

EXECUTIVE SUMMARY

CDDEP THE CENTER FOR
Disease Dynamics,
Economics & Policy
WASHINGTON DC • NEW DELHI



Global
Antibiotic
Resistance
Partnership



THE STATE OF THE WORLD'S ANTIBIOTICS 2015

© Center for Disease Dynamics, Economics & Policy, 2015.
Reproduction is authorized provided the source is acknowledged.

A full version of this report is available at www.cddep.org/swa

This report is based on research funded in part by the Bill & Melinda Gates Foundation. The findings and conclusions contained within are those of the authors and do not necessarily reflect positions or policies of the Bill & Melinda Gates Foundation.

Related research and additional information on antibiotic resistance and other global health priorities are available at www.cddep.org

The Global Antibiotic Resistance Partnership (GARP) is a network of interdisciplinary working groups in multiple countries in Africa and Asia that are catalyzing the development and implementation of national action plans to address antimicrobial resistance. Further information is available at www.cddep.org/garp

Suggested citation

Center for Disease Dynamics, Economics & Policy. 2015.
State of the World's Antibiotics, 2015. CDDEP: Washington, D.C.

CENTER FOR DISEASE DYNAMICS, ECONOMICS & POLICY
1400 Eye Street, NW
Suite 500
Washington, DC 20005
USA

THE STATE OF THE WORLD'S ANTIBIOTICS 2015

AUTHORS

HELLEN GELBAND

MOLLY MILLER-PETRIE

SURAJ PANT

SUMANTH GANDRA

JORDAN LEVINSON

DEVRA BARTER

ANDREA WHITE

RAMANAN LAXMINARAYAN

CONTRIBUTORS

NK Ganguly for the GARP-India Working Group

Samuel Kariuki, Linus Ndegwa, and **Eveline Wesangula** for the GARP-Kenya Working Group

Betuel Sigaúque and **Esperança Sevens** for the GARP-Mozambique Working Group

Buddha Basnyat, Paras Pokharel, Sameer Mani Dixit, and **Santoshi Giri** for the GARP-Nepal Working Group

Adriano Duse, Olga Perovic, and **Kim Faure** for the GARP-South Africa Working Group

Said Aboud, Robinson Mdegela, and **Khadija Msami** for the GARP-Tanzania Working Group

Denis K. Byarugaba, Donna A. Kusemererwa, and **James Lakony** for the GARP-Uganda Working Group

Nguyen Van Kinh, Heiman Wertheim, and **Do Thuy Nga** for the GARP-Vietnam Working Group

CDDEP BOARD OF DIRECTORS

Adel Mahmoud, Chairman; Professor, Woodrow Wilson School and Department of Molecular Biology, Princeton University

Sir George Alleyne, Chancellor, University of the West Indies

George Bickerstaff, Managing Director, M.M. Dillon & Co.

Mark Cohen, Professor of Law and Management, Vanderbilt University

Maureen Cropper, Professor, Department of Economics, University of Maryland

Edward Hand, Senior Strategy Advisor, Resources for the Future

Sir Richard Peto, Professor, Medical Statistics and Epidemiology, University of Oxford

Ramanan Laxminarayan, Director, Senior Fellow, CDDEP





ACRONYMS

AGAR	Australian Group on Antimicrobial Resistance	GARP	Global Antibiotic Resistance Partnership (CDDEP)
CARA	Canadian Antimicrobial Resistance Alliance	LMICs	Low- and middle-income countries
CDC	Centers for Disease Control and Prevention (United States)	NARST	National Antimicrobial Resistance Surveillance Center, Thailand
CDDEP	Center for Disease Dynamics, Economics & Policy	NME	New molecular entity
CRE	Carbapenem-resistant Enterobacteriaceae	MRSA	Methicillin-resistant <i>Staphylococcus aureus</i>
EARs-Net	European Antimicrobial Resistance Surveillance Network	SASCM	South African Society for Clinical Microbiology
ESBL	Extended-spectrum beta-lactamase	TSN	The Surveillance Network (United States)
ESR	The Institute of Environmental Science and Research (New Zealand)	VINARES	Vietnam Resistance Project
		WHO	World Health Organization

EXECUTIVE SUMMARY

Since their introduction into medicine in the 1940s, antibiotics have been central to modern healthcare. Their role has expanded from treating serious infections to preventing infections in surgical patients, protecting cancer patients and people with compromised immune systems, and promoting growth and preventing disease in livestock and other food animals.

Now, however, once-treatable infections are becoming difficult to cure, raising costs to healthcare facilities, and patient mortality is rising, with costs to both individuals and society. Decreasing antibiotic effectiveness has risen from being a minor problem to a broad threat, regardless of a country's income or the sophistication of its healthcare system. Many pathogens are resistant to more than one antibiotic, and new, last-resort antibiotics are expensive and often out of reach for those who need them.

Antibiotic resistance is a direct result of antibiotic use. The greater the volume of antibiotics used, the greater the chances that antibiotic-resistant populations of bacteria will prevail in the contest for survival of the fittest at the bacterial level.

Two trends are contributing to a global scale-up in antibiotic consumption. First, rising incomes are increasing access to antibiotics. That is saving lives but also increasing use—both appropriate and inappropriate—which in turn is driving resistance. Second, the increased demand for animal protein and resulting intensification of food animal production is leading to greater use of antibiotics in agriculture, again driving resistance.

This State of the World's Antibiotics report records the status of this important global resource and provides critical policy analysis on three issues:

- global patterns and trends in antibiotic resistance and antibiotic use in human beings and animals;
- the existing antibiotic supply and the research and development pipeline; and
- interventions that have been shown to help rationalize antibiotic use and are practicable in all countries.

We present a comprehensive country-level policy response, consisting of six strategies, based on the experience of the Global Antibiotic Resistance Partnership (GARP), which has fostered the development of locally driven antibiotic policy in eight countries. The strategies should be particularly relevant for the many countries that have not yet formally addressed antibiotic resistance.

PATTERNS AND TRENDS IN ANTIBIOTIC RESISTANCE (CHAPTER 1)

Evidence from around the world indicates an overall decline in the total stock of antibiotic effectiveness: resistance to all first-line and last-resort antibiotics is rising. The patterns of which bacteria are resistant to specific antibiotics differ

The greater the volume of antibiotics used, the greater the chances that antibiotic-resistant populations of bacteria will prevail in the contest for survival of the fittest at the bacterial level.

regionally and by country, mirroring patterns of infectious disease and antibiotic use.

The U.S. Centers for Disease Control and Prevention (CDC) estimates that antibiotic resistance is responsible for more than 2 million infections and 23,000 deaths each year in the United States, at a direct cost of \$20 billion and additional productivity losses of \$35 billion (CDC 2013). In Europe, an estimated 25,000 deaths are attributable to antibiotic-resistant infections, costing €1.5 billion annually in direct and indirect costs (EMA and ECDC 2009). Although reliable estimates of economic losses in the developing world are not available, it is estimated that 58,000 neonatal sepsis deaths are attributable to drug-resistant infections in India alone (Laxminarayan et al. 2013). Studies from Tanzania and Mozambique indicate that resistant infections result in increased mortality in neonates and children under five (Kayange et al. 2010; Roca et al. 2008).

Resistant bacteria in humans

Methicillin-resistant *Staphylococcus aureus* (MRSA) has declined in incidence in Europe, the United States and Canada over the past eight years, to 18 percent, 44 percent, and 16 percent, respectively (EARS-Net 2014; CDDEP 2015b; Public Health Agency of Canada 2015). It also has begun to decline in South Africa (to 28 percent), where antibiotic stewardship is taking hold (Kariuki and Dougan 2014; CDDEP 2015b) (Figure ES-1). In sub-Saharan Africa, India, Latin America, and Australia, it is still rising (AGAR 2013; CDDEP 2015b), recorded at 47 percent in India in 2014, and 90 percent in Latin American hospitals in 2013 (PAHO, forthcoming).

***Escherichia coli* (*E. coli*) and related bacteria** have become resistant to newer third-generation cephalosporins, indicating that they are difficult-to-treat extended-spectrum beta-lactamase (ESBL) producers. In 2013, in 17 of 22 European countries, 85 to 100 percent of *E. coli* isolates were ESBL positive (EARS-Net 2014). In 2009 and 2010, 28 percent of all Enterobacteriaceae (the *E. coli* family) from urinary tract infections in 11 countries in Asia were ESBL producers, and resistance to third- and fourth-generation cephalosporins ranged from 26 to 50 percent (Lu et al. 2012). In Latin America in 2014 resistance in *Klebsiella pneumoniae* ranged from 19 percent in Peru to 87 percent in Bolivia (PAHO, forthcoming). In sub-Saharan Africa, median prevalence of

resistance to third-generation cephalosporins ranged up to 47 percent (Leopold et al. 2014).

Carbapenem-resistant Enterobacteriaceae (CRE) are resistant even to last-resort carbapenems. In Europe, five countries reported increases in 2013, starting from low levels of less than 10 percent (EARS-Net 2014). In U.S. hospitals, 11 percent of *K. pneumoniae* and 2 percent of *E. coli* were resistant to carbapenems in 2012 (CDC 2013). In Latin America in 2013, resistance of *K. pneumoniae* to carbapenems ranged from full susceptibility in the Dominican Republic to 28 percent resistant in Guatemala (PAHO, forthcoming). In India, 13 percent of *E. coli* were resistant to carbapenems in 2013. For *K. pneumoniae*, 57 percent were resistant in 2014 (CDDEP 2015b).

Clostridium difficile infections are related to antibiotic use: the bacteria are not affected by most antibiotics and therefore proliferate in the human intestine after most other bacteria are killed by antibiotics. *C. difficile* causes an estimated 14,000 deaths per year in the United States (CDC 2013).

Evidence from around the world indicates an overall decline in the total stock of antibiotic effectiveness: resistance to all first-line and last-resort antibiotics is rising.

ResistanceMap, an interactive, data-rich visualization tool, brings together the most current antibiotic resistance surveillance statistics from the United States, Europe, and many low- and middle-income countries (LMICs) (www.resistancemap.org).

Resistant bacteria in food animals and the environment

Poultry, cattle, and swine raised with antibiotics harbor significant populations of antibiotic-resistant bacteria, which are transmitted to humans through direct contact with the animals and through their meat, eggs, and milk (Marshall and Levy 2011). Some proportion of the antibiotics used in agriculture and aquaculture ends up in the broader

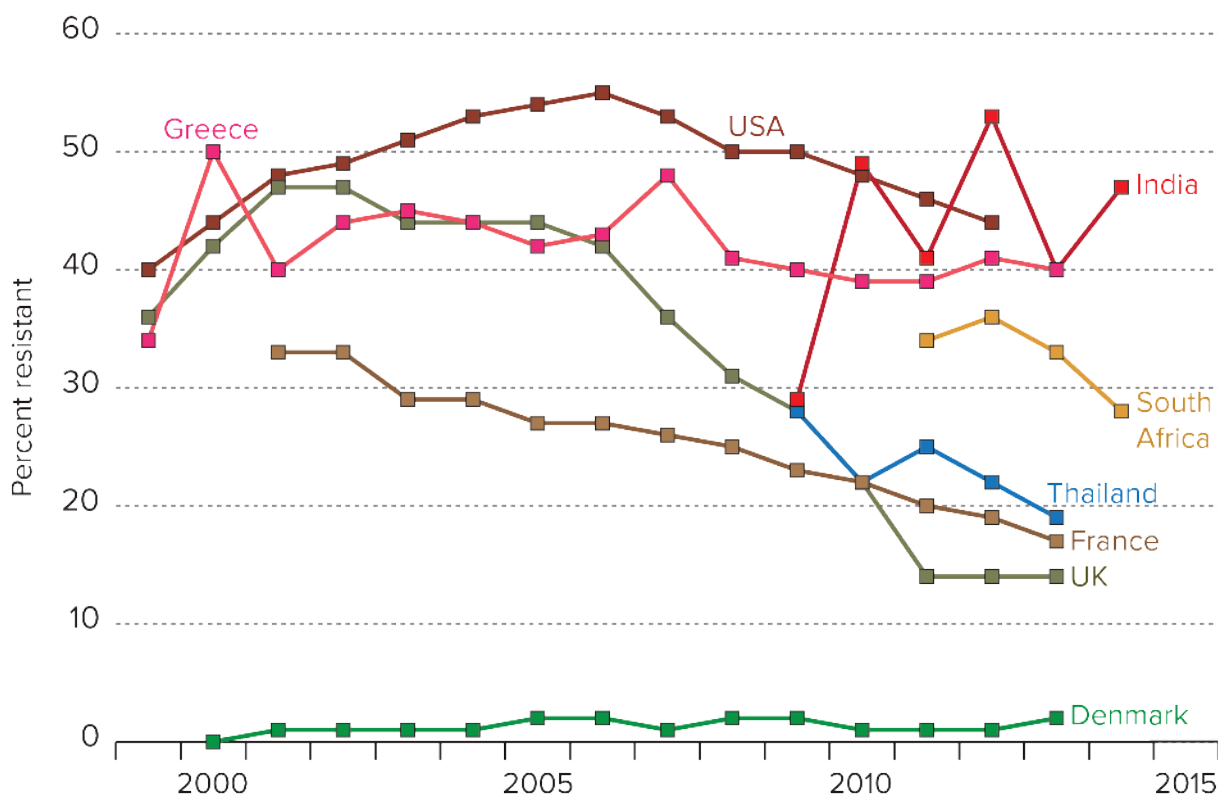


FIGURE ES-11: Percentage of *Staphylococcus aureus* isolates that are methicillin resistant (MRSA) in selected countries, 1999–2014

Source: CDDEP 2015

Depending on the country, resistance to one or more of the following drugs may have been used to test for MRSA: Oxacillin, cefoxitin, flucloxacillin, cloxacillin, dicloxacillin, and methicillin. Intermediate-resistant isolates are included as resistant.

¹ CDDEP 2015 sources include: AGAR (Australia), CARA (Canada), EARS-Net (Europe), ESR (New Zealand), NARST (Thailand), SASCM (South Africa), SRL Diagnostics (India), TSN (USA), and VINARES (Vietnam).

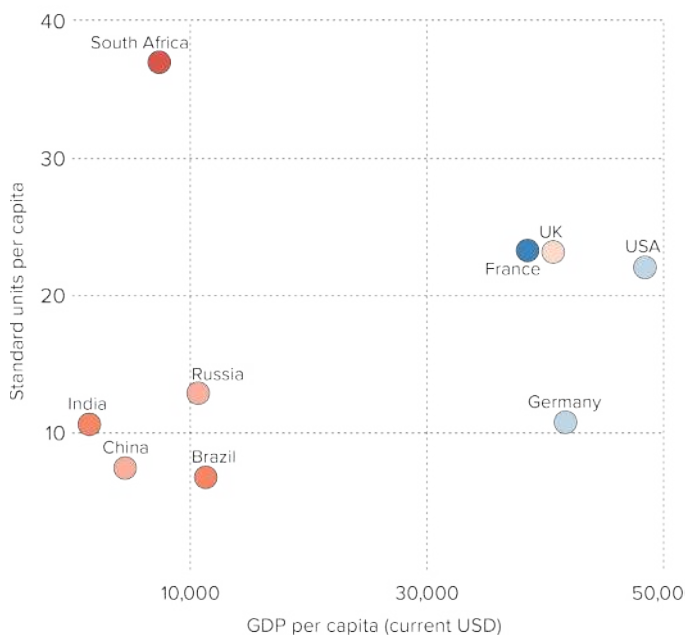


FIGURE ES-2: Antibiotic use per capita by income in selected countries, 2010

Source: Van Boeckel et al. 2014 (based on IMS MIDAS) and World Bank 2015

*Much of the increase in antibiotic consumption in South Africa can be attributed to the WHO recommended use of co-trimoxazole as prophylaxis for HIV patients.

environment (Daghrir and Drogui 2013), which adds to the total global burden of antibiotic resistance in both animals and humans.

PATTERNS AND TRENDS IN ANTIBIOTIC USE

Human consumption (Chapter 2)

Demand for antibiotics continues to rise, particularly to treat children with potentially fatal sepsis and pneumonia: in 2013, pneumonia was responsible for an estimated 935,000 deaths in children under five worldwide (Liu et al. 2015). If given effective antibiotic treatment, most of these children would not have died.

Between 2000 and 2010, total global antibiotic consumption grew by more than 30 percent, from approximately 50 billion to 70 billion standard units, based on data from 71 countries, including most high-population countries (Van Boeckel et al. 2014). Per capita consumption is generally higher in high-income countries, but the greatest increase in antibiotic use between 2000 and 2010 was in LMICs, where use continues to rise (Figure ES-2).

In most countries, about 20 percent of antibiotics are used in hospitals and other healthcare facilities, and 80 percent are used in the community, either prescribed by healthcare providers or purchased directly by consumers or caregivers without prescription (Kotwani and Holloway 2011). Perhaps half of community use is inappropriate, for coughs and colds that will not benefit from treatment, but it adds to the burden of antibiotic resistance. Hospitals generate some of the most dangerous and difficult-to-treat infections, a

Demand for antibiotics continues to rise, particularly to treat children with potentially fatal sepsis and pneumonia.

result of heavy use of antibiotics (especially in LMICs, where antibiotics may substitute for infection control), immune-compromised and elderly patients, and overcrowding.

Agricultural consumption (Chapter 3)

Increasing prosperity and population growth drive an increasing demand for animal protein. To satisfy this need, many farmers are transitioning to intensive agriculture and often use antibiotics to optimize production.

Antibiotics are used not only to treat individual animals with bacterial infections and prevent infections in herds or flocks, but also to promote growth—a controversial and high-use application. Worldwide, in 2010, at least 63,200 tons of antibiotics were consumed in livestock—likely to be more than all human consumption (Van Boeckel et al. 2015). By 2030, this figure is projected to rise by two-thirds, to 105,600 tons, to meet the demands of a projected 8.5 billion human population (United Nations 2015). Two-thirds of the projected increase is accounted for by increases in the number of animals raised for food production and the remaining one-third by the shift from small-scale to industrial-scale production (Van Boeckel et al. 2015) (Figure ES-3).

Antibiotic growth promotion is the focus of most legal and regulatory efforts to reduce animal antibiotic use because it provides no health benefit to the animals but accelerates antibiotic resistance. Recent analyses suggest that growth promoters have a smaller effect on animal growth than assumed, particularly in production systems that are otherwise optimized (Laxminarayan et al. 2015). The countries with the greatest expected increases in food demand and animal antibiotic use currently have the least efficient farming systems. Emphasis should be on improving productivity without antibiotic growth promoters, as is increasingly the case in high-income countries.

NEW ANTIBIOTICS AND OTHER INTERVENTIONS (CHAPTER 4)

Antibiotics are among the most familiar of medicines and are used liberally by people all over the world. The societal consequence of loss of effectiveness is of little concern to the individual user or prescriber, since resistance affects the next patient. These characteristics combine to foster gross antibiotic overuse and accelerate antibiotic resistance.

Importantly, for at least some antibiotics, resistance levels decrease with declining use, conserving and even recovering some antibiotic effectiveness. In some high-income countries, where antibiotic stewardship has taken hold and public health is good, antibiotic resistance levels have stabilized or declined: when antibiotic use declines, the prevalence of antibiotic-resistant bacteria tends to fall. Vaccines against a range of diseases and improved water and sanitation have moderated antibiotic demand in higher-income countries, and per capita use has begun to level off in many of these countries.

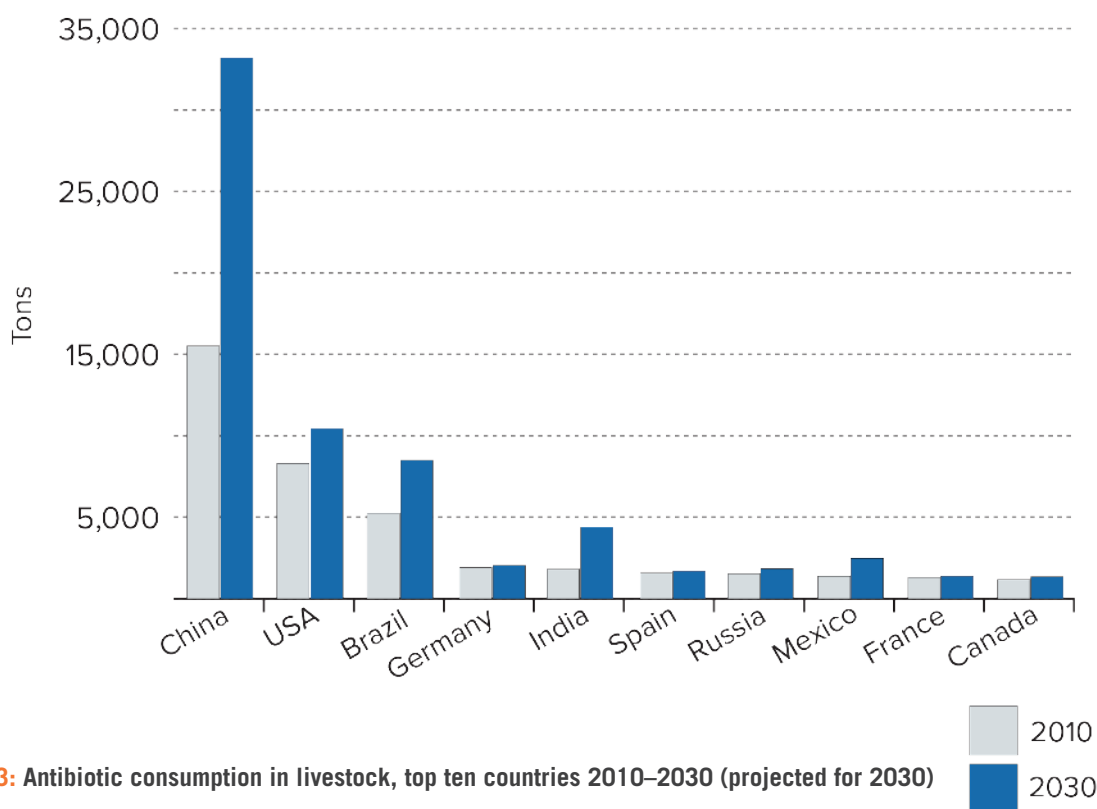


FIGURE ES-3: Antibiotic consumption in livestock, top ten countries 2010–2030 (projected for 2030)

Source: Van Boeckel et al. 2015

The global capacity to treat common infections depends on maintaining an adequate supply of antibiotic effectiveness. Over the past 10 years, the discussion has been dominated by an “empty pipeline” argument, with proposed solutions involving financial incentives for drug developers. Independent analysis suggests that the pipeline has been consistently productive for the past three decades (Outterson et al. 2013) (Figure ES-4). New incentives to spur drug development, by themselves, would do nothing to realign existing incentives for the overuse of antibiotics, nor would they incentivize the development of antibiotics targeted to the most urgent needs. Moreover, new drugs are not widely available in LMICs, where they are unaffordable for patients and healthcare systems (Kariuki et al. 2015).

Feasible, practicable interventions, however, could contribute to maintaining antibiotic effectiveness. Changing the norms regarding how antibiotics are perceived and used requires behavioral change. Alternative and complementary approaches to infection control and treatment, such as improved diagnostic tools, new vaccines, and bacteriophages, will also help maintain the effectiveness of current and emerging antibiotics. Global antibiotic stewardship in the broadest sense should make it possible not only to conserve the current effectiveness of existing antibiotics, but even to reclaim some of effectiveness that has been lost.

EXTENDING ANTIBIOTIC EFFECTIVENESS (CHAPTER 5)

Antibiotic resistance is a global problem, but antibiotic use has its greatest effects locally. It is in every country’s self-interest—for the health of its own population—to prolong antibiotic effectiveness. This means reducing use where possible and making sure that antibiotics are accessible when needed. Rather

Increasing prosperity and population growth drive an increasing demand for animal protein. To satisfy this need, many farmers are transitioning to intensive agriculture and often use antibiotics to optimize production.

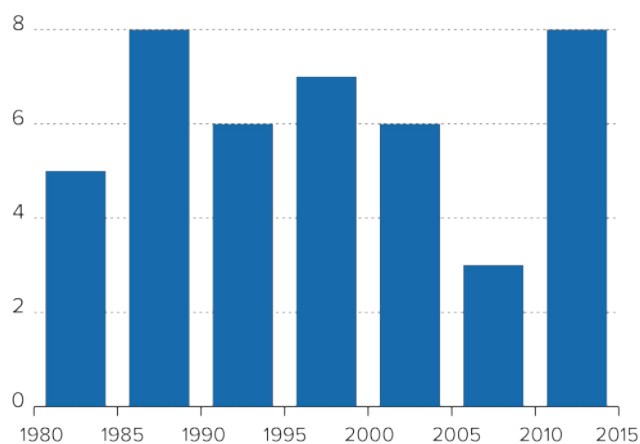


FIGURE ES-4: Systemic new molecular entity (NME) antibiotics still marketed in the US by period of introduction, 1980–2015*

Source: Outterson et al. 2013

*As of August 21, 2015; additional market discontinuations since 2009 are not calculated. Bedaquiline, approved for multidrug-resistant tuberculosis in 2012, is included.

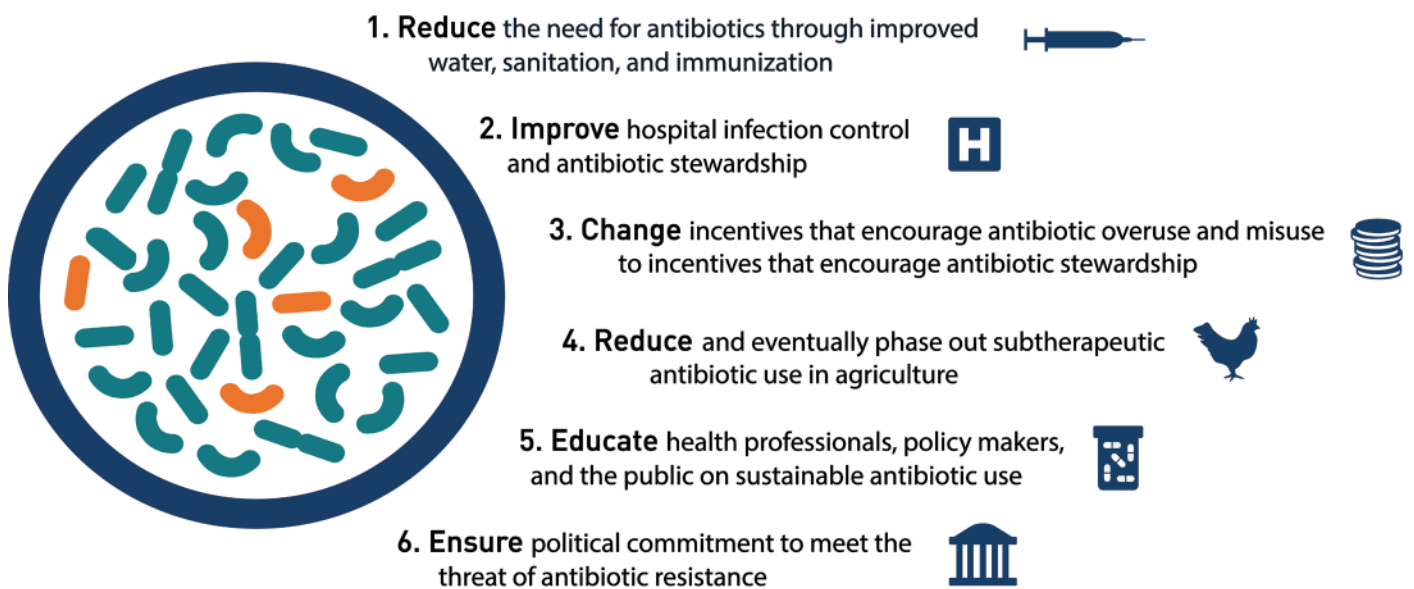


FIGURE ES-5: Six strategies needed in national antibiotic policies

than regulating individual actions, however, policymakers should address the mindset about antibiotics. Instead of being the default treatment for a host of mild ailments—particularly coughs, colds, and uncomplicated diarrhea—antibiotics must be considered life-saving medicines to be used when needed.

The transformation will be not easy, but social norms can and do change—witness the change in attitudes toward cigarette smoking. A set of coordinated antibiotic resistance strategies can start the norm-changing process.

GARP has worked with eight countries to establish the capacity and methods for developing antibiotic resistance policies. Six strategies will contribute to slowing resistance and maintaining the effectiveness of current drugs (Figure ES-5):

1. *Reduce the need for antibiotics through improved water, sanitation, and immunization.*
Improving coverage for existing vaccines and adding new ones, improving access to clean water and sewerage systems, and ensuring a safe and healthful food supply all reduce the need for antibiotics, thereby reducing antibiotic resistance rates.
2. *Improve hospital infection control and antibiotic stewardship.*
Better hygiene, particularly hand washing with soap or using alcohol disinfectant between patients, and antibiotic stewardship programs reduce infection rates. Surveillance of resistance and hospital-acquired infections gives administrators information for management and policy decisions.
3. *Change incentives that encourage antibiotic overuse and misuse to incentives that encourage antibiotic stewardship.*
Eliminating economic incentives that encourage the overuse of antibiotics all along the supply chain—in hospitals, in communities, and in agriculture—can conserve antibiotic effectiveness.
4. *Reduce and eventually phase out antibiotic use in agriculture.*

Instead of being the default treatment for a host of mild ailments—particularly coughs, colds, and uncomplicated diarrhea—antibiotics must be considered life-saving medicines to be used when needed.

Eliminating antibiotic use for growth promotion and minimizing use for disease prophylaxis need not jeopardize animal or human health.

5. *Educate and inform health professionals, policymakers, and the public on sustainable antibiotic use.*
Education and guidelines for healthcare professionals, engagement with policymakers, and national awareness campaigns for the public will begin changing the norms in antibiotic use and promote conservation.
6. *Ensure political commitment to meet the threat of antibiotic resistance.*
Presenting the case to policymakers and gaining their political and financial support are critical to success.

GLOBAL AND NATIONAL COMMITMENTS

In May 2015, the World Health Assembly endorsed the Global Action Plan on Antimicrobial Resistance, which calls on all countries to adopt national strategies within two years (WHO 2015). With support from WHO and the international community, this resolution could catalyze change—or, like similar resolutions over the past decade, it may be ignored.

In the United States, the National Action Plan for Combating Antibiotic-Resistant Bacteria (White House 2015) stresses the need to slow the spread of antibiotic resistance through stewardship at all levels. The European Union has taken a similar stance (European Commission 2011). Southeast Asian WHO countries committed to addressing the issue in the Jaipur Declaration (WHO 2011). The process is also

under way in South Africa, started by the work of GARP and continued through a broad coalition of government and private sector leaders.

The evidence in this report, documenting the seriousness of the problem and offering a successful approach to country-level action, supports both the urgency and the feasibility of making progress in conserving antibiotic effectiveness. The Center for Disease Dynamics, Economics & Policy (CDDEP) will continue collecting reliable data from around the world on antibiotic use and resistance, making the information available to all through ResistanceMap (www.resistancemap.org), and monitoring progress on global antibiotic stewardship.

REFERENCES

- Australian Group on Antimicrobial Resistance (AGAR). 2014. *Enterobacteriaceae Sepsis Outcome Programme, 2013 Antimicrobial Susceptibility Report*. Perth.
- . 2013. *Staphylococcus aureus Sepsis Outcome Programme (ASSOP), Annual Report 2013*. Perth.
- Centers for Disease Control and Prevention (CDC). 2013. *Antibiotic Resistance Threats in the United States*. Atlanta.
- Center for Disease Dynamics, Economics & Policy (CDDEP). 2015. ResistanceMap. Accessed on August 20, 2015. Retrieved from www.cddep.org/projects/resistance-map and www.resistancemap.org.
- Daghri, R., and Drogui, P. 2013. Tetracycline Antibiotics in the Environment: A Review. *Environmental Chemistry Letters*, 11(3):209–227.
- Denisuik, A., Simner, P., Taylor, F., Adam, H., Lagace-Wiens, P., Mulvey, M. et al. 2012. Dramatic Increase in the Prevalence of ESBL-Producing *Escherichia coli* in Canadian Hospitals over a 5-year Period. *Presented at the 52nd Interscience Conference on Antimicrobial Agents and Chemotherapy, September 9–12, 2012*. San Francisco.
- European Antimicrobial Resistance Surveillance Network (EARS-Net). 2014. *EARS-Net Report, Quarters 1–4*. Dublin.
- European Medicines Agency (EMA) and European Centre for Disease Prevention and Control (ECDC). 2009. *The Bacterial Challenge: Time to React a Call to Narrow the Gap Between Multidrug-Resistant Bacteria in the EU and Development of New Antibacterial Agents*. Stockholm.
- European Commission. 2011. *Action Plan Against Antimicrobial Resistance*. Brussels.
- Kariuki, S., and Dougan, G. 2014. Antibacterial Resistance in Sub-Saharan Africa: An Underestimated Emergency. *Annals of the New York Academy of Sciences*, 1323:43–55.
- Kariuki, S., Gordan, M. A., Feasey, N., and Parry C. M. 2015. Antimicrobial Resistance and Management of Invasive *Salmonella* Disease. *Vaccine*, 33(Suppl 3):C21-9.
- Kayange, N., Kamugisha, E., Mwizamholya, D. L., Jeremiah, S., and Mshana, S. E. 2010. Predictors of Positive Blood Culture and Deaths Among Neonates with Suspected Neonatal Sepsis in a Tertiary Hospital, Mwanza-Tanzania. *BMC Pediatrics*, 10(1):39. <http://doi.org/10.1186/1471-2431-10-39>.
- Kotwani, A., and Holloway, K. 2011. Trends in Antibiotic Use Among Outpatients in New Delhi, India. *BMC Infectious Diseases*, 11(1):99. <http://doi.org/10.1186/1471-2334-11-99>.
- Laxminarayan, R., Duse, A., Wattal, C., Zaidi, A. K. M., Wertheim, H. F. L., Sumpradit, N., et al. 2013. Antibiotic Resistance—The Need for Global Solutions. *The Lancet Infectious Diseases*, 13(12):1057–98. [http://doi.org/10.1016/S1473-3099\(13\)70318-9](http://doi.org/10.1016/S1473-3099(13)70318-9).
- Laxminarayan, R., Van Boeckel, T., and Teillant, A. 2015. The Economic Costs of Withdrawing Antimicrobial Growth Promoters from the Livestock Sector. *OECD Food, Agriculture and Fisheries Papers*, (78):doi:10.1787/18156797.
- Leopold, S. J., van Leth, F., Tarekegn, H., and Schultz, C. 2014. Antimicrobial Drug Resistance Among Clinically Relevant Bacterial Isolates in Sub-Saharan Africa: A Systematic Review. *The Journal of Antimicrobial Chemotherapy*, 69(9):2337–53.
- Liu, L., Oza, S., Hogan, D., Perin, J., Rudan, I., Lawn, J. E. et al. 2015. Global, Regional, and National Causes of Child Mortality in 2000–13, with Projections to Inform Post-2015 Priorities: An Updated Systematic Analysis. *The Lancet*, 385(9966):430–440.
- Lu, P. L., Liu, Y. C., Toh, H. S., Lee, Y. L., Liu, Y. M., Ho, C. M., et al. 2012. Epidemiology and Antimicrobial Susceptibility Profiles of Gram-Negative Bacteria Causing Urinary Tract Infections In the Asia-Pacific Region: 2009–2010 Results from the Study for Monitoring Antimicrobial Resistance Trends (SMART). *International Journal of Antimicrobial Agents*, 40 (Suppl):S37–43. [http://doi.org/10.1016/S0924-8579\(12\)70008-0](http://doi.org/10.1016/S0924-8579(12)70008-0).
- Marshall, B. M., and Levy, S. B. 2011. Food Animals and Antimicrobials: Impacts on Human Health. *Clinical Microbiology Reviews*, 24(4):718–33. doi:10.1128/CMR.00002-11.
- Outterson, K., Powers, J. H., Seoane-Vazquez, E., Rodriguez-Monguio, R., and Kesselheim, A. S. 2013. Approval and Withdrawal of New Antibiotics and Other Anti-infectives in the U.S., 1980–2009. *Journal of Law, Medicine and Ethics*, 41(3):688–696. <http://doi.org/10.1111/jlme.12079>.
- Pan American Health Organization (PAHO). Forthcoming. *Informe Anual de la Red de Monitoreo/Vigilancia de la Resistencia a los Antibióticos y de Infecciones Asociadas a la Atención de la Salud 2014*. Washington.
- Public Health Agency of Canada. 2015. *Canadian Antimicrobial Resistance Surveillance System Report 2015*. Ottawa.

- Roca, A., Quintó, L., Abacassamo, F., Morais, L., Vallès, X., Espasa, M., et al. 2008. Invasive *Haemophilus influenzae* Disease in Children Less than 5 years of Age in Manhica, a Rural area of Southern Mozambique. *Tropical Medicine & International Health*, 13(6):818–26. <http://doi.org/10.1111/j.1365-3156.2008.02061.x>.
- Salles, M. J. C., Zurita, J., Mejia, C., and Villegas, M. V. 2013. Resistant Gram-Negative Infections in the Outpatient Setting in Latin America. *Epidemiology and Infection*, 141(12):2459–72. <http://doi.org/10.1017/S095026881300191X>.
- United Nations, Department of Economic and Social Affairs, Population Division. 2015. *World Population Prospects: The 2015 Revision, Key Findings and Advance Tables*. Working Paper No. ESA/P/WP.241.
- Van Boeckel, T. P., Brower, C., Gilbert, M., Grenfell, B. T., Levin, S. Robinson, T. P., et al. 2015. Global Trends in Antimicrobial Use in Food Animals. *Proceedings of the National Academy of Sciences*, 112(18):5649–54. <http://doi.org/10.1073/pnas.1503141112>.
- Van Boeckel, T. P., Gandra, S., Ashok, A., Caudron, Q., Grenfell, B. T., Levin, S. A., and Laxminarayan, R. 2014. Global Antibiotic Consumption 2000 to 2010: an Analysis of National Pharmaceutical Sales Data. *The Lancet Infectious Diseases*, 3099(14):1–9. [http://doi.org/10.1016/S1473-3099\(14\)70780-7](http://doi.org/10.1016/S1473-3099(14)70780-7).
- White House. 2015. *National Action Plan for Combating Antibiotic-Resistant Bacteria*. Washington.
- World Bank. GDP per capita. Accessed on August 22, 2015. Retrieved from <http://data.worldbank.org/indicator/NY.GDP.PCAP.CD>.
- World Health Organization (WHO). 2015. *Antimicrobial Resistance: Draft Global Action Plan on Antimicrobial Resistance*. Geneva.

ABOUT THE CENTER FOR DISEASE DYNAMICS, ECONOMICS & POLICY

The Center for Disease Dynamics, Economics & Policy (CDDEP) was founded with the objective of using research to support better decision-making in health policy. CDDEP researchers employ a range of expertise—including economics, epidemiology, disease modeling, risk analysis, and statistics—to conduct actionable, policy-oriented research on malaria, antibiotic resistance, disease control priorities, environmental health, alcohol and tobacco, and other global health priorities.

CDDEP projects are global in scope, spanning Africa, Asia, and North America and include scientific studies and policy engagement. The CDDEP team is experienced in addressing country-specific and regional issues, as well as the local and global aspects of global challenges, such as antibiotic resistance and pandemic influenza. CDDEP research is notable for innovative approaches to design and analysis, which are shared widely through publications, presentations and web-based programs.

CDDEP has offices in Washington, D.C. and New Delhi and relies on a distinguished team of scientists, public health experts, and economists around the world.