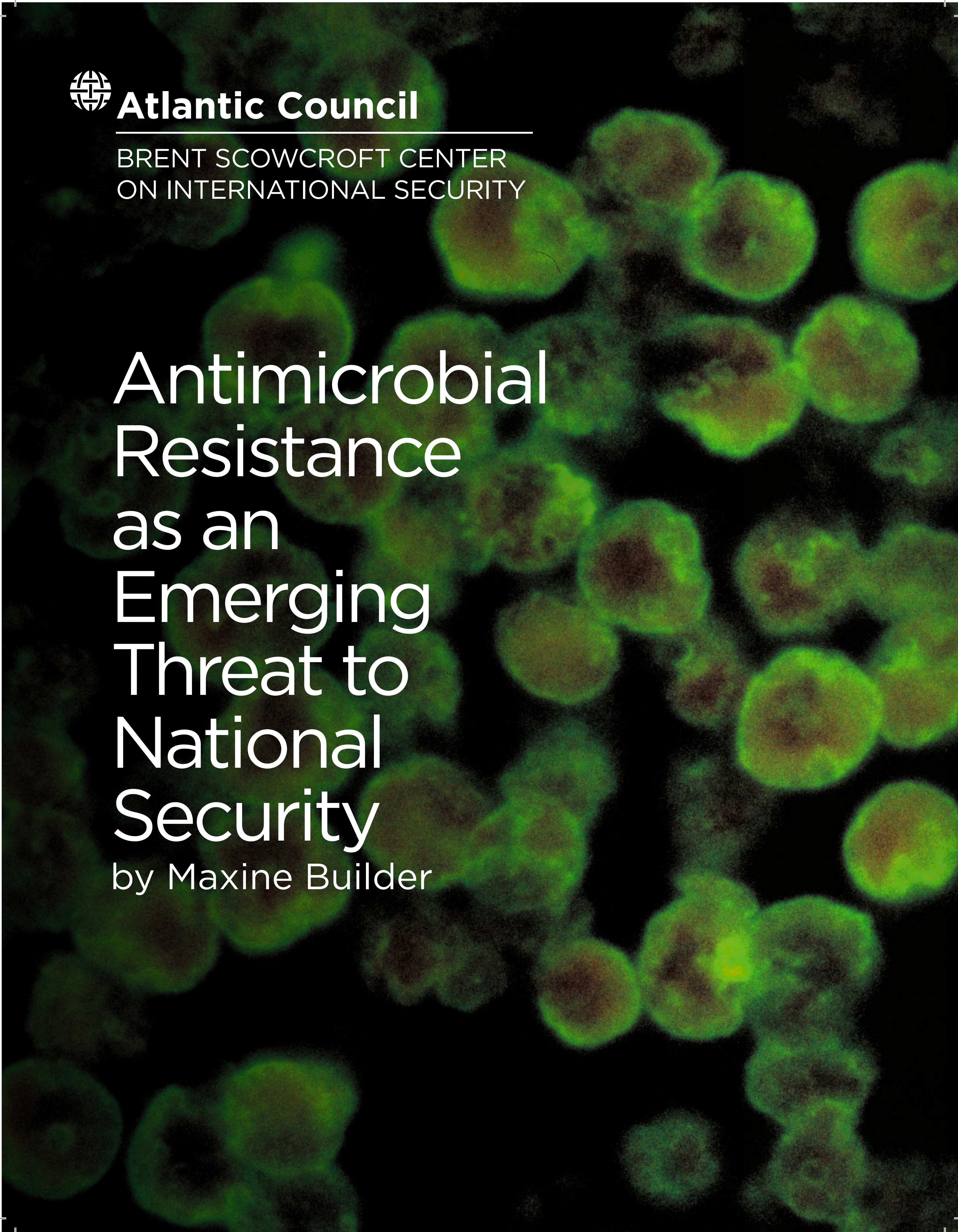


Atlantic Council

BRENT SCOWCROFT CENTER
ON INTERNATIONAL SECURITY

Antimicrobial Resistance as an Emerging Threat to National Security

by Maxine Builder

Antimicrobial Resistance as an Emerging Threat to National Security

BY MAXINE BUILDER

Atlantic Council

Atlantic Council
1030 15th Street, NW, 12th Floor
Washington, DC 20005

ISBN: 978-1-61977-050-8
December 2014

Transatlantic Partnership for the Global Future

The Transatlantic Partnership for the Global Future brings together experts from government, business, academia, and the science and technology communities to address critical global challenges and assess their effects on the future of transatlantic relations. The Partnership is a collaboration between the Brent Scowcroft Center on International Security's Strategic Foresight Initiative and the Government of Sweden. Together, we seek to make foresight actionable by connecting long-term trends to current challenges to inform policy and strategy choices.

REGERINGSKANSLIET

Government Offices of Sweden

This report is written and published in accordance with the Atlantic Council Policy on Intellectual Independence. The author is solely responsible for its analysis and recommendations. The Atlantic Council, its partners, and funders do not determine, nor do they necessarily endorse or advocate for, any of this report's particular conclusions.

Executive Summary

Growing rates of antimicrobial resistance (AMR) pose a threat to public health that could undo many of the medical advances made over the last seventy years, eroding the global medical safety net and posing a significant threat to national security. Diseases once eliminated by a single course of antibiotics show drug resistance, often to several different classes of drugs. Some of the implications of increasing rates of AMR are intuitive, such as longer duration of illness, extended hospital stays, and higher rates of mortality. But other effects of a postantibiotics world are less obvious, such as the inability to perform life-saving operations or the ability for a simple scratch on the arm to kill. Humanity could soon find itself living in a reality in which communicable diseases such as tuberculosis, cholera, pneumonia, and other common infections cannot be controlled. This potentially catastrophic problem still can be abated, and the global health community, including the World Health Organization (WHO), has highlighted AMR as a priority in global health. But all sectors of the international community, not simply those in public health, need to take immediate steps to reverse the current trends and eliminate the systematic misuse of antimicrobial drugs, especially in livestock, and restore the pipeline of new antimicrobial drugs.

> All sectors of the international community need to take immediate steps to reverse the current trends and eliminate the systematic misuse of antimicrobial drugs and restore the pipeline of new antimicrobial drugs.

The significant health and economic costs of AMR are difficult to quantify due to incomplete data that often underreports the extent of the problem, since there are no standard metrics or consensus on methodology to measure rates of AMR. But even the piecemeal statistics that exist paint a bleak picture. In a 2013 report, the US Centers for Disease Control and Prevention (CDC) reports at least two million Americans acquire serious infections to one or more strains of AMR bacteria annually, and at least 23,000 people die of these infections.[1] A 2008 study estimated the excess direct costs to the US medical system attributable to AMR infections at $20 billion, with additional estimated productivity losses to be as high as $35 billion.[2] With the increase in resistant infections and continuing rise in medical costs, the cost to the American medical system no doubt also has increased.

This trend is not a uniquely American problem; it is truly global in scope. The European Union (EU) reports about 25,000 deaths annually due to drug-resistant bacteria, at an overall, combined cost of $2 billion in healthcare costs and productivity losses.[3] There were over 14.7 million incidents of moderate-to-severe adverse reactions to antibiotics each year between 2001 and 2005 in China. Of these, 150,000 patients died annually.[4] The most recent available data on China estimates that treatment of AMR infections during that same time period cost at least $477 million, with productivity losses of more than $55 million each year.[5] A 2005 study of the United Kingdom (UK) found that the real annual gross domestic losses due to AMR were between 0.4 and 1.6 percent.[6] Although slightly outdated, this estimate may be a useful guide in assessing the global impact of AMR, and given the trend of increasing resistance, it is likely that the impact will also increase accordingly. That said, it is prudent to repeat that the disparities in the quality of data reporting standards across China, the United States, the United Kingdom, and the European Union make it difficult to directly compare the severity of the impacts AMR has on each entity.

1 Centers for Disease Control and Prevention, *Antibiotic Resistance Threats in the United States, 2013* (Washington, DC: US Department of Health and Human Services, 2013), p. 11.

2 Ibid, p. 26.

3 Davies et al., *The Drugs Don't Work*, p. 31.

4 Yan Li, "China's Misuse of Antibiotics Should Be Curbed," *The BMJ* 348, February 12, 2014, p. g1083.

5 Janet Currie, Wanchuan Lin, and Wei Zhang, "Patient Knowledge and Antibiotic Abuse: Evidence from an Audit Study in China," Working Paper 16602, National Bureau of Economic Research, December 2010, p. 4.

6 Richard D. Smith, et al., "Assessing the Macroeconomic Impact of a Healthcare Problem: The Application of Computable General Equilibrium Analysis to Antimicrobial Resistance," *Journal of Health Economics* 24, November 2005, p. 1069.

The primary cause of AMR globally is antibiotic overuse and misuse, be it from doctors inappropriately prescribing antibiotics to treat viral infections or individuals seeking over-the-counter antibiotics for self-treatment. But another driver, less obvious than overuse in humans, is the use of antimicrobials in livestock, and the ratio of use in animals as compared to humans is astounding. In the United States, about 80 percent of all antibiotics are consumed in either agriculture or aquaculture. Generally, these drugs are administered to livestock as growth promoters and are medically unnecessary. Resistance in livestock quickly spreads to humans, and many community-acquired infections are the result of a contaminated food supply. Although most infections are acquired in the community, most deaths attributed to resistant infections occur in healthcare settings, and healthcare-acquired (or nosocomial) infections are another driver of AMR.

At this point, AMR does not pose an immediate and direct threat to national security. Rather, this is a creeping global security crisis. If current trends continue, these drugs upon which the world relies will lose effectiveness. The gains made in fighting infectious diseases will be reversed, and a wide range of routine surgeries and easily treatable infections will become much more dangerous and deadly. This will cause the health of the world's working population to deteriorate, and the economic productivity and social cohesion of the globe to decline. At any time, a "black swan" event—triggered by an outbreak of drug-resistant tuberculosis, cholera, or pneumonia, for example—could prove catastrophic, endangering the fabric of societies and our globalized economy, forcing a stop to international trade and travel to prevent further spread.

The issue of AMR is a tragedy of the commons in which individual incentives lead to the overuse and eventual destruction of a shared resource. International cooperation is required to walk back from this ledge and avoid a postantibiotics world, even though it is impossible to completely reverse the damage already done.

If current trends continue, these drugs will lose effectiveness. The gains made in fighting infectious diseases will be reversed, and a wide range of routine surgeries and easily treatable infections will become much more dangerous and deadly.

Table of Contents

The Growing Scale of AMR

In the preantibiotic era, an infection as simple as a sore throat could be a death sentence. A cut on the arm, if infected, could lead to a life-threatening fever or even organ failure. Diseases that are now barely thought of in the United States and Europe, such as pneumonia, tuberculosis, and dysentery, ran rampant in the early twentieth century; communicable diseases such as these caused one-third of all deaths in the United States in 1900.[1] Over the past seventy years, the global burden of disease has shifted from communicable diseases to noncommunicable diseases, such as heart disease and cancer, in part because of the widespread introduction of antibiotics. The WHO estimates that antimicrobial drugs, such as antibiotics, add an average of twenty years to the life of every individual.[2]

Antimicrobials refer to three specific classes of drug—antibiotics, antivirals, and antifungals—that are responsible for fighting bacteria, viruses, and fungi, respectively. Resistance is a naturally occurring process that arises as a result of normal mutations in microbes, but the rate at which resistance is spreading has been rapidly growing with increased reliance on antimicrobial drugs. All antimicrobial usage creates a selection pressure that provides a competitive advantage to certain mutated strains that survive a course of antimicrobial drugs. The drugs will eliminate the weaker organisms, leaving the strong ones behind, allowing them to adapt and subsequently reproduce.[3] Although resistance occurs in all three classes of drugs, most of the recent alarm has been raised around the issue of antibiotic resistance. In its most recent report on the AMR threat, the WHO focused its survey on the threat of antibacterial resistance in common bacterial pathogens.[4]

Evolution in microorganisms, even without the presence of antimicrobial drugs, is quick. It takes bacterial colonies, such as *Escherichia coli* (*E. coli*), only twelve to twenty-four hours to spread and divide into a new generation. In optimal conditions, the generation time can be as rapid as twenty minutes.[5] Resistance to an antimicrobial can therefore develop in days, and spread easily among microorganisms, either vertically or horizontally. Vertical transfer of resistance happens during the normal reproductive process of microbes, from one generation to the next. Horizontal transfer occurs when individual microorganisms share or exchange sections of genetic material; this kind of transfer can happen both within and between species, meaning once resistance is found in one species it can spread to another.

Drug resistance can also spread through plasmids, tiny DNA packages that bacteria draw upon for resistance when antibiotics are present. When the threat passes, bacteria will pop the plasmids back out into the surrounding biofilm, allowing emphasis to switch to bacterial virulence genes. Drug resistance therefore can be swapped between bacteria as needed, much like a lending library. New Delhi metallo-beta-lactamase 1 (NDM-1) is one such plasmid. First identified in a Swedish patient of Indian origin in 2008, it since has spread globally with reports from the United States, the United Kingdom, the Netherlands, Oman, Hong Kong, and Kenya. Absorption of this plasmid renders bacteria functionally incurable, making treatment far more difficult, and sometimes leaving palliative care as the only treatment option. Many of the patients who contracted NDM-positive bacteria had no history of foreign travel, demonstrating the role of globalization in dissemination of resistance, and the insipid ability of resistant microbes to rapidly spread around the world.[6]

The increase in AMR in this antibiotics era has been swift. A study of 1,729 *E. coli* samples from the United States over six decades found the proportion of multidrug resistant pathogens increased from 7.2 percent in the 1950s to 63.6 percent in the early 2000s.[7] In China, rates of antibiotic resistance among the ten most common bacteria, including *E. coli*, increased by 22 percent in less than a decade, between 1994 and 2001 (the most recent period for which data is available).[8] It should be noted that *E. coli*, particularly carbapenem-resistant strains, are resistant to all or nearly all antibiotics available today; the CDC, in its 2013 threat assessment of antibiotic resistance, classified it in the highest priority threat level.[9]

The increase in AMR is correlated with the increased consumption of antibiotics, which has several drivers.[10] Part of the increase in overall antibiotics usage comes

1 "Achievements in Public Health, 1900-1999: Control of Infectious Diseases," *Morbidity and Mortality Weekly Report* 48 (July 30, 1999): 621.
2 Sally C. Davies, Jonathan Grant, and Mike Catchpole, *The Drugs Don't Work: A Global Threat* (London: Penguin Specials, 2013): ix.
3 Ruifang Zhang et al., "Antibiotic Resistance as a Global Threat: Evidence from China, Kuwait and the United States," *Globalization and Health* 2, April 7, 2007, p. 6.
4 World Health Organization, *Antimicrobial Resistance: Global Report on Surveillance 2014* (Geneva, Switzerland: World Health Organization, April 2014): pp. ix-x.
5 Davies et al., *The Drugs Don't Work: A Global Threat*, pp. 5-7.
6 Alan P. Johnson and Neil Woodford, "Global Spread of Antibiotic Resistance: the Example of New Delhi Metallo-β-lactamase (NDM)-mediated Carbapenem Resistance," *Journal of Medical Microbiology* 62, April 2013, pp. 499-500.
7 Johns Hopkins Center for a Livable Future, *Industrial Food Animal Production in America: Examining the Impact of the Pew Commission's Priority Recommendations* (Baltimore: Johns Hopkins, 2013), p. 4.
8 Zhang et al., "Antibiotic Resistance as a Global Threat," p. 6.
9 CDC, *Antibiotic Resistance Threats in the United States, 2013*, p. 53.
10 Brian G. Bell et al., "A Systematic Review and Meta-analysis of the Effects of Antibiotic Consumption on Antibiotic Resistance," *BMC Infectious Diseases* 14, 2014, pp. 8-9.

from inappropriate prescription of antibiotics. Total rates of prescriptions for antibiotics in the United States have been decreasing, but of those outpatient prescriptions, as many as 50 percent are medically unnecessary. The superfluous use of broad-spectrum antibiotics in fighting infections increases the rate of resistance by giving bacteria the opportunity to develop resistance to a wider range of drugs. Despite this danger, the proportion of prescriptions for broad-spectrum antibiotics, which act against all families of bacteria (as compared to narrow-spectrum antibiotics that are targeted to one specific family), increased from 41.0 percent to 76.8 percent between 1995 and 2002.[11]

The use of antibiotics in treatment of infections is well known and understood by most people, but antibiotics are also regularly used in prevention of infections. The preventative administration of antibiotics allows for the safe completion of complex and invasive surgical procedures, such as hip replacements, organ transplants, and open-heart surgeries. These operations would be too dangerous to even attempt without the prophylactic use of antibiotics, due to the high risk of postoperative infections. An estimated 30 to 40 percent of patients undergoing a total hip replacement would have a postoperative infection if not for precautionary antibiotics. Of those infectious, about 30 percent would be fatal.[12] If the drugs lose effectiveness, these surgeries would be medically too risky, and the inability to complete these currently routine and quality-of-life improving procedures would be a major feature of a postantibiotics world.

In Europe, about 50 percent of people believe that antibiotics can be used to treat influenza or a cold, even though both are viral infections.

Increased antibiotics usage—both medically appropriate and not—is not limited to developed countries. Developing countries, particularly in Asia and Latin America, also have been using more antibiotics. The increase is associated with the recent increase in wealth, allowing for greater access to these previously costly drugs. In India, for example, per capita antibiotics use increased by 37 percent in five years, between 2005 and 2010.[13] Rates are higher in China, where the Ministry of Health estimates each Chinese individual consumes about 138 grams of antibiotics per year, about ten times more than each individual in the United States.[14]

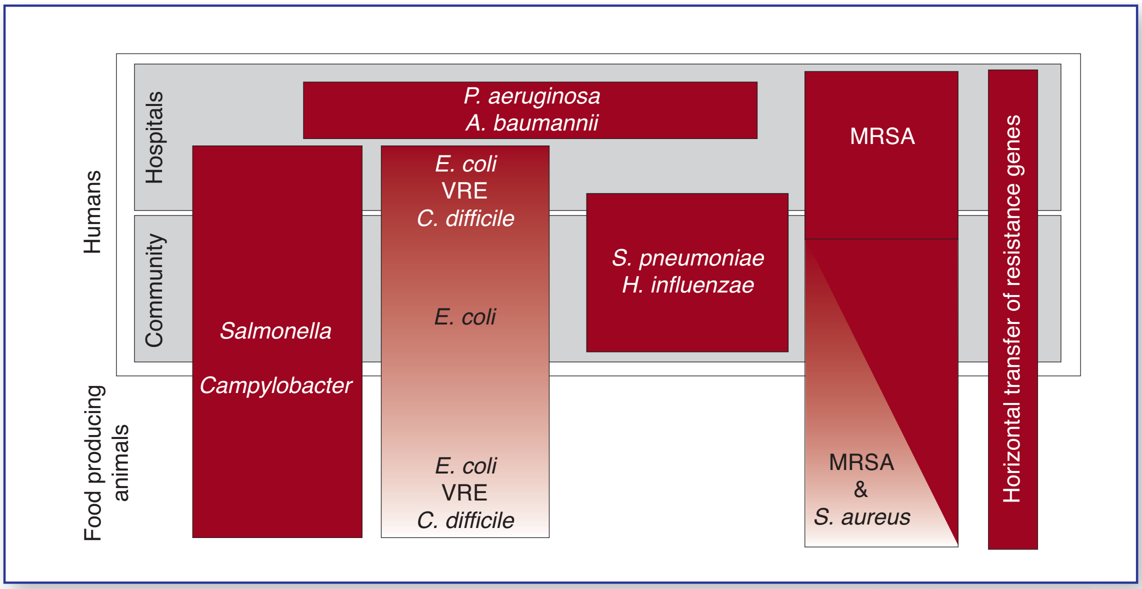
In developing countries, the danger of infectious diseases is still high, further complicating the issue of AMR. There is a common belief that these drugs are a panacea, so individuals will indiscriminately take the drugs regardless of diagnosis or symptoms in the hopes of seeing a quick cure. This perception is not limited to developing countries. In Europe, for example, about 50 percent of people believe that antibiotics can be used to treat influenza or a cold, even though both are viral infections against which antibiotics are useless.[15]

The ability to obtain antibiotics without a prescription in many developing countries encourages this inappropriate and unnecessary usage. In a Brazilian study, antibiotics could be obtained without a prescription from 70 to 97 percent of surveyed pharmacies, and in the few cases where antibiotics were denied to customers, it was only due to lack of prescription 7.5 percent of the time.[16] The rates were similar in a comparable survey of Indian pharmacies; a little over 50 percent of pharmacists issued antimicrobial drugs without a prescription, and 79 percent of pharmacists did not ask the customer about his or her symptoms before administering these drugs.[17] The lack of a strong regulatory system leads to widespread misuse and abuse of antibiotics, again leading to higher risk of AMR.

The higher rates of substandard and counterfeit drugs in developing countries exacerbate the problem of resistance, and many individuals—even when prescribed by a doctor—unintentionally take antibiotics at subtherapeutic levels. Approximately 10 percent of India's pharmaceutical market, a measure that includes antimicrobials, is comprised of substandard or illegal

11 Christianne L. Roumie, et al., "Trends in Antibiotic Prescribing for Adults in the United States—1995 to 2002," *Journal of General Internal Medicine* 20, August 2005, pp. 697-702.
12 Richard Smith and Joanna Coast, "The True Cost of Antimicrobial Resistance," *The BMJ* 346, March 11, 2013, p.f1493.
13 Ramanan Laxminarayan and David L. Heymann, "Challenges of Drug Resistance in the Developing World," *The BMJ* 344, April 3, 2012, p. e1567.
14 Li, "China's Misuse of Antibiotics Should Be Curbed," p. g1083.
15 Davies et al., *The Drugs Don't Work*, p. 47.
16 Dalton Espíndola Volpato et al., "Use of Antibiotics without Medical Prescription," *Brazilian Journal of Infectious Diseases* 9, August 2005, pp. 288-91.
17 U.P. Rathnakar et al., "A Study on the Sale of Antimicrobial Agents without Prescriptions in Pharmacies in an Urban Area in South India," *Journal of Clinical and Diagnostic Research* 6, August 2012, pp. 952-53.

Reservoirs of AMR Bacteria Causing Human Infections



Schematic overview of some of the most important antimicrobial resistant pathogens and the overlap between the different reservoirs. As indicated some pathogens are strictly confined within the human reservoir, whereas others have a mainly or partly animal reservoir.

Source: Centers for Disease Control and Prevention, *Antibiotic Resistance Threats in the United States*, 2013.

drugs.[18] In the same way that taking an incomplete course of antibiotics hastens resistance, taking substandard antimicrobial drugs has a comparable effect because it does not fully eliminate all of the microbes and allows those that remain an opportunity to adapt and evolve.

China, the world's largest consumer of antibiotics, has been struggling with these issues associated with the rational use of antibiotics. Chinese doctors are guilty of overprescribing and misprescribing antibiotics to patients at higher rates than anywhere else. Two-thirds of inpatients in China are prescribed antibiotics, as compared to about one-third of inpatients in other countries.[19] This increased rate of prescription is not necessarily related to a higher rate of bacterial infections. Rather, approximately 75 percent of Chinese patients diagnosed with seasonal influenza are prescribed antibiotics to treat this viral infection.[20] A survey of clinics in rural western China found approximately 50 percent of prescriptions contained antibiotics.[21]

These inappropriate prescriptions could be a result of poor education among doctors about proper antibiotics usage, but there could be a more selfish motive. Physicians' salaries are linked to prescription rates so Chinese doctors have a personal incentive to write prescriptions, and will receive payments of up to 20 percent of the value of the prescription, along with kickbacks from pharmaceutical companies.[22] This creates an economy of physician-induced demand, skewing the actual need for these drugs and encouraging irresponsible use of antibiotics. The Chinese government has, since 2011, begun to realign incentives to promote more rational antibiotics usage. Data released by the Chinese Ministry of Health indicates that these policies—including target-setting and education—have caused the percentage of prescriptions of antimicrobials to fall below 60 percent among inpatients, but that number is still well above the average for developed countries.[23]

Antibiotics Overuse in Livestock

Misuse and overuse of antibiotics in humans are important drivers of AMR, but just as important, though less obvious, is the overuse of antibiotics in livestock as antibiotic growth promoters (AGPs). The ratio of use of antibiotics in animals compared to humans is astounding. In the United States, about 80 percent of all antibiotics are consumed in either agriculture or aquaculture. In absolute terms, approximately 13,540,000 kilograms of antibiotics are purchased for use in livestock, as compared to only

18 *Ibid.*
19 Janet Currie, Wanchuan Lin, and Wei Zhang, "Patient Knowledge and Antibiotic Abuse: Evidence from an Audit Study in China," Working Paper 16602, National Bureau of Economic Research, December 2010, p. 1.
20 Li, "China's Misuse of Antibiotics Should Be Curbed," p. g1083.
21 Yonghong Xiao et al., "Changes in Chinese Policies to Promote the Rational Use of Antibiotics," *PLOS Medicine* 10, November 19, 2013, p. e1001556.
22 Currie et al., "Patient Knowledge and Antibiotic Abuse," p. 4.
23 Xiao et al., "Changes in Chinese Policies to Promote the Rational Use of Antibiotics," p. e1001556.

3,290,000 kilograms for use in humans.[24] Antibiotic use in livestock is neither collected by nor reported to any US government agency, so these numbers are pulled from sales data collected by pharmaceutical companies as a proxy for actual usage.

AGPs are not technically considered antibiotics by the pharmaceutical industry, but they are only one chemical group different from the human antibiotics to which they are related. The change is so minor the drugs are functionally the same, and when resistance develops against the growth promoter, resistance also develops in human antimicrobial drugs. AGPs are added directly to the feed of livestock in agriculture and the water of fish in aquaculture, so there is daily exposure. The drugs cause an increase in fat content, increasing the amount of cholesterol and causing the animal to weigh more, but also have the effect of encouraging resistance. Although it is important to give antibiotics to diseased livestock, the use of antibiotics as growth promoters is medically unnecessary and drives up the rates of resistance with few benefits to food security. As demonstrated by countries that have eliminated the use of AGPs, it is possible to have a secure and consistent food supply without reliance on these drugs. If anything, the health risks incurred by increased outbreaks of food-borne illnesses may outweigh benefits of using AGPs, especially since the mechanisms by which resistance is passed from livestock to humans are well documented.

> People with high levels of exposure to manure were 38 percent more likely to acquire community-acquired MRSA and 30 percent more likely to acquire healthcare-associated MRSA.

Livestock-acquired methicillin-resistant *Staphyococcus aureus* (*S. aureus*) (LA-MRSA) was first reported in Europe in 2004 among farm workers. This population is at an increased risk due to regular, direct contact with animals. A sample of twenty swineherds in Canada found 25 percent of the pigs were positive for MRSA, along with 20 percent of the swine farm workers.[25] There is also strong evidence that individuals living near pig farms or agricultural fields fertilized with pig manure are more likely to acquire a resistant infection, such as MRSA. MRSA is one of the most virulent AMR infections, resistant to multiple antibiotics.[26] In its prioritization of microorganisms in terms of antibiotic resistance threats, the CDC categorized MRSA in the second most urgent category, a serious threat.[27] People with high levels of exposure to manure—based on proximity to farms, size of farms, and amount of manure used—were 38 percent more likely to acquire community-acquired MRSA (CA-MRSA) and 30 percent more likely to acquire healthcare-associated MRSA (HA-MRSA).[28]

But living or working near a farm is not the only risk factor, and living far from the source does not provide protection. Resistant bacteria can spread to other environments, from rivers and streams to the Arctic. Feces of polar bears in Svalbard, Norway, an archipelago in the Barents Sea, with little human contact, contained low levels of resistance, likely to be anthropogenic.[29] Once resistant genes exist in the environment, it is all but impossible to mitigate their spread to other species. Up to 75 percent of antibiotics fed to livestock are excreted unaltered into the environment and may remain in the soil, and resistant bacteria from the feces can remain on crops, or in fertilizer.[30]

Resistance can also spread by human consumption of resistant bacteria when food is improperly handled or not cooked thoroughly. The bacteria will then colonize the human gut, making people ill and further spreading resistance. Bacteria can also spread resistance across species within the human gut once introduced, and resistant genes disseminate through the food chain.[31]

---

24 Aidan Hollis and Ziana Ahmed, "Preserving Antibiotics, Rationally," *New England Journal of Medicine* 369, December 26, 2013, p. 2474.

25 Tara C. Smith, et al., "Methicillin-Resistant *Staphylococcus aureus* in Pigs and Farm Workers on Conventional and Antibiotic-Free Swine Farms in the USA," *PLOS One* 8, May 7, 2013, p. e63704.

26 B.S. Cooper, et al., "Methicillin-resistant *Staphylococcus aureus* in Hospitals and the Community: Stealth Dynamics and Control Catastrophes," *Proceedings of the National Academy of Sciences of the United States of America* 101, July 6, 2004, p. 10223.

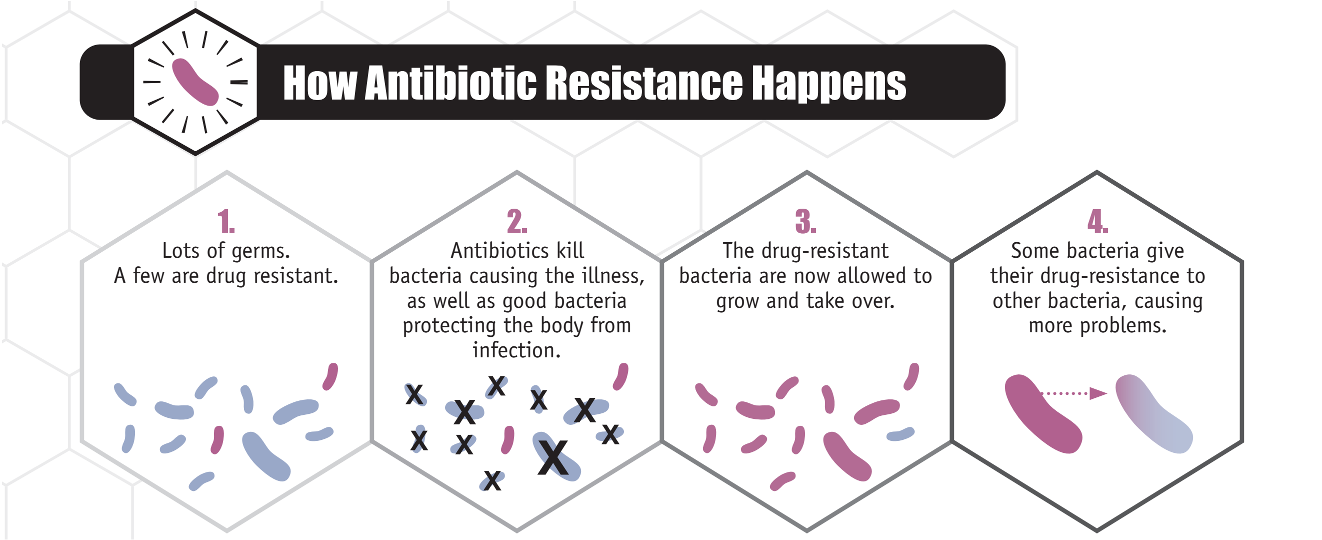
27 CDC, *Antibiotic Resistance Threats*, p. 58. A 'serious' threat is defined by the CDC as a bacteria of serious concern that requires prompt and sustained action to prohibit its growth.

28 Sarah Zhang, "Pig-manure Fertilizer Linked to Human MRSA Infections," *Nature*, September 16, 2013, http://www.nature.com/news/pig-manure-fertilizer-linked-to-human-mrsa-infections-1.13752.

29 Trine Glad, et al., "Bacterial Diversity in Feces from Polar Bear (*Ursus maritimus*) in Arctic Svalbard," *BMC Microbiology* 10, 2010, p. 10.

30 Johns Hopkins Center, *Industrial Food Animal Production in America*, 6; CDC, *Antibiotic Resistance Threats*, 14.

31 CDC, *Antibiotic Resistance Threats*, 14; Anthony E. van den Bogaard and Ellen E. Stobberingh, "Epidemiology of Resistance to Antibiotics: Links between Animals and Humans," *International Journal of Antimicrobial Agents* 14, 2000, p. 332.



Source: Centers for Disease Control and Prevention, *Antibiotic Resistance Threats in the United States*, 2013.

There is little opposition to the administration of antibiotics to livestock in order to treat infected animals, but there is increasing pressure to eliminate nontherapeutic uses of antibiotics and AGPs in livestock. EU countries are leaders in this regard. Sweden banned farm use of antibiotic growth promoters in 1986.[32] Denmark banned AGPs next, followed by the United Kingdom, and eventually the entire European Union banned usage of all AGPs in 2006.[33] Evidence from these countries demonstrates it is possible to maintain high levels of meat production while decreasing use of unnecessary antibiotics, and, in turn, decreasing rates of resistance. In Denmark, production of swine increased by 47 percent between 1992 and 2008, as antimicrobial use dropped by 51 percent.[34] The costs incurred by removing AGPs from pig and poultry production were estimated at $1.42 per pig produced, with no changes in poultry production.[35]

There is limited data to determine the health effects on humans, but no major outbreaks of AMR infections have occurred in humans since the ban, and the prevalence of resistant microbes, especially among enterococci, has dramatically decreased among livestock.[36] In the United States, where there is still debate on this issue, the US Food and Drug Administration (FDA) finally launched a plan to reduce antibiotics used in livestock in April 2012. Although voluntary, it does seem as though US agricultural companies are willing to make the necessary changes. As of March 26, 2014, twenty-five of twenty-six veterinary drug manufacturers agreed to cooperate with new labeling guidelines that ban over-the-counter sales of AGPs that are medically identical to antibiotics used in humans.[37]

Community-acquired and Nosocomial Infections

Resistance in livestock quickly spreads to humans, and many community-acquired infections are the result of a contaminated food supply. Some common community-acquired infections include *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Neisseria meningitides*, and *E. coli*, and many have evolved to reach unexpected levels of resistance to first-line antibiotics like penicillin.[38] Another example of the risk posed by AMR community-acquired infections is community-acquired MRSA (CA-MRSA), which began circulating in US communities in the 1990s. A metaanalysis of studies of CA-MRSA in the United States found the prevalence of MRSA increased, from 32.7 percent in 1998 to 53.8 percent in 2007; of these, CA-MRSA also increased in prevalence, increasing its share of MRSA from 22.3 percent of cases in 1998 to 66.1 percent in 2007.[39] These reservoirs of MRSA outside of healthcare facilities means that attempts to contain MRSA in the hospital setting are unlikely to succeed without a similar infection control mechanism

32 Dan Charles, "FDA Launches Voluntary Plan to Reduce Use of Antibiotics in Animals," National Public Radio, April 11, 2012, http://www.npr.org/blogs/thesalt/2012/04/11/150432234/fda-launches-voluntary-plan-to-reduce-use-of-antibiotics-in-animals; Carol Coglianim, Herman Goosens, and Christina Greko, "Restricting Antimicrobial Use in Food Animals: Lessons from Europe," *Microbe* 6, 2011, p. 274.
33 Cogliani et al., "Restricting Antimicrobial Use in Food Animals," p. 278.
34 Ibid, p. 276.
35 World Health Organization, *Impacts of Antimicrobial Growth Promoter Termination in Denmark*, WHO/CDS/CPE/ZFK/2003.1 (Foulum, Denmark: World Health Organization, 2003), p. 8.
36 Ibid.
37 Maryn McKenna, "Farm-Drug Companies Agree to Antibiotics Ban. More of the Same, or Fresh Start?" *Wired*, March 28, 2014, http://www.wired.com/2014/03/fda-213-companies/.
38 Herman Goosens and Marc J.W. Sprenger, "Community Acquired Infections and Bacterial Resistance," *The BMJ*, 317, September 5, 1998, p. 654.
39 Robertino M. Mera, "Increasing Role of *Staphylococcus aureus* and Community-Acquired Methicillin-Resistant *Staphylococcus aureus* Infections in the United States: A 10-Year Trend of Replacement and Expansion," *Microbial Drug Resistance* 17, June 2011, pp. 321-28.

in the community.[40] CA-MRSA has an impact on a much broader segment of the population; at-risk groups include professional and amateur athletes, indigenous populations, military personnel, urban underserved communities, and children.[41]

Most infections are acquired in the community, but most deaths attributed to resistant infections occur in the healthcare setting. Healthcare facilities have long been recognized as a breeding ground for resistant infections. Healthy individuals have a natural resistance to infection, but patients in hospitals—including people with underlying diseases, newborn babies, and the elderly—are less likely to have strong levels of general resistance.

A bigger problem than patient immunity is that patients have many opportune points of infection; intravenous drip lines, catheters, surgical wounds, and injections can quickly become colonization sites for bacteria. Hospital-acquired infections spread through contact with healthcare personnel, contact with other patients, or contact with the inanimate environment.[42] They also can occur as a result of improper infection control techniques while conducting any of the aforementioned invasive procedures, and, even more simply, because of improper hand washing among healthcare workers. About 40 percent of hospital-acquired infections are a direct result of improper hand washing among healthcare workers and are therefore preventable with proper hygiene, which will stop further spread within the healthcare setting.[43] Rapid identification of healthcare workers who are carriers of infections, as well as correctly sterilizing equipment can greatly reduce hospital transmission. There are also several cases where doctors leave and go to another hospital, rather than be identified as carriers.

The prevalence of nosocomial infections has been increasing over the last twenty years, along with the increase in the number of long-term care facilities like nursing homes that are now performing many of the same functions as acute-care facilities like hospitals.[44] MRSA, the same pathogen affecting livestock and the community at large, has been challenge for healthcare systems.

Hospitals and healthcare facilities provide an ideal environment to incubate more virulent strains of resistant microbes, and nosocomial infections are associated with longer lengths of stay, higher medical costs, and greater death rates. Patients infected with hospital-acquired MRSA (HA-MRSA), for example, spend about twenty days in the hospital, about three times the average stay for any other kind of infection. Treating MRSA infection costs 6 to 10 percent more than treating a nondrug resistant strain of *S. aureus*, and the average attributable death rate for patients with MRSA is 21 percent, as compared to 8 percent for a nonresistant *S. aureus* infection.[45]

The prevalence of MRSA has been increasing in the United States, and its epidemiological spread demonstrates the global nature of resistance. First reported in 1961 in the United Kingdom, MRSA became endemic in hospitals by the 1980s, and the rate of infection in the healthcare setting has been rising ever since. The number of hospitalizations in the United States due to *S. aureus* infections increased by 62 percent between 1999 and 2005, of which about 58 percent were methicillin-resistant in 2005.[46] The prevalence of MRSA in US intensive care units (ICU) doubled in ten years, between 1992 and 2002, from 36 percent to 62 percent of all *S. aureus* hospitalizations.[47] Rates of MRSA in European hospitals, as a proportion of invasive *S. aureus* isolates, range from 1 percent in hospitals in Denmark and the Netherlands to 44 percent in the United Kingdom and Greece.[48]

The pathogen's current endemic status in American healthcare facilities is partly a function of the global spread of resistance. Hospital-acquired strains spread from the United Kingdom in 1961 to Sydney, Australia, in 1965 and then to Boston, Massachusetts, in 1968, followed by more recent reports from Canada, Taiwan, Brazil, and several other European nations.[49]

Another important hospital-associated infection is *Clostridium difficile* (*C. difficile*) infections. Although not yet significantly resistant to antibiotics, *C. difficile* infections correlate to antibiotics usage, and have been classified in the highest threat level by the CDC. These infections kill about 14,000 patients per year and cause over $1 billion in excess medical costs in

40 Michael Z. David and Robert S. Daum, "Community-Associated Methicillin-Resistant *Staphylococcus aureus*," *Clinical Microbiology Reviews* 23, July 2010, p. 618.
41 Ibid, p. 636.
42 A. Prüss, E. Giroult, and P. Rushbrook, eds., *Safe Management of Wastes from Healthcare Activities* (Geneva: World Health Organization, 1999), pp. 148-49.
43 Ken Inweregbu, Jayshree Dave, and Alison Pittard, "Nosocomial Infections," *Continuing Education in Anaesthesia, Critical Care & Pain* 5, 2005, pp.14-17.
44 Ibid.
45 Robert J. Rubin, et al., "The Economic Impact of *Staphylococcus aureus* Infection in New York City Hospitals," *Emerging Infectious Diseases* 5, January-February 1999, p.15.
46 Eili Klein, David L. Smith, and Ramanan Laxminarayan, "Hospitalizations and Deaths Caused by Methicillin-Resistant *Staphylococcus aureus*, United States, 1999-2005," *Emerging Infectious Diseases* 13, December 2007, pp. 1841-42.
47 L. Clifford McDonald, "Trends in Antimicrobial Resistance in Health Care-Associated Pathogens and Effect on Treatment," *Clinical Infectious Diseases* 42, 2006), pp. S65-71.
48 Cooper, et al., "Methicillin-resistant *Staphylococcus aureaus* in Hospitals and the Community," p. 10223.
49 "Methicillin-Resistant *Staphylococcus aureus* (MRSA)," National Institute of Allergy and Infectious Diseases, last modified March 4, 2008, http://www.niaid.nih.gov/topics/antimicrobialresistance/examples/mrsa/pages/history.aspx; David and Daum, "Community-Associated Methicillin-Resistant *Staphylococcus aureus*," pp. 619-20.

the United States.[50] The infection is a challenge to treat, since administration of more antibiotics will also kill off healthy bacteria that fight *C. difficile*. As such, individuals are turning to less orthodox methods of treatment, including fecal transplants.[51] *C. difficile* most often occurs in people who are hospitalized or have just left the hospital; about 50 percent of infected patients first show symptoms while in the hospital, and the most common mechanism of exposure is through the hands of healthcare workers.[52]

Although difficult, it is possible to mitigate the spread of HA-MRSA, *C. difficile*, and other comparable infections often with relatively simple techniques. The US Department of Veterans Affairs (VA) has been particularly successful in this regard. The VA instituted a MRSA Prevention Initiative in January 2009 in its 133 long-term care facilities, which included interventions as simple as emphasizing the importance of hand hygiene, isolating infected patients, and an "institutional culture change in which infection prevention and control became everyone's responsibility." In less than three years, the overall rate of HA-MRSA infections declined by 36 percent. What is worrisome is that the MRSA admission prevalence increased over the same time period, from 23.3 percent to 28.7 percent.[53] Conventional wisdom states that hospital-acquired infections will move into the community, but this data from the VA indicates that the opposite is also true. As there is more movement between long-term healthcare facilities, hospitals, and the community, the line between these two ecosystems is blurring.

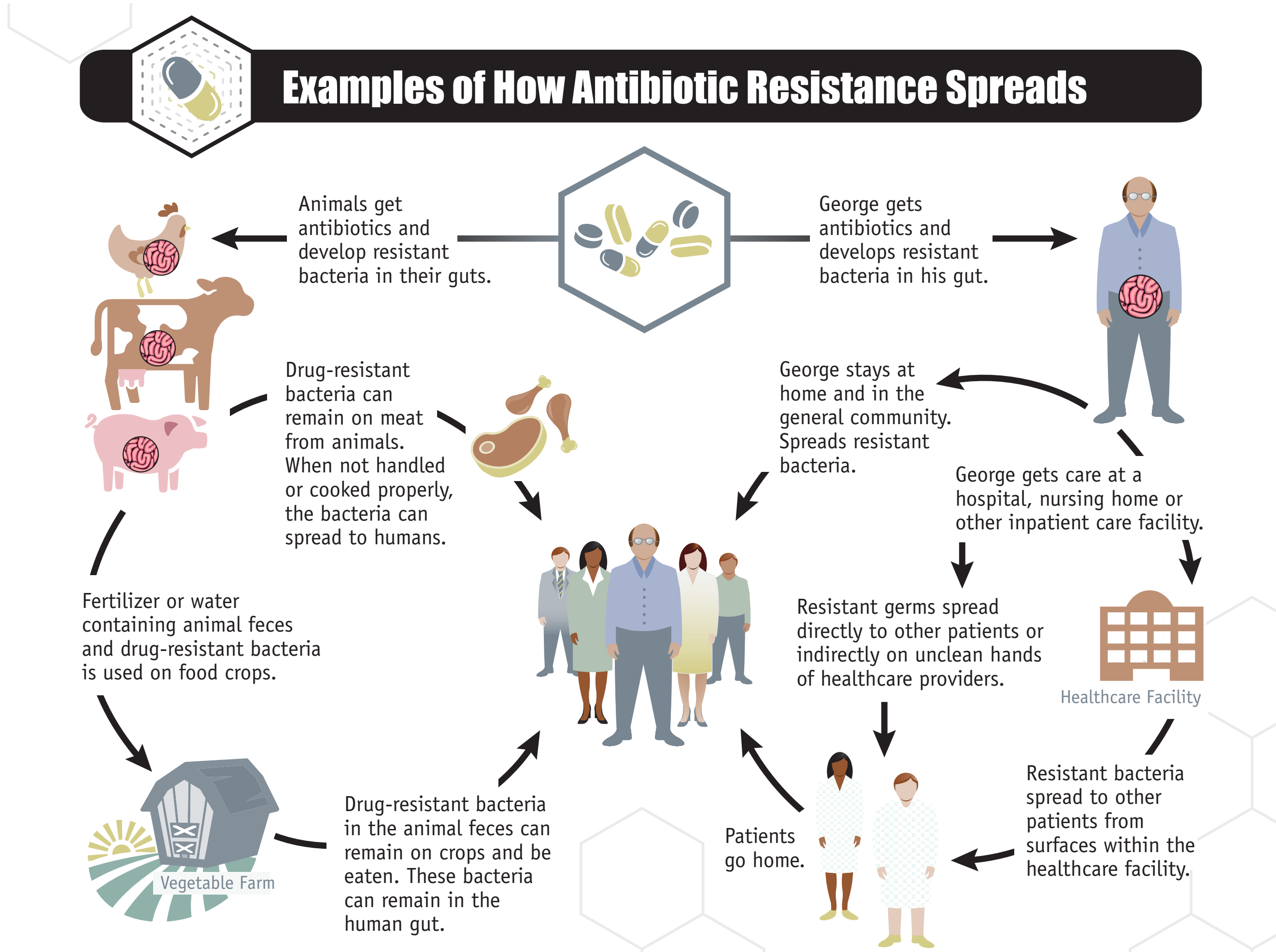
A Dried-Up Research and Development Pipeline

If drugs are becoming less effective, a rational solution would be to increase the supply and availability of safe, effective, or new antibiotics, but there are supply chain issues impeding this possibility. There is a societal need for new drugs, but the incentives for research and development are misaligned, and the pipeline for antimicrobial drugs is all but dried up. The number of new anti-infectives has been dropping consistently over the last thirty years; the US FDA approved thirty-five anti-infectives in the 1980s, a number that fell to twenty-seven in the 2000s. In the subclass of antibiotics, the FDA approved twenty-nine drugs in the 1980s, twenty-one in the 1990s, and nine in the 2000s.[54] Most newly approved drugs are actually modifications or different formulations of existing drugs, rather than a novel drug. No new class of antibacterial has been discovered since 1987.[55]

This drought is primarily a function of the economics of drug development and distribution, including hyperbolic discounting faced by pharmaceutical companies. Antimicrobial drugs are not accurately priced. Their market price is relatively low, which increases access, but the low prices do not take into account the long-term or future costs incurred by possible resistance or decreased effectiveness. A common argument against development of new antimicrobials is the high cost of research and testing, but the investment in developing a new antibiotic is no less expensive than that of developing a new cancer drug. The biggest difference is that market forces allow pharmaceutical companies to charge significantly more for the cancer drug than for the new antibiotic. Any new antibiotics will also have to compete with generic antibiotics, further lowering potential profit margins.

Ways to realign incentives include encouraging public-private partnerships to develop new drugs, offering an advanced price or market commitment for a new antimicrobial, and extending the patent period for new drugs.[56] Putting new antimicrobial drugs on the market could relieve some of the pressure from current drugs and allow doctors to prescribe more targeted antimicrobial drugs, rather than rely on broad-spectrum antibiotics. But approving new drugs without a strong framework of stewardship and responsibility does no long-term good. As Dennis Maki, professor at the University of Wisconsin School of Medicine and Public Health, said at a meeting of the Infectious Diseases Society of America, "The development of new antibiotics without having mechanisms to insure their appropriate use is much like supplying your alcoholic patients with a finer brandy."[57]

50 CDC, *Antibiotic Resistance Threats*, pp. 50-51.
51 Olga Khazan, "After Antibiotics, the Feces Pill Remains," *Atlantic*, December 2, 2013, http://www.theatlantic.com/health/archive/2013/12/after-antibiotics-the-feces-pill-remains/281925/.
52 CDC, *Antibiotic Resistance Threats*, pp. 50-51; Lynne Sehulster and Raymond Y.W. Chinn, "Guidelines for Environmental Infection Control in Health-Care Facilities," *Morbidity and Mortality Weekly Report* 52, June 6, 2003.
53 Martin E. Evans et al., "Nationwide Reduction of Health Care-associated Methicillin-resistant *Staphylococcus aureus* Infections in Veterans Affairs Long-term Care Facilities," *American Journal of Infection Control* 42, 2014, p. 60.
54 Kevin Outterson, et al., "Approval and Withdrawal of New Antibiotics and Other Antiinfectives in the US, 1980-2009," *Journal of Law, Medicine & Ethics* 41, Fall 2013, p. 690.
55 Davies et al., *The Drugs Don't Work*, p. 56.
56 Ibid, pp. 57-60.
57 Kevin Outterson, "New Business Models for Sustainable Antibiotics," Centre on Global Health Security Working Group Paper 1, Chatham House, February 2014, p. 8.



Source: Centers for Disease Control and Prevention, *Antibiotic Resistance Threats in the United States*, 2013.

The Growing Costs of AMR

There are real economic costs associated with the increase of AMR. A reduction in effectiveness of existing antibiotics by just 1 percent could impose costs of up to $3 trillion in lost human health.[58] AMR infections are harder to fight off, leading to more severe illnesses, longer hospital stays, and higher mortality rates. According to the CDC, at least two million Americans acquire serious infections due to at least one strain of resistant bacteria annually, and at least 23,000 people die of these infections.[59] In the European Union, drug resistant bacteria are responsible for at least 25,000 deaths a year.[60] There were also more than 14.7 million incidents of moderate-to-severe adverse reactions each year between 2001 and 2005 in China, and 150,000 patients died annually as a result of these adverse reactions.[61] This number from China does not include those who have died of resistant infections, which would likely increase the death toll further. In understanding these data, it is important to remember there is no standard or, as the WHO phrases it, "global consensus on methodology and data collection" for AMR surveillance.[62] This makes comparisons across countries even more difficult, and highlights how the data could be easily skewed.

A reduction in effectiveness of existing antibiotics by just 1 percent could impose costs of up to $3 trillion in lost human health.

There is also a significant economic impact associated with AMR. The estimated cost in the United States alone is $20 billion, with an additional $35 billion in lost productivity.[63] With the increase in resistant infections and rise in medical costs in the United States, it is expected that the cost to the medical system due to AMR has continued to increase since these data were released. In the European Union, the healthcare costs and productivity losses associated with AMR are estimated to be over $2 billion; the lower costs as compared to those in the United States are likely attributable to the difference in healthcare systems.[64] A 2005 study of the United Kingdom estimated that real annual gross domestic product losses due to AMR were between 0.4 and 1.6 percent.[65] This estimate may be a useful guide to the global impact of AMR, which will likely increase if AMR goes unchecked.

The most recent available data from China are even more unreliable, but just as stark. Treating antibiotic resistant infections in China between 2001 and 2005 cost at least $477 million, with estimated productivity losses of more than $55 million annually.[66]

All these figures are likely underestimates. In the United States, for example, surveillance and reporting mechanisms for AMR are limited, and there are no standard criteria to determine when an individual's death is primarily attributable to an AMR infection, rather than to a coexisting illness or different cause. While these figures do not capture the full extent of the problem, they nevertheless provide a sense of the scale, as well as the stakes associated with ignoring this urgent issue. The problem is, troublingly, likely to be much bigger in scale, and it will certainly continue to grow without a timely international intervention.

58 Hollis and Ahmed, "Preserving Antibiotics: Rationally," p. 2476.
59 CDC, *Antibiotic Resistance Threats*, p. 11.
60 Davies et al., *The Drugs Don't Work*, p. 31.
61 Li, "China's Misuse of Antibiotics Should Be Curbed," p. g1083.
62 World Health Organization, *Antimicrobial Resistance: Global Report on Surveillance 2014*, p. x.
63 CDC, *Antibiotic Resistance Threats*, p. 26.
64 Davies et al., *The Drugs Don't Work*, p. 31.

65 Richard D. Smith, et al., "Assessing the Macroeconomic Impact of a Healthcare Problem," p. 1069.
66 Currie et al., "Patient Knowledge and Antibiotic Abuse," 4.

National Security Implications

AMR, like global warming, presents the world with a threat that can only be solved at the global level. Just as a molecule of carbon dioxide emitted anywhere contributes to the threat to the entire planet, resistance that appears in one part of the world can spread to undermine the health of the global community. The international community needs to address the long-term challenge of a possible postantibiotic world and to prepare to best manage and mitigate an AMR-induced crisis that could occur at any time. Antimicrobial drugs are a public good, akin to fisheries or forests, and need to be treated as such in broader political conversations.

At this point, AMR does not pose an immediate and direct threat to national security, but without an effective and swift response to the growing problem of AMR, the situation will continue to deteriorate on a global scale. This is a creeping national security crisis, and underestimates of the problem now may lead to disaster in the near future. If current trends continue, the drugs will lose effectiveness. The gains made in fighting infectious diseases will be reversed, and a wide range of routine surgeries and easily treatable infections will become much more dangerous and deadly. This will cause the health of the world's working population to deteriorate and the economic productivity and social cohesion of the globe to decline. At any time, a "black swan" event, triggered by an outbreak of drug-resistant tuberculosis, cholera, or pneumonia, for example, could prove catastrophic, endangering the fabric of societies and our globalized economy, forcing a halt to international trade and travel to prevent further spread.

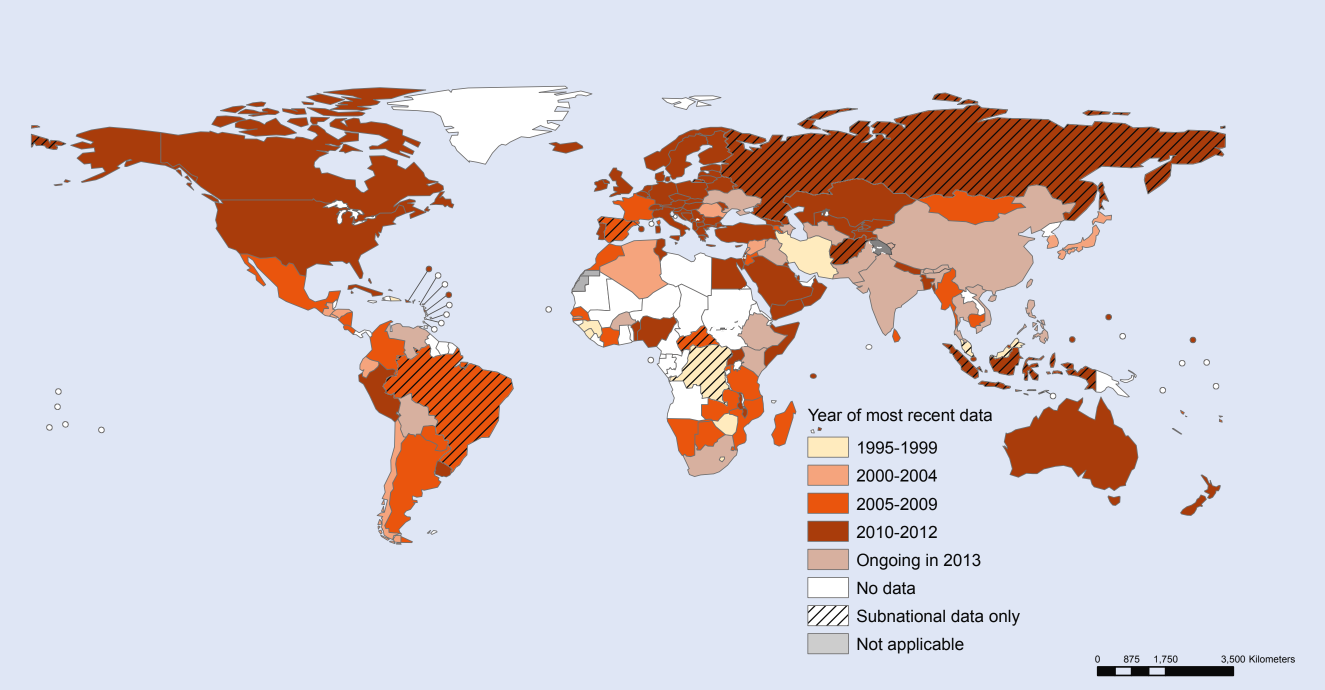
> Current trends of international trade and travel are exacerbating the spread of resistance, and conflict and displacement of populations only hasten this process.

As demonstrated by the rapid spread of NDM-1, current trends of international trade and travel are exacerbating the spread of resistance, and conflict and displacement of populations only hasten the process. The current conflict in Syria has caused the displacement of millions of people, and preventable communicable diseases, such as cholera and even polio, have run rampant in these populations, crossing borders quickly and often unnoticed. These diseases are neither being treated nor prevented because of a lack of resources and access to proper drugs, in spite of the technical ability to prevent and effectively treat these diseases. If the diseases circulating in these refugee communities become drug-resistant, it could lead to even higher mortality rates among this already vulnerable population, and it is more than likely that these resistant genes and strains will appear in the broader population, at which point the issue becomes more than one of public health, but also one of development and foreign affairs.

Concern about the threat of AMR to US national security has lead the US Department of Health and Human Services (HHS) to fund development of a new drug to address two antibiotic-resistant infections linked to bioterrorism threats. HHS announced in February 2014 that a public-private partnership will advance the development of Carbavance, a new option to treat bioterrorism threats and antibiotic-resistant infections. Carbavance will address melioidosis, also known as Whitmore's disease, and glanders–both of which are bacterial infections and can therefore become resistant to existing antibiotics. Already, approximately 40 percent of people who contract these bacteria will die, and up to 90 percent of those infected will die if not treated. "Antibiotic resistance adversely impacts our nation's ability to respond effectively to a bioterrorism attack and to everyday public health threats," said Dr. Robin Robinson, director of the Office of the Assistant for Preparedness and Response's Biomedical Advanced Research Development Authority, which will oversee the project. "By partnering with industry to develop novel antimicrobial drugs against biothreats that also treat drug-resistant bacteria, we can address health security and public health needs efficiently."[67]

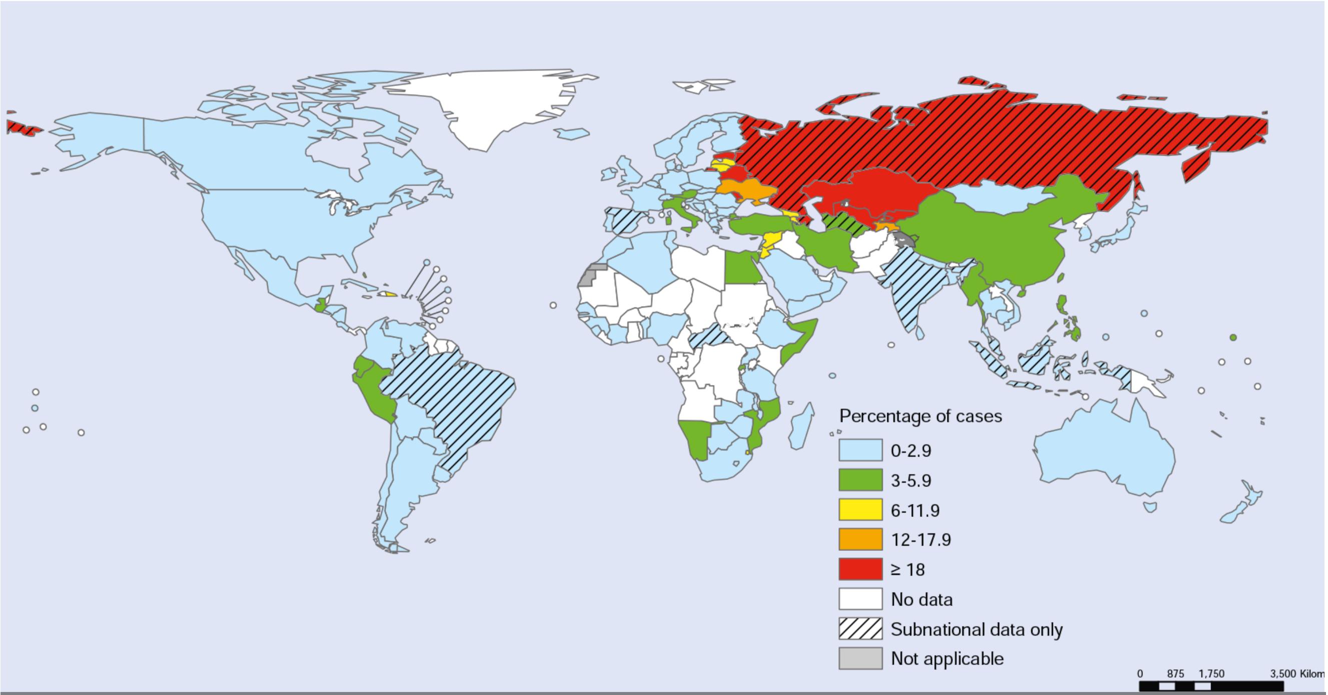
67 "Melioidosis, also called Whitmore's disease, can be mistaken for other diseases such as tuberculosis and common forms of pneumonia. The bacteria that cause melioidosis can be found in water and soil, and cause infection when a person touches or inhales the bacteria. The infection is common in parts of Southeast Asia and Australia. Glanders is a respiratory disease that can affect people, although it is primarily found in animals. The bacteria that cause glanders can affect skin, blood, lungs, or muscles, and may be transmitted through direct contact with infected animals or by inhaling contaminated aerosols or dust. Melioidosis and glanders can become resistant to existing antibiotics." See "HHS Funds Drug for Bioterrorism, Antimicrobial-resistant Infections," press release, February 15, 2014, http://www.hhs.gov/news/press/2014pres/02/20140205b.html.

Progress in Global Coverage of Surveillance Data on anti-TB Drug Resistance, 1994–2012



Source: World Health Organization, *Antimicrobial Resistance: Global Report on Surveillance*, 2014.

Proportion of New Tuberculosis Cases with Multidrug Resistance Worldwide



Source: World Health Organization, *Antimicrobial Resistance: Global Report on Surveillance*, 2014.

Policy Recommendations

To date, piecemeal steps have been taken to address the issue of AMR, with certain countries and organizations fighting against resistance while others benefit from the short-term advantages of using these drugs without considering the long-term consequences. In addition to the many worst-case scenarios outlined throughout this report—higher rates of mortality, and inability to perform life-saving operations, among others—there is the possibility of broader social problems. Food security may be threatened because of an inability to fight off infections in livestock and in agriculture. Overall, productivity will decrease as a result of more frequent and severe illnesses due to once easily treated infections, thereby threatening global economies. These problems are not just medical, and a postantibiotics world will ensure that health issues will stymie future progress and development in all fields.

There are ways to mitigate the damage done and to reverse the trends associated with increasing resistance:

- **Improve surveillance systems.** Because resistance is a global problem, a strong global disease surveillance system is required to catch new outbreaks. Accurate, complete data is required to understand the full scope of the problem, and to understand which interventions are working. Additionally, better public health surveillance would allow officials to quickly respond to the global spread of resistant microbes, preventing further infection.

- **Promote proper infection control techniques.** Managing AMR is, at its core, prevention of the spread of infectious diseases, and as such, implementation of proper infection control in healthcare facilities and the community is critical. As demonstrated by the experience of the VA in the United States, this includes steps as simple as promoting proper hygiene and correctly washing one's hands. It also includes quickly identifying patients with resistant infections and isolating them from the general population when appropriate, especially in hospitals and ICUs. It is important, however, not to get carried away with using antimicrobial soaps, which have been identified by the FDA as another source of resistance and are no more effective than regular soap and water.[68]

- **Educate about antimicrobial stewardship,** in both healthcare settings and the community. Patients need to learn that antibiotics are not an automatic solution to every health malady and doctors need to be firmer about not prescribing antibiotics unnecessarily, either to satisfy a difficult patient or to increase an individual doctor's paycheck. Antibiotics should never be prescribed for a viral infection, and patients who are prescribed antibiotics need to understand the importance of completing a full course of drugs, not stopping once he or she feels better.

- **Require a prescription for antibiotics and regulate quality.** Because antimicrobial drugs are a limited resource, there needs to be a qualified gatekeeper overseeing their administration. This also means de-linking physicians' salaries from antibiotic prescriptions so that there is not a skewed financial incentive to unnecessarily prescribe these drugs. Prescriptions for antibiotics should be required for all patients, be they human or animal, and access to over-the-counter antimicrobials needs to be stopped.

- **Eliminate the use of AGPs in livestock.** Considering that 80 percent of antibiotics in the United States are used in livestock, eliminating the nontherapeutic uses of antimicrobial drugs in livestock will decrease the prevalence of AMR infections in both livestock and humans without reducing food production. It also stymies the spread of resistant microbes into the broader food supply.

- **Increase the cost of antimicrobial drugs.** The phenomenon of hyperbolic discounting and the tragedy of the commons lead to a market price of antimicrobial drugs that does not reflect the long-term consequences of overuse. Increasing the market price will discourage unnecessary prescription or purchase, although there is a fine line between accurate pricing and access. Since most antibiotics have been off-patent for decades, it may be challenging to increase prices, but it is important to ensure the market price of these drugs reflects the true cost of both their present and future use.

- **Invest in research and development for new diagnostic tools and drugs.** The obvious solution to this problem is to research and

68 "FDA Taking Closer Look at 'Antibacterial' Soap," US Food and Drug Administration, last modified December 24, 2013, http://www.fda.gov/forconsumers/consumerupdates/ucm378393.htm.

develop new antimicrobials. Diagnostic tools also need to be improved, so as to give doctors the ability to quickly and correctly diagnose an infection and accurately prescribe the drug that will treat it. This could cut down, if not eliminate, unnecessary prescriptions of antimicrobial drugs. In addition to finding new classes of antimicrobial drugs, alternate therapies should be explored. One such option is phage, which are tiny viruses that infect and emit a toxin to poison a specific bacteria or fungi. Phage research has struggled to advance because there is no known way to manage phages in an uncontrolled environment, but the world is at such a crisis point that interest in phage research has resurrected.

Ultimately, the world needs to agree to implement all of the above recommendations on a global scale to protect the health, economic prosperity, and national security of individual nations. In order for these recommendations to be successful in stopping the current trends of AMR, there needs to be a strong mechanism for compliance. Ideally, this could come about as part of a broader culture change, in which the health of individuals, animals, and the environment are understood to be part of one framework.

If current trends of AMR continue and these recommendations are not taken seriously, the world will experience more severe illnesses and higher mortality rates as a direct result of infectious diseases. But the implications are much broader than that. The advances in quality of life made over the last seventy years during this antibiotic era will deteriorate rapidly without the continued efficacy and reliability of antimicrobial drugs. A major step to a more global approach is the Transatlantic Taskforce on Antimicrobial Resistance, which was established by presidential declaration in 2009 at the annual summit between the EU and US presidencies. The purpose of the task force is to identify urgent antimicrobial resistance issues that could be better addressed by intensified cooperation between the United States and the European Union within the following key areas:

1. Appropriate therapeutic use of antimicrobial drugs in the medical and veterinary communities;
2. Prevention of both healthcare- and community-associated drug-resistant infections;
3. Strategies for improving the pipeline of new antimicrobial drugs.[69]

At the 67th World Health Assembly in May 2014, the WHO released a draft global action plan on antimicrobial resistance that calls for several concrete steps to be taken over the next twelve months including the convening of a Strategic and Technical Advisory Group on Antimicrobial Resistance to provide recommendations to the director-general on next steps. Actions in this plan are expected to include strengthening lab and surveillance capacity in member states, promoting proper infection control techniques within countries, working with the Food and Agriculture Organization and the World Organization for Animal Health to limit use of AGPs in livestock, encouraging interest in this issue from the public, and increasing funding from national governments to support these efforts.[70] One important action already taken to foster public interest in this pressing issue has been the WHO's May 2014 release of a publication highlighting and summarizing this global threat. In the foreword to the full report, Dr. Keiji Fukuda, assistant director-general for health security at the WHO, uses strong language to describe the urgency of this issue: "A post-antibiotic era–in which common infections and minor injuries can kill–far from being an apocalyptic fantasy, is instead a very real possibility for the 21st century."[71] He also highlights the importance of improving monitoring systems, a main emphasis of this WHO report.

With these commitments from the WHO, it is clear the issue of AMR has become a priority for the global health community. Given the wide scope of the problem, though, interest needs to broaden beyond the realm of public health. If current trends of AMR continue, the world will experience more severe illnesses and higher mortality rates as a direct result of infectious diseases. But the implications are much broader than that. The advances in quality of life made over the last seventy years during this antibiotic era will deteriorate rapidly without the continued efficacy and reliability of antimicrobial drugs. The success of many recent interventions has demonstrated, however, that it is possible to walk back from this ledge, even if it is impossible to completely reverse the damage already done.

---

69 Through regular meetings and several public consultations, the members of the TATFAR have identified a set of 17 recommendations in these key areas where future cooperation would prove fruitful. Transatlantic Taskforce on Antimicrobial Resistance, *Recommendations for Future Collaboration between the US and EU* (2011), http://www.ecdc.europa.eu/en/activities/diseaseprogrammes/TATFAR/Documents/210911_TATFAR_Report.pdf.
70 Maryn McKenna, "World Health Organization Drafting Global Plan on Drug Resistance. Is That Enough?" *Wired*, May 26, 2014, http://www.wired.com/2014/05/wha67-resistance/; World Health Organization, *Draft Action Plan on Global Antimicrobial Resistance: Report by the Secretariat*, A67/39 Add.1 (Geneva, Switzerland: World Health Organization, 8 May 2014): pp. 1-3.
71 World Health Organization, *Antimicrobial Resistance: Global Report on Surveillance 2014*, p. ix.

About the Author

Maxine Builder is a research associate for global health at the Council on Foreign Relations, based in New York City. She holds a bachelor of arts in international relations.

Atlantic Council Board of Directors

The Atlantic Council is a nonpartisan organization that promotes constructive US leadership and engagement in international affairs based on the central role of the Atlantic community in meeting today's global challenges.

1030 15th Street, NW, 12th Floor, Washington, DC 20005

(202) 778-4952, www.AtlanticCouncil.org