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The Economic Costs of Antimicrobial Resistance

In April 2014, the *World Health Organization* (WHO) revealed in their "*Antimicrobial Resistance: Global Report on Surveillance*" that *Antimicrobial (Drug) Resistance* (AMR) has reached "*urgent*" levels, resulting in the possibility of common infections and minor injuries killing people, which *"threatens the achievements of modern medicine"*.[1] AMR is the *"reduced efficacy of antibacterial, antiparasitic, antiviral and antifungal drugs, making the treatment of patients difficult, costly, or even impossible."*[2] AMR is different from *antibiotic resistance*, which refers specifically to the resistance of certain antibiotics used for common bacteria that causes infections.[3] In contrast, AMR encompasses a broader resistance to medications that treat infections caused by microbes, such as: *"(1) parasites (e.g. Malaria), (2) viruses (e.g. HIV) and, (3) fungi (e.g. Candida)."*[4]

AMR was initially considered a *"human medical problem"* to which only patients with *hospital-acquired infections* (HAI), the critically ill, or the immunosuppressed would be likely to succumb.[5] Today, AMR has spread to the point that "*the general population is considered to be at risk*," at a time where "*common bacterial infections are becoming increasingly difficult to treat.*"[6] There are a number of natural (i.e., biological) and societal causes behind this current phenomena. Three biological explanations for AMR include:

(1) *Selective Pressure* - Microbes that are killed by an antimicrobial carry a resistant gene and survive. These survivors will replicate and quickly become the dominant type throughout the microbial population;
(2) *Mutation* - Microbes produce by dividing and during division mutation s may arise that allow the microbe to survive; and,
(3) *Gene Transfer* - Microbes may get genes from one another, including genes that make the microbe drug resistant.[7]

In addition to biological causes, societal pressures that can be attributed to increased AMR include:

(1) Inappropriate prescription of antimicrobials by healthcare providers,
(2) Inadequate diagnostics, which result in the prescription of antimicrobials *"just-in-case"*;
(3) The extensive use of antimicrobials in the hospital; and,
(4) The addition of antibiotics to agricultural feeds, which promotes drug resistance.[8]

The negative medical and economic effects of AMR may be significant if this phenomenon continues without resolution. For example, anyone who receives care in a medical setting (inpatient or outpatient), could potentially succumb to an infection.[9] AMR could also impact the future of preventative care, especially in developed countries where antimicrobial drugs are methods for secondary care, because:

> "*…health care systems in high income countries are heavily dependent on the use of antimicrobial drugs, not only for the treatment of primary infections, but also for many aspects of secondary health care, such as cancer treatment or prevention of iatrogenic infection in surgical care. Therefore, in high-income countries, hospital-acquired infections are a major concern*."[10]

At least two million Americans annually become infected with bacteria that are resistant to antimicrobial drugs, and at least 23,000 individuals die each year as a result.[11] By 2050, if this problem continues, more than 10 million people per year will die due to AMR.[12] In 2000, *The Alliance for the Prudent Use of Antibiotics* (APUA) and Chicago's Cook County Hospital conducted a chart-by-chart review of 1,391 hospitalized patients, 188 of which patients had *antibiotic-resistant infections* (ARIs). The medical costs ranged from $18,588 to $29,069 per patient, with a hospital stay lasting between 6.4 and 12.7 days.[13] These avoidable infections resulted in more than 8 million additional hospital days, and approximately $5.5 million in additional costs.[14]

In addition to the negative medical effects of AMR, this phenomenon is also resulting in substantial economic costs. A 1992 *Institute of Medicine* (IOM) report estimated the annual costs of antibiotic-resistance bacteria in the U.S. to be at least $4 to $5 billion.[15] Over the next 35 years, the accumulated loss of global output due to AMR, will total $100 trillion, more than 1.5 times the current annual global GDP.[16] These increased costs stem from a variety of mechanisms, including:

(1) Additional labs and X-rays;
(2) Alternative, more expensive treatments;
(3) More elaborate infection control procedures;

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(4) Reduced quality of life;
(5) Increases in private insurance coverage premiums;
(6) Increased overall healthcare expenditure;
(7) Increased cost of disease surveillance;
(8) Increased family burden of infected individual; and,
(9) Increased cost to firms of absentee workers.[17]

If resistance rates continue to increase at the current pace, additional *indirect costs* may arise from affected individuals who refrain from undertaking certain economic activities, such as travel and trade, or experience general negative psychological effects such as panic.[18] Due to the current lack of urgency among the U.S. population related to AMR, the indirect costs have been shown to be substantial, although these costs have, to date, been understudied and poorly understood by scientists.[19]

Despite the apparent lack of urgency regarding AMR among the general population, the federal government, as well as various governmental agencies, are taking substantial steps to combat AMR through budgetary appropriations and program. On February 2, 2015, President Obama released his proposed budget for fiscal year 2016, which included more than $1.2 billion to be allocated across various agencies to: (1) improve antibiotic stewardship; (2) strengthen risk assessment and reporting; and, (3) promote research in health and agricultural sectors.[20]

On a provider level, healthcare organizations are implementing practicing antibiotic stewardship programs,[21] which programs may include the following components:

(1) Appointing an individual physician leader to be responsible and accountable for the program's outcomes;
(2) Appointing a single pharmacist leader to be responsible for improving antibiotic use
(3) Implementing recommended actions such as *"systematic evaluation of ongoing treatment need after a set period of initial treatment";*
(4) Implementing an effective form of tracking and reporting of antibiotic use and resistance; and,
(5) Educating clinicians about resistance and optimal prescribing.[22] While these measures certainly will not eradicate infections, the above efforts can aid in improving the treatment of infections and reduce the adverse events linked to inappropriate antibiotic use.

These programs strive to combat the rapid increase of AMR, not just to decrease the medical and economic costs related to the phenomenon, but also to increase the overall health of, and ability to treat, the general U.S. population well into the future.

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