevention strategies once again take on salience.

The Global Action Plan has incorporated this principle. Reducing the incidence of infections is one of the five objectives. Two complementary facets of the preventative agenda involve: (1) expanding access to water and sanitation; and (2) universalizing basic hygiene practices, particularly in health care facilities.

1. **Countries can harness the power of water and sanitation investments to check infections, fight AMR, and support economic growth.** Expanding access to sanitation and clean water is among the most powerful AMR-sensitive investments available. Improved access to clean water and sanitation delivers robust public health benefits in its own right. In addition, by preventing infections and reducing the need for antibiotics, these measures also reduce the pressures that drive antimicrobial resistance (Wellcome Trust 2016). The combined health impacts translate into remarkable gains in life expectancy, which imply productivity and economic gains for countries, as well. As leaders weigh the costs and benefits of development investments, it is important to incorporate public-health benefits, including AMR containment effects, in the expected gains from investing in water and sanitation.
2. **Hygiene in health facilities: simple tools, strong impacts.** The settings where water, sanitation, and hygiene practices can combine to powerfully impact AMR include health facilities. Infection prevention and control (IPC) strategies in health care settings are pillars of the AMR containment agenda, recognized in the infection-prevention objective of the Global Action Plan.

Basic hand hygiene (hand washing with soap and water or alcohol-based products) has repeatedly been cited as the single most important practice to reduce health care associated infections. Improved hand hygiene has been associated with a sustained decrease in the incidence of AMR infections in health care settings (Rainey and Weinger 2016). Today, in countries at all income levels, these basic tools are not being rigorously applied. While this is alarming, it also represents an opportunity for low-cost, high-yield action against AMR.

WHO, UNICEF, and partners have set out a global agenda for universal access to water, sanitation, and hygiene in health care facilities. By implementing the plan, governments, international organizations, donors, and civil society partners can achieve substantial gains against AMR (Rainey and Weinger 2016).

Country Leadership, Global Partnership

Today, political momentum for action on AMR is growing. At the United Nations General Assembly (UNGA) special session on AMR, in September 2016, 193 Member States pledged to “develop . . . multi-sectoral national action plans, programmes, and policy initiatives, in line with a One Health approach and the global action plan.”

AMR containment will depend on country-led efforts implemented in countries. But effective AMR containment also demands coordinated action across national borders. Adequately resourced multilateral agencies can multiply the impact of country policies. Multilateral organizations mobilize international attention, facilitate cooperation and knowledge sharing, provide technical advice and standards, and catalyze multi-sectorial action. Successful AMR strategies will also engage private firms, research institutions, global and local civil society, and other partners.

What Will the World Bank Group Do?

The agenda for AMR action outlined in this report implies responsibilities for the World Bank Group.

Creating a Global Investment Framework for AMR Action

Thanks to the Global Action Plan and the efforts of many partners, substantial consensus exists on the types of policies and interventions needed to contain AMR. Moreover, we now have a reasonable idea of how much AMR containment will cost. The sums are modest by global investment standards, as we’ve seen, and the likely rewards exceptionally high. But the money still has to be put on the table.

The World Bank Group will work with countries and partners to develop an investment framework to deliver the objectives of the AMR Global Action Plan. The framework will include rigorous costing of priority AMR interventions at country, regional, and global levels. Costed plans for AMR will be integrated with broader country agendas for emergency preparedness, response, and resilience, which are gaining momentum through the WHO Monitoring and Evaluation Framework, the OIE Performance of Veterinary Services (PVS) pathway, and other mechanisms.

The AMR investment framework will be informed by the results of the International Working Group on Financing of Preparedness, whose research is currently in progress, and by experience with the Pandemic Emergency Financing Facility (PEF), created under World Bank leadership following the 2015 Ebola outbreak in Western Africa. The investment framework will emphasize integration of AMR activities and funding into finance mechanisms that will be sustainable over time.

In laying foundations for the global investment framework, World Bank experts will work at the country level with policy makers and technical colleagues to develop national AMR financing assessments, aligned with countries’ AMR National Action Plans (NAPs). Country financing assessments will identify

national priorities, needs, gaps, and best-value interventions. They will explore resource mobilization options, looking across sectors and including public and private sources.

The global AMR investment framework will then incorporate the results of country planning and costing exercises to develop a comprehensive instrument that can map and quantify needs worldwide and coordinate global investments in AMR action. The framework will be a decision tool for policy makers, planners, development finance institutions, donors, and other partners in the AMR effort, helping ensure that AMR finance flows to where it is most needed and achieves the greatest impact.

We consider the creation of a global AMR investment framework as a key step towards the realization of the Global Action Plan and as a logical follow-up to the September 2016 UNGA special session. The World Bank will deliver an initial version of the AMR investment framework by the time of the official AMR progress report to the UN General Assembly in September 2019.

An AMR Lens on Development Finance

The World Bank Group will review its own investment lending policies and instruments to support the AMR agenda across relevant sectors. We will also strengthen our institutional capacity on the ground in technical areas that can optimize our services to countries as they advance national AMR agendas.

Relevant sectors for World Bank Group investing include, but are not limited to, agriculture; water and sanitation; and urban development, in addition to the health, nutrition, and population sector itself. As the Bank Group weighs investment options in dialog with country leaders and partners, we will apply an AMR lens to identify those projects that hold promise for AMR-sensitive impacts. We will design projects to maximize these impacts.

The World Bank Group will also progressively incorporate AMR-related gains into the calculations used when assessing likely costs and benefits of projects competing for support. Over time, the systematic inclusion of an AMR perspective in investment conversations may evolve towards the creation of a formal screening instrument similar to the World Bank's mandatory Climate and Disaster Risk Screening tools.

Mobilizing Finance for AMR Innovation across Agriculture and Health

Investment in the AMR knowledge agenda must nurture new technologies in both animal and human health. It should also create connections and harness synergies between the two. To foster this kind of innovation, the World Bank will seek to engage existing multidisciplinary research networks, donors, and other partners around the idea of a combined animal and human health research center on AMR. Promising conversations have begun, and may advance to a detailed feasibility study. The effort may develop as a multifaceted collaboration, along the lines of the successful Coalition for Epidemic Preparedness Innovations (CEPI).

Bringing the Private Sector on Board

The private sector can contribute substantially to tackling AMR, and private-sector capacities and creativity in this area are only just beginning to be tapped. The World Bank Group's ability to engage national and global business actors is a strong comparative advantage.

The International Finance Corporation (IFC) is the arm of the Bank Group that invests in and advises private-sector companies. IFC is active in the animal protein sector through investment and advisory work. In engagement with its clients in animal production, IFC reviews operational practices and provides benchmarking for clients on good industry practices, including the use of veterinary services and antibiotics. IFC will seek to deepen this partnership by developing a more focused advisory offering as part of its animal protein advisory platform. Where government regulations evolve

towards a more focused use of antibiotics, IFC will seek to partner with private producers and their associations to support the transition of the sector through management practices and investment.

IFC is also active in the private health care sector, mainly through the support of health service providers and companies that manufacture or distribute affordable pharmaceuticals or medical devices. IFC has developed a Quality Assessment Tool used to assess health service companies on various clinical governance and patient safety criteria. IFC plans to enhance this tool and, in the process, incorporate best practices for implementing policies, protocols, and training around antimicrobial drug use.

A clear opportunity for private-sector engagement in the AMR challenge is for pharmaceutical and biotech firms to pursue development of new antimicrobials and related technologies, such as rapid diagnostic tests that could inform antimicrobial prescribing decisions at the point of care. The complex topic of antimicrobial drug development is well analyzed elsewhere (Review on Antimicrobial Resistance 2015). Here, we note only that the World Bank Group and other development finance institutions might play a role in creating fresh incentives for pharmaceutical companies to engage in antimicrobial research. One approach is “delinking” company profits for any new antimicrobial product from the actual sales volumes, through a number of possible mechanisms. Country policy makers, in particular among the G77, have pressed for the implementation of delinking strategies.

Leveraging UHC Reforms to Reach AMR Objectives

In the World Bank’s health sector practice, action on AMR containment will mesh with ongoing work programs on (1) health systems strengthening through UHC reforms, and (2) emergency preparedness and resilience.

Many countries are currently carrying forward ambitious UHC reforms with World Bank support, and more are poised to adopt UHC goals. As suggested above, countries’ commitment to implement UHC provides multiple opportunities to reinforce AMR containment. The World Bank will work through its policy dialog and technical collaboration around UHC to support countries in leveraging health systems reforms to accelerate progress on AMR.

AMR and Resilient Health Systems: The Agendas Converge

Currently, the World Bank is financing improvements in core public-health functions in multiple countries, notably for disease surveillance and laboratory strengthening. These investments reflect a broad consensus on the need to strengthen global health security and reinforce preparedness.

We have emphasized that AMR is part of a wider spectrum of infectious threats that generate outbreaks with epidemic and pandemic potential. Thus, the AMR and health emergency preparedness agendas are intertwined. The consolidation of core human and animal public-health capacities; the creation of health systems resilient to emergencies; and the AMR fight reflect largely convergent and mutually reinforcing agendas. The World Bank will expand its action to help countries capitalize on these synergies.

Action Today—To Preserve Tomorrow

Many important aspects of the AMR threat lie beyond the scope of this report. Yet we hope our work can clarify implications of AMR that have been insufficiently understood, and help point the way toward viable solutions.

Those who will benefit most do not have a voice. Many of them have not yet been born. AMR is indeed a threat to our economic future, but above all to the future of our children. Bold action today can safeguard the health and prosperity of those who will come after us.

References

- FAO (United Nations Food and Agriculture Organization). 2016. *The FAO Action Plan on Antimicrobial Resistance 2016–2020*. Rome: FAO.
- OIE (World Animal Health Organisation). 2016. *The OIE Strategy on Antimicrobial Resistance and the Prudent Use of Antimicrobials*. Paris: OIE.
- Rainey R. and Weinger M. 2016. “The role of water, sanitation and hygiene (WASH) in healthcare settings to reduce transmission of antimicrobial resistance.” In World Alliance Against Antibiotic Resistance (WAAAR). *AMR Control 2016*. Available at: <http://resistancecontrol.info/infection-prevention-and-control/the-role-of-water-sanitation-and-hygiene-wash-in-healthcare-settings-to-reduce-transmission-of-antimicrobial-resistance/>
- Review on Antimicrobial Resistance. 2015. *Securing New Drugs for Future Generations: The Pipeline of Antibiotics*. London: Wellcome Trust and Government of the United Kingdom.
- . 2016. *Tackling Drug-Resistant Infections Globally: Final Report and Recommendations*. London: Wellcome Trust and Government of the United Kingdom.
- Wellcome Trust. 2016. *Evidence for Action on Antimicrobial Resistance*. London: Wellcome Trust.
- WHO (World Health Organization). 2015. *Global Action Plan on Antimicrobial Resistance, 2015–2019*. Geneva: WHO.

Today, in countries at all income levels, people are dying from infections that used to be curable.

Antimicrobial medicines, including the antibiotics that treat bacterial infections, have been mainstays of health care for 70 years. These medications have saved hundreds of millions of lives and substantially accelerated economic growth. Now, they are losing their power, as disease-causing microbes relentlessly mutate to elude them, health systems fail to manage drugs wisely, and research on new antimicrobials remains stalled.

Harmful microorganisms' acquired capacity to withstand the drugs designed to kill them is called antimicrobial resistance (AMR). While AMR has long preoccupied the health sector, this report expands the conversation from medicine and public health to economics. The report uses World Bank Group economic simulation tools to put a price tag on AMR's destructive impacts on the global economy from 2017 through 2050. It shows that, unchecked, drug-resistant infections will severely reduce global economic output and hobble development progress in the decades ahead.

But these destructive effects can be avoided. The report highlights actions low- and middle-income countries and their development partners can take to counter AMR, and estimates the investment required.

Analyzing costs and benefits under multiple outcome scenarios, the report shows that putting resources into AMR containment now is one of the highest-yield investments countries can make. By investing in the fight against drug resistance, low-, middle-, and high-income countries will all reap exceptional economic rewards.

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