Diagnostic Data and Community Surveillance:

A Contemporary Approach to Implementing Antimicrobial Stewardship Monitoring

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THE FIGHT AGAINST antimicrobial resistance (AMR) demands both effort and commitment from everyone involved in healthcare and the understanding and enforcement of policy disciplines. Among the hurdles that healthcare leaders face, *unifying information and training across diverse healthcare disciplines on resistant infections* may present the two greatest challenges. Despite oversight measures such as US Senate bill 1311 [which requires hospitals to have an antimicrobial stewardship program (ASP)],[17] gaps in awareness, resources, and education can impact the ability of these measures to reach their maximum potential.

An ASP is a comprehensive, systematic effort to promote the appropriate use of antimicrobials (including antibiotics) and is considered the best response from hospitals to avoid the medical and economic risks of AMR. Per APIC, ASPs should be designed to improve patient outcomes, reduce microbial resistance, and decrease the spread of infections caused by multidrug-resistant organisms (see, e.g., Association for Professionals in Infection Control and Epidemiology, https://apic.org/professional-practice/practice-resources/antimicrobial-stewardship/). The critical connection with precision medicine is to ensure that the most appropriate antimicrobial is delivered to the infected population while keeping in mind the vagaries of responses by individuals.[1]

Many US hospitals have a program that meets all seven CDC objectives (see https://www.cdc.gov/antibiotic-use/core-elements/index.html), but the quality of those programs and the results they deliver can vary widely. Optimizing a facility's stewardship program can support better prescribing practices, and help that hospital achieve heightened clinical, financial, and operational goals, and most of all, patient outcomes. However, the installation and practices of stewardship programs vary, and in some cases the sole "steward" for an entire hospital is the resident pharmacist.

Access to quality diagnostic tools for susceptibility testing or a system of community surveillance tools is critical for the implementation of an ASP. Most hospital systems, however, utilize traditional methods to control infectious diseases that are more readily available but less AMR focused. Healthcare centers in rural areas, for example, may lack the resources to retain either infectious disease pharmacists or infectious disease physicians, or nursing staff trained in antimicrobial stewardship.

With new efforts to fight AMR,[2] surveillance tools have become comparatively simpler, less costly, and quicker to implement. Hospitals can access this network of data to help inform a battle strategy for fighting AMR in facilities lacking infectious disease expertise, thereby allowing smaller facilities to join the effort. Successful ASPs should include consistent education and implementation of the diagnostic and data sharing tools available to support optimized use of antimicrobials. Diagnostics, continued education, data, and surveillance are among the primary methods to achieve these public health objectives.

Cases of successful ASPs have been reported worldwide. Australia, for example, made AMS a criterion for health services accreditation in 2013; while the extent of its impact is still to be determined, such measures will no doubt shift the emphasis of "stewardship in everyday clinical practice." China has experienced a sharp uptick of multidrug resistant organisms (or MDROs, which we will describe in more detail later), so the Chinese Ministry of Health launched a campaign to raise awareness of AMS in healthcare settings. Preliminary analyses imply that this has led to a reduction in antibiotic use. And Chile, a country once notorious for dispensing antibiotics easily without requiring prescriptions, enacted a ban in 1999 on over-the-counter use of antibiotics without a prescription, which led to usage levels remaining lower than they were in their pre-intervention period, even today.[3]

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The Value of Diagnostics, Data, and Surveillance

A clinician's first steps in antimicrobial decision-making starts with determining whether the patient has an infection that requires antimicrobials. These steps include arranging for the appropriate lab tests (with relevant supplies and cultures) before recommending a course of treatment. Due to the rise in MDROs, integral parts of clinical decision making – such as identifying bacteria and assessing their response to antibiotics – have grown increasingly important.[9] Clinicians without access to rapid diagnostic tests (RDTs) cannot always wait for test results before initiating antimicrobial treatment and must rely on empiric therapy. RDTs support a clinician's evidence-based decision making and can improve patient outcomes.

Today, new technologies for RDTs abound – for example, polymerase chain reaction (PCR) technology,[8] a newer method, brings the ability to detect, identify, and track resistance in a relatively short time. The next advance is multiplex PCR (mPCR), which enables PCR panels that provide for time-saving processes by testing a patient for a broad range of pathogens, allowing for more rapid (and accurate) diagnoses. With advanced testing now available through rapid diagnostics, healthcare systems can better support monitoring and surveillance efforts, changing the game for tracking the introduction and spread of an infection.

Even more important, however, is educating and raising the awareness of practitioners regarding the advantages of these newly developed healthcare tools for improved treatment. Further empowered by systematic surveillance, practitioners will be able to raise the standard of care, as measured by improved public health and patient outcome metrics.

When deciding an appropriate treatment plan for a patient, speed and precision of diagnostic solutions are crucial to successfully coordinate stewardship initiatives across hospital departments. Some advanced analytics platforms are capable of consolidating and monitoring real-time infectious disease data by integrating feeds from multiple data sources to track a spectrum of bacterial pathogens and antibiotic resistance markers, including MDRO trend data that can be easily shared inside the hospital. Additionally, this spectrum of collected data can support better empiric therapy. Antibiograms, for example, can now be based on more components upon which hospitals heavily rely when evaluating information about bacterial pathogens.

What is an antibiogram?

An antibiogram is an overall profile of antimicrobial susceptibility testing results of a specific microorganism to a battery of antimicrobial drugs. This profile is generated by the laboratory using aggregate data from a hospital or healthcare system; data are summarized periodically and presented showing percentages of organisms tested that are susceptible to a particular antimicrobial drug. Only results for antimicrobial drugs that are routinely tested and clinically useful should be presented to clinicians.

See, e.g., https://www.health.state.mn.us/diseases/antibioticresistance/abx/antibiograms.pdf

In brief, diagnostic capabilities can contribute value across the entire patient journey and help improve a facility's stewardship program metrics. Increased application of diagnostic data and other infectious disease monitoring tools, however, are still needed to inform antimicrobial prescribing practices. As a case in point, consider

Figure 1: Rapid diagnostics lowers unnecessary prescriptions[7]

Figure 1, which shows that nearly three quarters of antibiotics recipients in the United States have been prescribed unnecessarily (that is, antibiotics are prescribed due to urgency but lack full diagnosis).

Some clinicians even advise that stewardship strategies begin as early in a patient's healthcare journey as pediatric treatment to alleviate the efforts on both national and global levels (see **Figure 2**). A child's caregiver, for example, may request antibiotics from their clinician unnecessarily without knowing that such practices can escalate the threat of AMR. Pediatricians must intervene and educate healthcare providers during these early moments to prevent downstream complications, including the likelihood that their pediatric patients become adults who carry resistance patterns.

As noted above, another tool for combating resistance spread is a syndromic panel, a time-saving physician's process of testing a patient for a broad range of pathogens with overlapping symptomology simultaneously. Syndromic panels have equipped clinicians to "rapidly identify bacteria, viruses, fungi, and parasites and are now fully integrated into the standard testing practices of many clinical laboratories."[9] Along with the key factors of surveillance and advanced testing now available through rapid diagnostics, these panels have changed the game. The education, awareness, and advantages of newly developed surveillance tools bring a wealth of information that raises the standard of care, tremendously improving healthcare overall.

Despite a promising arsenal of technological advancements, many healthcare leaders acknowledge there is still a long way to go. As shown in **Figure 3**, one estimate of global mortality caused by AMR by 2050 could reach staggering heights in all parts of the world (N.B. – the estimate was made prior to the onset of COVID-19).[7] This figure emphasizes an alarming reality of a public health crisis of global proportions growing increasingly difficult to control.

Genomic sequencing and similar techniques have been critical to tracking COVID-19 variants and infectious disease management (e.g., the rise in bacterial resistance). Metagenomic and next-generation sequencing (NGS) tools enable researchers to capture and share the data necessary to predict resistance trends and build antibiograms, a reporting component upon which hospitals heavily rely when evaluating information about bacterial pathogens. In addition, advanced analytics software connects diagnostic data inside US hospitals, providing critical lab and clinical data across departments, processes, and vendors.

In an interconnected world, local use of diagnostics and advanced monitoring and surveillance solutions can foster communication and collaboration among regions to address the spread of AMR. An up-to-date global view of microbial genetics would support clinicians, microbiologists, and public health stakeholders in making informed decisions on antimicrobial use (see **Table 1**).

"A recent study drew conclusions upon the impact that coronavirus has on AMR, including patients infected with coronavirus being more likely to receive antimicrobial therapy due to overlapping symptoms."

The Value of Multidrug-Resistant Organism (MDRO) Surveillance

AMR is both a community problem and collective global problem – it knows neither borders nor boundaries. Due to a lack of access to advanced surveillance tools, many hospital systems utilize readily available, traditional methods to support ASP efforts. In addition to the seven CDC objectives for stewardship, the CDC also identifies the following seven control interventions within MDRO practice: administrative support, education, judicious use of antimicrobial agents, MDRO surveillance (described as a "critically important component of any MDRO program"), infection control precautions, environmental measures, and decolonization.[10]

Education to Optimize Utilization of Antimicrobials, Improve ASP Performance

Many field experts today with long tenures studying containment methods for AMR – including best practices within ASPs – recommend a simple but

Figure 2: How surveillance improves outcomes[7]

powerful solution for better infectious disease public health management as a highly effective one: education.

When healthcare centers offer comprehensive training programs to thoroughly equip their teams, they open the possibility for other public health tools and techniques: well-tailored patient therapies, advanced diagnostics processes, highly productive surveillance methods, and so on. When it comes to boosting advanced data solutions, it's not difficult to prove the value in offering ASP-related educational resources to healthcare professionals.

By its very nature, ASP is multi-disciplinary due in part to the seven elements stipulated by the CDC for these programs to work.[11] To ease installation and implementation, ASP-specific training programs have emerged, including Making a Difference in Infectious Disease (MAD-ID), which offers both basic and advanced levels of antimicrobial stewardship training.[12] For another example, the Infectious Disease Society of America (IDSA) curriculum "[was] designed to provide ID fellows with a foundation in antimicrobial stewardship, regardless of their ultimate career plans."[13] Such language indicates that antimicrobial stewardship training is not for siloed specialists; instead, everyone in healthcare should be encouraged to take advantage of this crucial resource.

It is important to note, however, that these programs are often limited to key job functions such as clinician or physician, pharmacist, and nurse; consequently, many competent key stewardship team players are denied an opportunity to provide better care to patients. One way to take down silos is for experienced antimicrobial stewards to take up the duty and opportunity to educate their peers and encourage acceptance of best stewardship practices. In one study, 77% of fellowship directors reported that stewardship

training "is very or extremely important for infectious disease fellows."[14]

Another study emphasized the need for "more robust evaluation ... [in] ... training prescribers" in antimicrobial stewardship, given "the global challenge of antimicrobial resistance."[15] Clinical providers, physicians' assistants, pharmacists, and advanced nurse practitioners that specialize in antibiotic resistance are suitable examples of who would benefit. The more diverse the professionals that participate in these kinds of training programs, the more participation will expand across specialties, practices, and departments. All stand to benefit, and more professionals are recognizing this.

Over time, clinical leaders have begun involving more of the right people in such training, expanding them into stewardship meetings, medical staff meetings, infection prevention meetings, and even in collaborations with laboratory technicians. Interest in stewardship training programs also continues to grow; this momentum typically fuels more expansive educational opportunities for antimicrobial stewardship. Stewardship teams focused on credentials have paved the way for training programs to grow and gain influence in healthcare organizations.

Table 1: CDC Assessment of Antibacterial Resistance Threats[8]

Urgent Threats
Clostridium difficile
Carbapenem-resistant Enterobacteriaceae (CRE)
Drug-resistant *Neisseria gonorrhoeae*
Serious Threats
Multidrug-resistant *Acinetobacter*
Drug-resistant *Campylobacter*
Fluconazole-resistant *Candida* (a fungus)
Extended spectrum beta-lactamase-producing Enterobacteriaceae (ESBLs)
Vancomycin-resistant Enterococci (VRE)
Multidrug-resistant *Pseudomonas aeruginosa*
Drug-resistant nontyphoidal *Salmonella*
Drug-resistant *Salmonella Typhimurium*
Drug-resistant *Shigella*
Methicillin-resistant *Staphylococcus aureus* (MRSA)
Drug-resistant *Streptococcus pneumoniae*
Drug-resistant tuberculosis
Concerning Threats
Vancomycin-resistant *Staphylococcus aureus* (VRSA)
Erythromycin-resistant Group A *Streptococcus*
Clindamycin-resistant Group B *Streptococcus*

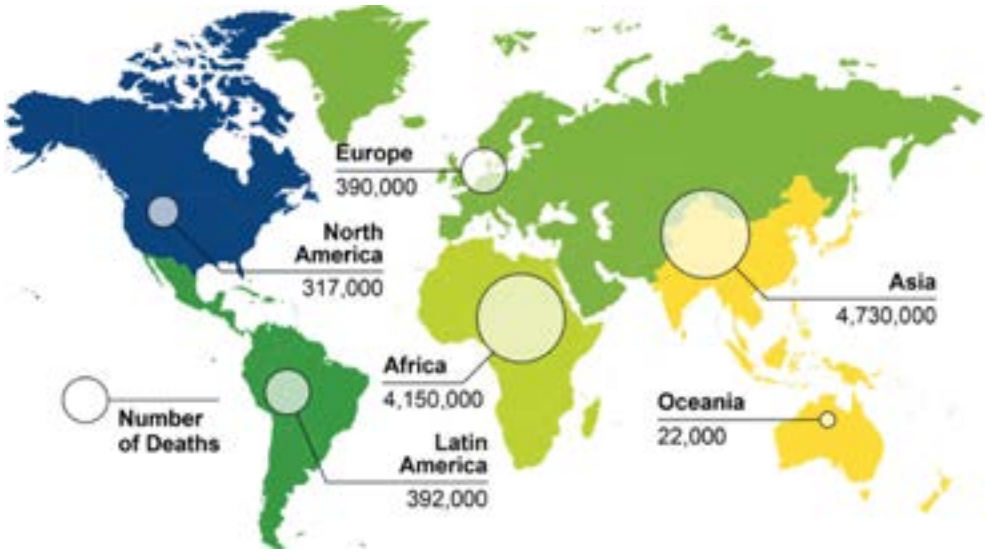

Figure 3: Predicted annual deaths from AMR by 2050[7]

> *"Even the federal government has played a role in propelling forward ASPs. Senate Bill (SB) 1311 requires care hospitals to adopt their own antimicrobial stewardship policies, one 'that includes a process to evaluate the judicious use of antibiotics.'"*

AMR and COVID-19

In 2014, the UK Prime Minister, David Cameron, commissioned a report, "The Review on Antimicrobial Resistance," to examine AMR as a global issue and the necessary measures to tackle it by way of a global effort. Cameron recognized that if an AMR spread were to get out of hand due to a "[failure] to act," this "unthinkable scenario" would be one in which we would be "cast back into the dark ages of medicine," with developing countries bearing the greatest harmful impact of this public health crisis. In the foreword of this report, Dr. Jim O'Neill, who chaired the Review of Antimicrobial Resistance, said, "Indeed, even at the current rates, it is fair to assume that over one million people will have died from AMR since I've started this Review in the summer of 2014."[16]

Today, in 2022, COVID-19 not only bears many ominous resemblances to AMR (similarly cited by many as a silent pandemic), but it also sheds further light on the critical need to address widespread adoption of ASPs (including casting a bright light on effective medicines versus the inappropriate use of ivermectin). In fact, the World Health Organization (WHO) named AMR among one of the top public health priorities, before the onset of the COVID-19 pandemic.[17] A recent study drew conclusions upon the impact that coronavirus has on AMR, including patients infected with coronavirus being more likely to receive antimicrobial therapy due to overlapping symptoms.[18]

Another study – the first one to examine the global impact of COVID-19 on AMR – highlighted key "actions to help ensure that AMR remains a global health priority," including facilitating "reliable AMR surveillance data, [developing] more sustainable IPC programs, promoting integrated antibiotic stewardship guidance, leveraging increased laboratory capabilities, and other system-strengthening efforts."[19] For instance, by using enhanced testing and surveillance tools, some US hospitals have been able to discover that the delta variant of COVID-19 exhibited a more widespread presence than that of other variants. As new variants continue to mutate, there is no question that testing will continue to play a core role in addressing threats such as COVID-19 and AMR concurrently. Amidst the global COVID-19 pandemic, the syndromic approach has also proven – and will continue to prove – highly effective within the efforts to slow the spread of AMR. With the omicron variant detected in most US states as of December 20, 2021, surveillance methods remain vital in tracking new variants that perpetuate this pandemic.

Despite the prospective future that ID workers face (antimicrobial drug consumption is estimated to rise by 67% by 2030), oversight in healthcare has

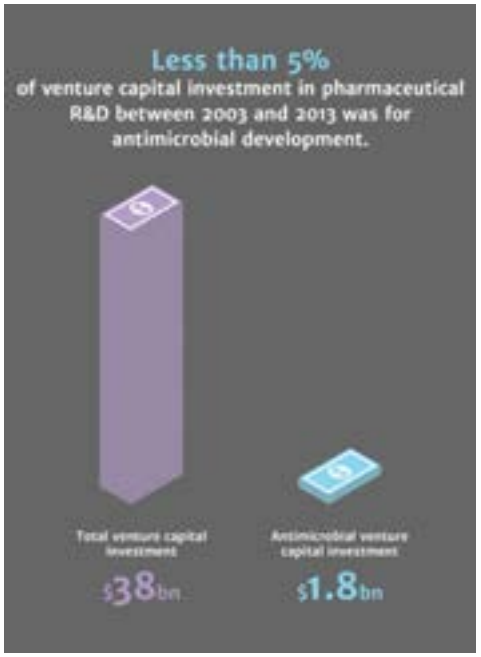

Figure 4: Reasons for Hope: The Most Effective Stewardship Strategies and Techniques

Antimicrobial R&D has not been an attractive investment to venture capitalists in previous years[5]

improved over the years – another major factor in boosting ASP efforts in hospitals. Even the federal government has played a role in propelling forward ASPs. Senate Bill (SB) 1311 requires care hospitals to adopt their own antimicrobial stewardship policies, one "that includes a process to evaluate the judicious use of antibiotics." [20]

A principal case of introducing or in some cases overhauling ASPs in hospital facilities, this bill requires specific conditions for hospitals, such as "[developing] a physician-supervised multidisciplinary antimicrobial stewardship committee, subcommittee, or workgroup," or "[reporting] [ASP] program activities to each appropriate hospital committee undertaking clinical quality improvement activities."

Since the passage of SB 1311, healthcare oversight in this area has stimulated the establishment of ASPs to an unprecedented degree. Take, for instance, the Centers for Medicare and Medicaid Services (CMS), which now requires antimicrobial stewardship participation quotas. Programs must either comply with and meet engagement quotas, or risk losing their funding.

Formerly, efforts to address resistant organisms have been broadly dismissed in healthcare, deemed unprofitable and thus unaffordable, given little attention as a result. Today, this pattern has flipped: such efforts are now more commonplace; in some cases, organizations need to be encouraged or even incentivized to offer AMR-combative programs. The awareness that patients continue to die from AMR-related infections has helped spark reform. Until recently, there was little motive to develop new drugs to circumnavigate resistant organisms (see **Figure 4**); now, mitigation options are much more heavily researched and funded. JoPM

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Table of Summary Points

- While some experts believe that new solutions to stop the spread of antimicrobial resistance (AMR) are working, AMR spread continues to raise concerns for the future of public health.
- In order to prevent antimicrobial resistance from continuing to spread, the effort and commitment of everyone in healthcare will be critical.
- If one were to have hopes of eradicating AMR, strong antimicrobial stewardship initiatives that require the incorporation of consistent education, community surveillance, and diagnostic and data sharing tools to support optimized use of antimicrobials must be implemented. This is especially true for hospitals and healthcare centers with limited resources and staff.
- As we've learned from the COVID-19 pandemic, access to fast and accurate testing is considered more critical now than ever before.
- As oversight in healthcare continues to improve, so also do the chances of these facilities carrying out faster and more accurate diagnosis and patient treatment plans, enhancing their antimicrobial stewardship programs, and creating a greater impact in combatting AMR.
- Equally (if not more) critical to having access to best-in-class technological capabilities is the need to educate and train healthcare professionals to bolster the stewardship efforts of hospital systems.

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