

Controlling Antimicrobial Resistance: The Need to Mobilize and Coordinate Public and Private Sector Action

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Antimicrobials—drugs that kill infectious bacteria, viruses, parasites and fungi—are a mainstay of modern medicine.

Their discovery has revolutionized health care. But limited development of new medicines, decades of outmoded use, prescribing practices and the application of these products in agriculture and animal husbandry have driven increases in the number of microbes resistant to these life-saving drugs. The health care environment itself has become a source point for spread of antimicrobial resistance (AMR). Improvements in clinical and laboratory practices, combined with effective deployment and use of medical technology, can help to ensure antimicrobials are utilized appropriately, reducing risk to patients and lowering costs associated with resistance.

The recently published report of *The Review on Antimicrobial Resistance*, chaired by Lord Jim O'Neill of the United Kingdom, projects a massive increase in mortality due to AMR, accompanied by a \$100 trillion lost global economic productivity between now and 2050. The major health risk of AMR affects both the global South and North, and is among one of the leading development challenges across the globe. The massive scope of this challenge will require the combined resources and focus of both the public and private sectors if this growing drug resistance is to be halted and reversed.

This paper discusses three essential elements of a

comprehensive approach to AMR: prevention and control of infections, diagnostic testing to support effective treatment decisions, and surveillance and reporting on appropriate use of antimicrobials.

THE CHALLENGE: ANTIMICROBIAL RESISTANCE IS INCREASING RAPIDLY WORLDWIDE

Resistance is not new. Decades ago, shortly after the discovery and initial use of antibiotics, resistant bacteria were identified, but cases were rare and alternative effective drugs were available. Today, drug-resistant organisms are increasingly common and widespread. Resistance to tuberculosis in the form of multi-drug resistant (MDR) and extensively resistant (XDR) TB is on the increase on a global scale, resistance to anti-malarials continues and new combinations of antiretrovirals, including the use of more expensive second and third line drugs, are needed to help address the needs of 37 million people living with HIV.

Approximately 700,000 people die every year because they have been infected with a drug-resistant pathogen¹. The annual figure is projected to grow to as high as 10 million deaths by 2050, making antimicrobial resistance among the leading causes of death, and killing more people than cancer does today².

RESPONDING TO THE CHALLENGE

Fundamental change is required across many fronts in order to respond to the challenge of AMR. Medical technology that can prevent the spread of infections as well as accurate diagnosis and treatment must be leveraged and incorporated across the continuum of care. In addition, ensuring that the right drug is delivered to the right patient at the right time requires improvements in the timely identification of infections and enhancements in the way the world monitors resistance. In parallel, a long-term transformation is required in the incentives for discovering and developing new antimicrobials and in the ways antimicrobials are used in agriculture and food supply.

PREVENTING AND CONTROLLING INFECTION IS A CRUCIAL STARTING POINT

Preventing the occurrence and spread of infections is the first line of defense in addressing AMR. Investments in improved water and sanitation are critical components of community-based prevention. Screening tests can be used in health care facilities when patients are admitted to determine if they are carrying a drug resistant organism acquired in the community that can be spread to other patients, helping to control transmission. Further, the spread of resistant organisms in health care facilities can be prevented when comprehensive infection prevention practices are followed.

The organisms that cause infections can live on a variety of surfaces in health care settings, including on unwashed hands as well as medical equipment that both patients and

health care workers touch. As a result, these deadly organisms can be easily transmitted and cause health care-associated infections (HAIs). The World Health Organization³, national public health agencies⁴ and professional societies⁵ have summarized the core components of infection prevention and control programs necessary to address the transmission of HAIs. All health care facilities need to follow these essential procedures to prevent the spread of infections. In addition, depending on the setting of care and type of procedure, specific evidence-based interventions enabled by medical technologies should be deployed.

The risk of infections due to resistant organisms, both in health care settings and in the wider community, fuels the use of multiple and, frequently, broad spectrum antimicrobials, which in turn drives further antimicrobial resistance. Even with the development of new antimicrobials that enable treatment of once drug-resistant infections, organisms will continue to evolve and develop resistance. Therefore, preventing the spread of infection will always be a critical component of controlling AMR.

THE IMPORTANCE OF ACCURATE DIAGNOSIS AND THE TRANSFORMATIVE EFFECT OF RAPID TESTS

Empirical decision-making based on clinical observation and prior experience often results in patients quickly receiving treatment that is potentially effective. However, this very common medical practice is also a major source of unnecessary antimicrobial use and expansion of resistance. These prescribing decisions, which are often based on limited or no diagnostic information, contribute significantly to the improper, or unnecessary use of these important drugs.

Common and accessible diagnostic tests can identify the organism causing the infection (bacteria, virus, parasite or fungus), allowing providers to distinguish between these sources of infection and determine appropriate treatment. Once the pathogenic organism has been identified, diagnostic tests can determine which specific antimicrobial a particular pathogen will respond to, guiding the physician in appropriate drug choice and dosage for difficult to treat infections. After an antimicrobial has been prescribed, diagnostics should be consistently used to confirm the effectiveness of drug treatment.

Because there is generally a lag between the prescribing decision and the availability of diagnostic test results, patients regularly take antimicrobials before the organism causing the infection has been accurately identified and its susceptibility to antimicrobials determined. New rapid diagnostic tests for bacterial infections, which allow for the identification of an infection in minutes instead of hours or days, have the potential to transform the treatment process from an empirical one to a precise one. Agencies such as the Foundation for Innovative New Diagnostics (FIND) and Médecins Sans Frontières (MSF) have developed target product profiles to encourage industries to develop rapid diagnostic tests that

can differentiate between bacterial and viral fevers.

In order for useful tests that are available today, as well as more advanced tests in future development to be purchased and used by health care systems, barriers around access and uptake need to be addressed. At the moment, diagnostics are often undervalued by health care systems and as a result seem very expensive or cumbersome compared to simply prescribing an antibiotic. This can be true in both higher and lower income settings. Effective diagnostics have the potential to break the vicious cycle of over-treatment or under-treatment. However, this will require overcoming the embedded practice of physicians prescribing antimicrobials in the absence of any diagnostic testing as well as recognition that the long-term impact of antimicrobial resistance outweighs the incremental near-term cost of conducting diagnostic tests.

SURVEILLANCE IS ESSENTIAL FOR CONTROLLING ANTIMICROBIAL RESISTANCE ON BOTH A PATIENT AND POPULATION LEVEL

Control of antimicrobial resistance requires surveillance to ensure that the appropriate therapy is provided to patients. Surveillance tools can streamline identification of patients at greatest risk of antimicrobial resistance by assimilating information generated by a variety of sources as part of routine care. The near real-time availability of this data can enable clinicians to make more targeted empirical decisions to optimize antimicrobial use.

It is also critical for health care facilities to collect and aggregate data on antimicrobial use and resistance to drive the organizational change required to address unnecessary and inappropriate use of antimicrobials. In addition, surveillance tools can be used to create an early warning system to detect HAI cases before an outbreak occurs, so preventive action or rapid control of an outbreak can be taken. The surveillance data generated can be transmitted to public health authorities in order to monitor local, regional, and national trends.

With increased use of diagnostics and rise of information-enabled instruments and devices, it will be important that the data captured by these technologies is leveraged to provide better surveillance information in real-time. In order to ensure this data is used effectively when generated on a much larger scale, the systems and governance standards need to be discussed and determined by governments, public health agencies, and regulatory bodies.

IMPORTANCE OF A COLLABORATIVE PUBLIC-PRIVATE SECTOR RESPONSE

The United Nations General Assembly (UNGA) convened a high-level meeting on AMR in September 2016, demonstrating global concern and action is needed to address AMR from many stakeholders across sectors. Given the very large current and future economic costs of resistance, as well as the tragic human health impacts, the public and private sectors must work together on a global scale to ensure that

all tools that can aid in the control AMR are being deployed. The development of new antibiotics is a critical component, but will not solve the problem alone. Medical technology that can prevent and control infections, provide accurate diagnosis, as well as track and report the spread of infections to inform treatment decisions must be leveraged across the continuum of care.

Now is the time for international agencies, governments, donors and the private sector to commit to working together to create the right incentives to encourage innovation in medical technologies to control AMR. The global community has come together to address issues such as immunization, HIV & AIDS, TB and Malaria with much success, and our experience from these initiatives can help inform the path forward for AMR. The private sector must continue to invest in developing medical technologies that improve prevention efforts and reduce the time to actionable diagnosis. Governments and policymakers need to ensure swift regulatory approvals for innovations in this space and adequate reimbursement for technologies designed to address this public health threat. This will not only save lives but also prevent the massive economic costs of inaction. **GHD**

REFERENCES

1. Review on AMR, *Antimicrobial resistance: Tackling a crisis for the health and wealth of nations*, 2014.
2. Review on AMR, *Tackling drug-resistant infections globally: Final report and recommendations*, 2016.
3. World Health Organization, *Core components for infection prevention and control programmes*, 2008
4. Siegel JD, Rhinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee, 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings <http://www.cdc.gov/ncidod/dhqp/pdf/isolation2007.pdf>
5. Deborah S. Yokoe, Deverick J. Anderson, Sean M. Berenholtz, David P. Calfee, Erik R. Dubberke, Katherine D. Eilingson, Dale N. Gerding, Janet P. Haas, Keith S. Kaye, Michael Klompas, Evelyn Lo, Jonas Marschall, Leonard A. Mermel, Lindsay E. Nicolle, Cassandra D. Salgado, Kristina Bryant, David Classen, Katrina Crist, Valerie M. Deloney, Neil O. Fishman, Nancy Foster, Donald A. Goldmann, Eve Humphreys, John A. Jernigan, Jennifer Padberg, Trish M. Perl, Kelly Podgorny, Edward J. Septimus, Margaret VanAmringe, Tom Weaver, Robert A. Weinstein, Robert Wise and Lisa L. Maragakis (2014). A Compendium of Strategies to Prevent Healthcare-Associated Infections in Acute Care Hospitals: 2014 Updates. *Infection Control & Hospital Epidemiology*, 35, pp S21-S31.

