SIDP PAC CARB response - January 7, 2019

GOAL 1: Slow the Emergence of Resistant Bacteria and Prevent the Spread of Resistant Infections

Recommendation 1: Strengthen requirements for educational programs that encourage appropriate antibiotic use across healthcare. The current recommendations in goal 1.1 are suggestive, voluntary and not standardized. Antibiotics are a complex class of drugs with unique properties that healthcare professionals should understand in order to ensure their safe use for the patient that they are intended for, as well as to prevent harm to a larger population. The Society of Infectious Diseases Pharmacists (SIDP) supports a stronger commitment to more robust standards that guide 1) the type of education required, 2) the frequency of education, and 3) promotion of the inclusion of formalized education as part of any future versions of mandates linked to federal funding, such as the CMS Conditions of Participation or the CDC's Antibiotic Solutions Initiative. Professional groups covered by these requirements should include physicians, advanced practice professionals, pharmacists, nurses, dentists, veterinarians, and agricultural industry members. Existing educational programs in human health target professionals in acute care settings, such as academic medical centers or larger community hospitals, where existing antibiotic stewardship resources exist. There is a need to expand educational goals to include specific milestones for critical access hospitals, outpatient clinics (including urgent care, dialysis centers, and ambulatory surgery centers), and long term care facilities. Educational programs should also incorporate strategies for how to engage the patient and the lay public regarding appropriate antibiotic use. SIDP recommends that strong considerations should be given to delegating these requirements to the state-level (e.g. state medical/pharmacy/veterinarian boards) and professional societies.

Recommendation 2: Protect the supply of existing drugs: National anti-infective drug shortages are associated with patient harm which can include an increased risk of *Clostridioides* (*Clostridium) difficile,* under-treatment of serious infections due to the lack of appropriate agents and overprescribing of unnecessary broad-spectrum antibiotics, such as carbapenems, which can increase the risk of antibiotic resistance. Therefore, we suggest a **new** priority that will further develop strategies to mitigate the impact of anti-infective shortages and decrease risk of shortages from occurring through enhanced communication and early response from manufacturers and the FDA. Key anti-infective agents that are both generic and essential to public health should be identified and public/private/academic partnerships should be developed to ensure a consistent supply of key agents is available.

References:

1. CDC Antibiotic Resistance Solutions Website - https://www.cdc.gov/drugresistance/solutions-initiative/index.html
2. ANA – CDC Whitepaper on the role of registered nurses in hospital antibiotic stewardship practices. https://www.cdc.gov/antibiotic-use/healthcare/pdfs/ANA-CDC-whitepaper.pdf
3. Heil EL, Kuti JL, Bearden DT, Gallagher J on behalf of the Society of Infectious Diseases Pharmacists. The essential role of pharmacists in antimicrobial stewardship. *Infection Control and Hospital Epidemiology* 2016; 753-754. https://doi.org/10.1017/ice.2016.82
4. Quadri F, Mazer-Amirshahi M, Fox ER, et al. Antibacterial drug shortages from 2001 to 2013: Implications for clinical practice. Clinical Infectious Diseases 2015; 60(12):1737-42. https://doi.org/10.1093/cid/civ201
5. Gross AE, Johannes R, Gupta V, et al. et al. The effect of a piperacillin/tazobactam shortage on antimicrobial prescribing and *Clostridium difficile* risk in 88 US Medical Centers. Clinical Infectious Diseases 2017; 65(4): 613-618. https://doi.org/10.1093/cid/cix379

Goal 2: Strengthen National One-Health Surveillance Efforts to Combat Resistance

Recommendation 1: Develop incentives to facilitate the ability to better track antibiotic use and resistance in the outpatient and long-term care settings. Sub-objective 2.2.1 currently provides suggestions for promoting increased reporting of hospital data, but an information deficit exists when it pertains to obtaining antibiotic utilization and resistance data in outpatient clinics and in long-term care. Many long term care facilities and outpatient clinics lack a basic electronic health record (EHR) infrastructure or, if they have one in place, the functionality is limited and it cannot produce an aggregate antibiotic use or resistance report that is actionable. Incentives or requirements from CMS are needed and could facilitate EHR adoption or EHR enhancements which will create a data infrastructure that allows for the submission of antibiotic use data through the NHSN AUR module. For the outpatient setting, a potential alternative approach that would capture most patient level antibiotic utilization could be through mandating/incentivizing insurers to track and report dispensed antibiotics from pharmacies or requiring/incentivizing the largest pharmacy chains to report their dispensing data. Increasing the availability of information related to antibiotic use from these facilities would help to fill the information gap across the healthcare continuum, and if shared with public health, will allow for improved detection and control of antibiotic resistant organisms, thus aligning with the "One Health" approach.

Recommendation 2: Support timely national and regional susceptibility reporting that is available "on demand". Although the CDC does have an interactive website for tracking antibiotic resistance data across the US (Patient Safety Atlas), it is limited to select pathogens that have been isolated from a short list of healthcare associated infections and has not been populated with new information since 2014. One suggestion is to create a recommendation for the CDC to integrate data from the Antibiotic Resistance laboratory network into this centralized, publically available website. This would allow healthcare professionals and researchers to track shifting resistance patterns and generate reports of interest on demand, similar to what is tracked by the Canadian Antimicrobial Resistance Alliance (CARA). A longer-term goal would be to enhance national reporting and expand from just tracking resistance, to also tracking mortality associated with infections due to resistant organisms, and have this information available in an easily searchable manner.

References:

Office of the National Coordinator for Health Information Technology. 'Office-based physician electronic health record adoption,'Health IT Quick Stat #50. December 2016. Available at https://dashboard.healthit.gov/quickstats/pages/physician-ehr-adoption-trends.php.

Philip W. Smith et al., "Antibiotic Stewardship Programs in Long-Term Care Facilities," Annals of Long-Term Care 19 no. 4 (2011): 1- 8, http://www.annalsoflongtermcare.com/article/antibiotic-stewardship-programs-long-term-care-facilities

Susan M. Rhee and Nimalie D. Stone, "Antimicrobial Stewardship in Long-Term Care Facilities," Infectious Disease Clinics of North America 28, no. 2 (2014): 237-46 ,http://dx.doi.org/10.1016/j.idc.2014.01.001.

Canadian Antimicrobial Resistance Alliance - http://can-r.com/

Centers for Disease Control – Lab Capacity: Antibiotic Resistance Laboratory Network (AR Lab Network). September 2018. Available at https://www.cdc.gov/drugresistance/solutions-initiative/ar-lab-network.html

Goal 3: Advance Development and Use of Rapid and Innovative Diagnostic Tests for Identification and Characterization of Resistant Bacteria

Recommendation 1: Invest in improved testing methodologies. We recommend guidance and incentives to investigate more accurate methods for detecting antibiotic resistant organisms. For example, better methods are needed for detecting linezolid and daptomycin-nonsusceptible *Enterococcus* species and vancomycin-intermediate *Staphylococcus aureus*. Currently methodologies are inaccurate and/or provide discordant results. In addition, incentives should be developed that promote research and commercialization of products that are less expensive, easy to use and more readily accessible to clinicians in under-resourced institutions such as rural hospitals, nursing homes, and at the point of care.

Recommendation 2: Develop goals that incentivize diagnostic stewardship. Inappropriate testing, overuse of tests, as well as underutilization of tests directly influences antibiotic use and can falsely elevate healthcare-associated infection reporting. Goals should be established that encourage development of guidelines, as well as policies that help to better guide when diagnostic testing (e.g. urinalysis/urine cultures, rapid diagnostics, etc.) should be performed (vs. avoided) in clinical care.

References:

Kirn TJ, Onyeaso E, Syed M, Weinstein MP. Systematic evaluation of commercial susceptibility testing methods for determining the *in vitro* activity of daptomycin versus Staphylococcus aureus and Enterococci. J Clin Microbiol. 2014.;52(6):1877-82. https://doi.org/10.1128/JCM.03439-13 .

Messacar K, Parker SK, Todd JK, Dominguez SR. Implementation of Rapid Molecular Infectious Disease Diagnostics: the Role of Diagnostic and Antimicrobial Stewardship. Journal of Clinical Microbiology 2017;55(3): 715-723. https://doi.org/10.1128/JCM.02264-16

Goal 4. Accelerate Basic and Applied Research and Development for New Antibiotics, Other Therapeutics, and Vaccines

Recommendation 1: Promote the development of new antibiotics - Ensure access to anti-infective agents through increased regulation, coordination with insurance providers, and public/private/academic manufacturing partnerships. There is an overall need for additional "push" and "pull" incentives that promote investment for discovery and development of new antibiotics. These include:

- Creating innovative new funding mechanisms and partnerships for antibiotic research
- Developing recommendations that reform CMS policy towards inpatient reimbursement of antibiotics outside of the current DRG payment system.
- Developing a system that incorporates local epidemiology and patient risk that moves away from a "one-size fits all" approach. Emphasis should be placed on reimbursement for appropriateness of use rather than amount of use.
- Developing a framework for value-based pricing/reimbursement like those used in hepatitis C therapies and cancer treatments
- Creating a working group that includes experienced representation from successful drug developers to formulate risk-balanced approach towards programs and priorities in the discovery of new treatments. While there have been very extensive and deliberate attempts to develop new modes and classes of treatments in the last 3 decades, the increased emphasis on such may be creating an imbalance of approaches that are directly impacted by public funding that comes at the expense of more tried and true approaches. It would be good for this group to assess whether the current funding mechanisms have a balanced "portfolio" of risk.

Recommendation 2: Increase funding to improve the management of patients with less common infectious diseases, as well as alternative treatment methods for infections caused by multi-drug resistant organisms. This would include support for post-approval trials (both prospective and retrospective) to evaluate or describe outcomes and safety in less commonly-occurring infections for FDA approved drugs. This support could be in the form of grants for clinicians or an industry incentive for non-registrational/indication type trials. Additional areas for funding could include clinical trials that focus on

repurposing existing antibiotics (e.g. combination therapy trials using two existing antibiotic classes), support for pharmacokinetic/pharmacodynamic studies to optimize dosing regimens in special populations (e.g. renal replacement therapy, critically ill), and novel therapeutics that focus on host-factors such as T-cell defects.

References:

Årdal C, Røttingen JA, Opalska A, Van Hengel AJ, Larsen J. Pull Incentives for Antibacterial Drug Development: An Analysis by the Transatlantic Task Force on Antimicrobial Resistance. Clinical Infectious Diseases 2017;65(8): 1378-1382. https://doi.org/10.1093/cid/cix526

Goal 5: Improve International Collaboration and Capacities for Antibiotic-resistance Prevention, Surveillance, Control, and Antibiotic Research and Development

Recommendation 1: The differing regulatory requirements for approval of new anti-infective and diagnostics between the U.S. and other countries can delay the adoption of new treatment/diagnostic strategies for patients in all parts of the world. We recommend identifying opportunities to harmonize and streamline some regulatory requirements through collaboration with other regulatory bodies outside the United States (e.g. harmonizing allowable study endpoints for new anti-infectives).

Recommendation 2: Promote international public-private or public – organizational partnerships to improve microbiologic testing capabilities and increase laboratory proficiency and capacity. Section 5.1 specifically addresses the interaction between other countries' ministry of health with US based governmental organizations, however we suggest creating goals that will promote more collaboration between non-governmental entities and professional societies in the US with those located in other countries.

Reference: None