CIDRAP Antimicrobial Stewardship Project

POLICY UPDATE

JULY 2017

As part of our <u>series</u> focusing on current policy issues regarding antimicrobial stewardship and the spread of antimicrobial resistance (AMR), this update addresses the central role of AMR data in the development of effective antimicrobial stewardship programs and highlights some of the key sources of data on drug-resistant pathogens and antibiotic consumption in healthcare and agriculture. We welcome feedback on any of the topics presented in this series. If you have comments or suggestions, please contact the CIDRAP-ASP project team via Twitter at <u>@CIDRAP_ASP</u> or email at <u>asp-cid@umn.edu</u>.

Data to Inform Antimicrobial Stewardship

If we cannot measure the development and spread of drug resistance, we cannot manage it. (Review on AMR 2016)

Accurate and comprehensive information on antimicrobial resistance (AMR) is critical for understanding how common infections such as pneumonia or gonorrhea can become untreatable and for describing changes in the scope and magnitude of drug resistance worldwide. Surveillance and monitoring of antibiotic consumption and microbial resistance patterns are considered essential components of national action plans to combat AMR (WHO 2015a) and can provide the basis for informed decision-making to enhance appropriate use of antibiotics and ultimately improve patient outcomes. For example, antibiograms, which display trends in antimicrobial susceptibilities of bacterial isolates, can help guide medication decisions, aggregate data on antibiotic prescribing practices in outpatient settings can be used to improve feedback to providers, and rates of *Clostridium difficile* infections in relation to antibiotic use can inform prescribing and hospital infection-prevention practices. Aggregated AMR data across countries and regions also can be used to enhance awareness of the overall burden of drug-resistant disease and enable effective advocacy for antibiotic stewardship in the public sector (Fukuda 2017, Woolhouse 2016). Public officials rely on the availability of comprehensive AMR data to address key policy issues, such as promoting the prudent use of antibiotics in animal agriculture and prioritizing unmet needs in the development of new antibiotics.

Drug-resistant disease can be monitored in various ways by collecting data on topics such as:

- The proportion of drug-resistant isolates in specimens obtained from patients with microbial infections
- Trends in resistance to first-line, broad-spectrum, or all antibiotics (pan-resistant)
- The number of deaths per year attributable to treatment failure from drug-resistant infections
- Rates of *C difficile* infections in acute-care or long-term care settings
- Surveillance of resistant bacteria (and genomes or mobile genetic elements that encode resistance and can spread to other bacteria) in the food system

There are also many different approaches for assessing antibiotic use or consumption, such as collecting the following types of data:

- Rates of antibiotic prescribing for specific diagnoses, such as acute respiratory infections
- Point-prevalence surveys of antibiotic use in healthcare or on farms
- Risk-adjusted benchmarking for antibiotic use in acute-care hospitals
- Sales of antibiotics used in livestock feed and/or water for growth-promoting or preventive purposes, based on manufacturers or wholesalers
- Reimbursement data from health insurers

- National medicine agency procurement data
- National customs and import records

AMR Data Reporting – International Collaboration

In May 2015, World Health Organization (WHO) member states adopted the Global Action Plan on AMR (<u>WHO 2015b</u>), which is organized around five strategic objectives, two of which focus on enhancing the collection of data on AMR and antimicrobial use:

- 1. Improve awareness and understanding of antimicrobial resistance through effective communication, education and training.
- 2. Strengthen the knowledge and evidence base through surveillance and research (to collect and analyze data and monitor trends regarding drug-resistant pathogens).
- 3. Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures.
- Optimize the use of antimicrobial medicines in human and animal health (including the development of stewardship programs to monitor and optimize antimicrobial use at national and local levels).
- 5. Develop the economic case for sustainable investment that takes account of the needs of all countries and to increase investment in new medicines, diagnostic tools, vaccines, and other interventions.

The WHO Global Action Plan urges member states to develop national action plans for AMR based on these global objectives, taking into account national and regional priorities and governance. At the United Nations (UN) General Assembly high-level meeting on AMR in September 2016, all 193 UN member states agreed to develop national action plans aligned with the WHO's Global Action Plan on AMR and a One Health approach (WHO 2017a). The WHO Interagency Coordination Group on AMR was established in March 2017 to provide practical guidance in support of the Global Action Plan on AMR (UN Secretary-General 2017).

As of April 2017, the WHO reported that 67 member states had completed their national action plans on AMR, and 62 others are in the process of doing so, representing the largest and most populous countries and all regions. The WHO, the UN Food and Agriculture Organization (FAO), and the World Organization for Animal Health (OIE) initiated a survey to monitor each country's progress and identify areas needing more support to complete the national action plans (<u>WHO 2017a</u>).

The WHO also reported the establishment of the Global Antimicrobial Surveillance System (GLASS), with 43 countries either enrolled or in the process of enrolling. The GLASS is designed to facilitate collection, analysis, and reporting of harmonized, aggregated data on drug-resistant infections, focusing initially on bacterial pathogens in humans. The overall goal of GLASS is to strengthen the evidence base for linkages among AMR in healthcare, the food system, and the environment (<u>WHO 2017b</u>, <u>WHO 2015a</u>, <u>WHO 2015a</u>, <u>WHO 2015a</u>, <u>WHO 2015a</u>). Specific objectives of the GLASS include:

- Foster national surveillance systems and harmonized global standards for AMR surveillance.
- Estimate the extent and burden of AMR globally by selected indicators.
- Analyze and report global data on AMR regularly.
- Detect emerging AMR and its international spread.
- Inform implementation of targeted prevention and control programs.
- Evaluate stewardship interventions.

AMR Data Reporting – US Policy

Under the Joint Commission's Antimicrobial Stewardship Standard, effective Jan 1, 2017, the collection and reporting of data on antibiotic prescribing and drug resistance are required for accreditation of US hospitals, critical-access hospitals, and nursing-care centers (Joint Commission 2016). Reporting of AMRrelated data will also be used as a basis for reimbursement under a federal Center for Medicare and Medicaid Services (CMS) final rule. Nursing and long-term care centers, affecting approximately 15,000 US facilities that receive CMS funding, will be required as a condition of participation (effective Nov 28, 2017) to establish antimicrobial stewardship programs (ASPs) that include antibiotic use protocols and monitoring (<u>HHS 2016a</u>). A similar requirement for reimbursement is expected to be included in the CMS's proposed rule for US hospitals and acute-care facilities; as of July 2017, this rule had not been issued in final form (<u>HHS 2016b</u>).

In the National Action Plan for Combatting Antibiotic-Resistant Bacteria (White House 2015) the US government emphasized the need for enhanced data collection, monitoring, and surveillance to strengthen global antimicrobial stewardship efforts. Subsequent legislation supported this goal by including provisions for federal agencies to strengthen collection and reporting of AMR data. The 21st Century Cures Act (PL 114-255), enacted in December 2016, requires the Department of Health and Human Services (HHS) to (1) publish annual data on AMR trends and ASPs, (2) establish a mechanism for facilities to report antimicrobial stewardship activities and evaluate drug-resistance data, and (3) encourage federal healthcare facilities to report on antimicrobial use, AMR, and stewardship efforts.

Sources of Data on AMR and Antibiotic Usage

The tables below provide a summary of selected open (nonproprietary) sources of national and international data on AMR and antibiotic usage in humans and animals. Several databases focusing on the collection of data on antimicrobial-resistance genes or genetic elements are also listed.

International Data	Sponsor(s)	Scope
AMC Network Antimicrobial Medicines Consumption Network [link] [WHO ROE 2017]	WHO Regional Office for Europe	Monitors the consumption of antimicrobial medicines in non-EU countries and Kosovo in the WHO European Region. The network helps to strengthen capacity for national surveillance programs, which provide data that can be used as a basis for antimicrobial stewardship and monitoring. Sources include import data and sales records.
CAESAR Central Asian & Eastern European Surveillance of Antimicrobial Resistance [link]	ESCMID, RIVM (Netherlands), and WHO Regional Office for Europe	A network of national AMR surveillance systems that includes all countries of the WHO European Region that are not part of EARS-Net (see below).
EARS-Net European Antimicrobial Resistance Surveillance Network [link]	ECDC	Collects routine clinical antimicrobial susceptibility data from invasive isolates reported from local and clinical laboratories in 30 countries, forming the largest publicly funded system for AMR surveillance in Europe. Testing results are available online in the European Surveillance Atlas [link]
ESAC-Net European Surveillance of Antimicrobial Consumption Network [<u>link</u>]	ECDC	Collects and analyzes data on antimicrobial consumption in the community and the hospital sector from a network of national surveillance systems in EU, EEA, and EFTA countries. The data are displayed and reported through the access-limited European Surveillance System (TESSy) database [link].
Euro-GASP European Gonococcal Antimicrobial Surveillance Programme [<u>link</u>]	ECDC	Monitors gonococcal AMR in EU/EEA countries by testing a representative number of isolates from each member state per year against therapeutically relevant antimicrobials, including the use of sentinel surveillance to detect changes in resistance patterns and

		inform treatment guidelines.
GASP Global Gonococcal Antimicrobial Surveillance Programme [link] [Wi 2017]	WHO	Monitors gonococcal AMR through a collaborative global network of reference laboratories and coordinating centers, in collaboration with other international (eg, Euro-GASP) and national programs.
GLASS Global Antimicrobial Resistance Surveillance System [link]	WHO	Launched in 2015 to provide a standardized approach to the collection, analysis, and sharing of global AMR data to inform evidence-based action and advocacy to combat AMR. GLASS combines clinical, laboratory, and epidemiologic data on drug-resistant pathogens and supports national capacity building for AMR data collection and reporting. As of June 2017, 51 countries have expressed interest in enrolling in GLASS and 40 are fully enrolled [link].
Global-PPS Global Point Prevalence Survey on Antimicrobial Consumption and Resistance [link]	bioMérieux	Collects data from 64 countries to monitor rates of antimicrobial prescribing in hospitalized patients, establishing a global network for point-prevalence surveys. The project aims to provide a tool to evaluate antimicrobial prescribing practices in hospitals, identify targets for improving antimicrobial prescribing, and enhance antimicrobial prescribing practices globally.
HAI-Net PPS Point prevalence survey of healthcare-associated infections and antimicrobial use [link]	ECDC	Provides point-prevalence survey data on HAIs and antimicrobial use in acute-care hospitals in Europe through the TESSy database.
ResistanceMap [link]	CDDEP	Summarizes and displays national and subnational data on AMR and antimicrobial use worldwide in an interactive collection of charts and maps. The information includes antibiotic consumption data from 75 countries and 17 classes of antibiotics.
ResistanceOpen [link] [MacFadden 2016]	Boston Children's Hospital— HealthMap	Collects publicly available AMR data (eg, hospital antibiograms and AMI reports) and displays the information geographically in a collaborative online database. The platform is intended to aggregate and disseminate existing but disparate AMR information to enhance situational analysis, antimicrobial stewardship, and policy responses to the global problem of AMR.

European Society of Clinical Microbiology and Infectious Diseases; EU, European Union; HAI, healthcare-associated infection; RIVM, Dutch National Institute for Public Health and the Environment; WHO, World Health Organization.

National Data	Sponsor	Scope
AGAR	Australian	Performs continuous resistance surveillance of Staphylococcus aureus,
Australian Group on Antimicrobial	Commission on	Enterobacteriaceae, Pseudomonas aeruginosa, Acinetobacter
Resistance [link]	Safety and	spp and Enterococcus spp from blood cultures, based on data
	Quality in	submitted from healthcare institutions in all states and territories in
	Health Care	Australia.
AURA	Australian	Collects passive and targeted surveillance data on AMR and
Antimicrobial Use and Resistance	Commission on	antimicrobial use in hospitals and the community to inform strategies
in Australia [<u>link]</u>	Safety and	to curb AMR in Australia.
	Quality in	
	Health Care	
BSAC	Pharmaceutical	Collects a selection of pathogens from up to 6,000 clinical isolates
British Society for Antimicrobial	company	annually, including community- and hospital-acquired bacteremia and
Chemotherapy Resistance	sponsors	respiratory infections, from patients in the UK and Ireland for
Surveillance Project [link]		confirmation (as antibiotic-susceptible, intermediate, or resistant) and
		further analysis in a central laboratory. The data are disseminated in
		an interactive online database.
CARA	Health Canada	Provides AMR data in an interactive online tool, CAN-R, based on
Canadian Antimicrobial		national AMR surveillance studies, such as CANWARD (assessing AMR
Resistance Alliance [link]		and pathogen prevalence in Canadian hospitals), antibiograms, and

		SAVE (Streptococcus pneumoniae serotyping and antimicrobial susceptibility).
CARSS Canadian Antimicrobial Resistance Surveillance System [link] [Gov. of Canada 2016]	Health Canada	 Collects data from four surveillance systems on AMR and antimicrobial use in Canada: Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS), monitors priority bacteria transmitted through animals (see table below) Canadian Nosocomial Infection Surveillance Program (CNISP), provides rates and trends of HAIs at Canadian healthcare facilities Enhanced surveillance of antimicrobial-resistant gonorrhea program (ESAG), is aimed at rapid identification of changes in antimicrobial susceptibility and assessment of AMR risk factors to enable early identification and prevention of the spread of drug-resistant gonorrhea and identify appropriate treatment regimens. Canadian Tuberculosis Laboratory Surveillance System (CTLSS), collects data on drug susceptibility tests results for Mycobacterium tuberculosis isolates in all provinces and territories.
DRI Drug Resistance Index [<u>link</u>]	CDDEP	An online tool for tracking antibiotic resistance. The DRI provides a composite measure of the ability of antibiotics to treat infections with
 EIP Emerging Infections Programs [link] surveillance, including: ABCs: Active Bacterial Core surveillance [link] HAIC: Healthcare-Associated Infections—Community Interface [link] FoodNet: Foodborne Diseases Active Surveillance Network [link] ESPAUR English Surveillance Programme for Antibiotic Utilisation and Resistance [link] [Public Health England 2016] [Chaplin 2017] 	US CDC	 the extent of their use in clinical practice. ABCs provides clinical information and resistance data for invasive bacterial pathogens that cause infections predominantly in nonhospitalized patients: <i>S pneumoniae</i>, groups A and B <i>Streptococcus</i>, and MRSA. HAIC provides clinical information and resistance data for bacteria and fungi that cause infections in healthcare settings and in the community: <i>C difficile</i>, <i>Candida</i>, CRE, multidrug-resistant <i>Acinetobacter</i>. FoodNet provides clinical and epidemiologic data on human isolates from infections transmitted through food, including <i>Salmonella</i>, <i>Campylobacter</i>, <i>Escherichia coli</i> O157, and <i>Shigella</i>. Develops, maintains and disseminates data on AMR, antimicrobial prescribing in each healthcare sector, and antimicrobial stewardship in England, as part of the PHE's Antibiotic Guardian campaign aimed at healthcare professionals and the public to improve antibiotic prescribing and stewardship. AMR data are available via Fingertips, an
 Gonococcal Antimicrobial Surveillance Programs GISP: US Gonococcal Isolate Surveillance Project [link] AGSP: Australian Gonococcal Surveillance Programme [link] GRASP: UK Gonococcal Resistance to Antimicrobials Surveillance Programme [link] 	US CDC Australian Department of Health PHE	interactive online tool [link]. GISP: monitors trends in <i>Neisseria gonorrhoeae</i> antimicrobial susceptibilities in the United States. AGSP monitors AMR in <i>N gonorrhoeae</i> and helps to define standard protocols for antibiotic treatment of gonococcal infection in Australia. GRASP provides data on trends in antimicrobial resistance and decreased susceptibility in gonococcal infection in England and Wales.
NARMS National Antimicrobial Resistance Monitoring System for Enteric Bacteria [<u>CDC link</u>] [<u>FDA link</u>] [<u>USDA link</u>]	US CDC, FDA, and USDA, and state and local health departments	Tracks changes in the antimicrobial susceptibility of certain enteric bacteria found in ill people (CDC), retail meats (FDA), and food animals (USDA) in the United States. Antibiotic resistance data from bacteria transmitted commonly through food and isolated from humans are displayed in <i>NARMS Now: Human Data</i> [link], an online tool containing data on <i>Campylobacter, E coli</i> O157, <i>Salmonella</i> , and <i>Shigella</i> displayed by bacterial species and serotype, antibiotic, year, and state.
NETHMAP [<u>link]</u>	SWAB and RIVM	Tracks AMR trends and antibiotic use in the Netherlands, published in an annual report that provides an overview of the use of antibiotics and AMR against the most common and human pathogenic bacteria and fungi in the Netherlands.

		NethMap parallels the monitoring system of AMR and antibiotic usage in animals in the Netherlands, MARAN (see table below).
NHSN National Healthcare Safety Network [<u>link</u>] Antibiotic Resistance Patient Safety Atlas [<u>link</u>]	US CDC	 Tracks AMR testing data on select HAIs (eg, central line–associated bloodstream infections, catheter-associated urinary tract infections, and surgical-site infections) and 31 drug-bug profiles (eg, MRSA, CRE, and multidrug-resistant <i>P aeruginosa</i>) among patients in US hospitals. Aggregated national, regional, and state-level AMR-related data on HAIs, reported voluntarily to the CDC through the NHSN, are displayed in the online database Antibiotic Resistance Patient Safety Atlas. Additional data reported to NHSN and collected in the atlas include: Antibiotic stewardship practices data [link] collected from acute-care facilities participating in the NHSN. Antibiotic prescription data [link] on oral antibiotics dispensed to outpatients in US community pharmacies and mail-order pharmacies.
Abbreviations: AMR antimicrobiz	al resistance: CDC	Centers for Disease Control and Prevention: CRE, carbapenem-resistant

Abbreviations: AMR, antimicrobial resistance; CDC, Centers for Disease Control and Prevention; CRE, carbapenem-resistant Enterobacteriaceae; FDA, Food and Drug Administration; HAI, healthcare-associated infection; MRSA, methicillin-resistant Staphylococcus aureus; RIVM, Dutch National Institute for Public Health and the Environment; SWAB, Dutch Foundation of the Working Party on Antibiotic Policy; UK, United Kingdom; US, United States; USDA, US Department of Agriculture.

Animal Data	Sponsor	Scope
CIPARS Canadian Integrated Program for Antimicrobial Resistance Surveillance [link]	Public Health Agency of Canada	Monitors trends in AMR and antimicrobial use in selected bacterial organisms from human, animal, and food sources across Canada.
DANMAP Danish Integrated Antimicrobial Resistance Monitoring and Research Programme [<u>link</u>]	Danish Ministry of Food, Agriculture, and Fisheries and the Danish Ministry of Health	Monitors consumption of antimicrobial agents for food animals and humans; monitor the occurrence of AMR in bacteria isolated from food animals, food of animal origin, and humans; evaluates links between AMR and antimicrobial consumption; and identifies routes of transmission and areas for further research studies.
ESVAC European Surveillance of Veterinary Antimicrobial Consumption [link]	EMA	Collects information on how antimicrobial medicines are used in animals across the EU, applicable to the identification of possible risk factors for development and spread of AMR in animals.
MARAN Monitoring of Antimicrobial Resistance and Antibiotic Usage in Animals in the Netherlands [link] [NETHMAP 2013]	Wageningen University & Research	Monitors overall sales data at the national level and usage data per animal species in the Netherlands, supporting the analysis of trends in the exposure of farm animals to antibiotics.
NARMS National Antimicrobial Resistance Monitoring System for Enteric Bacteria [USDA link]	CDC, FDA, USDA, and state and local health departments	Monitors AMR in zoonotic pathogens from food animals by testing isolates of non-typhoid <i>Salmonella</i> , <i>Campylobacter</i> , <i>E coli</i> , and <i>Enterococcus</i> obtained from diagnostic animal specimens, healthy onfarm animals, and food-producing animals at slaughter. The panel of antimicrobial agents chosen is representative of common antimicrobials used in both human and veterinary medicine. Data are reported in annual NARMS integrated reports [link] and in interactive data displays [link].
SVARM Swedish Veterinary Antimicrobial Resistance Monitoring [link]	National Veterinary Institute (Sweden)	Monitors antimicrobial susceptibility of zoonotic bacteria (Salmonella and Campylobacter spp), specific animal pathogens, and commensal enteric bacteria (E coli and Enterococcus spp)
		ters for Disease Control and Prevention; EMA, European Medicines inistration; USDA, US Department of Agriculture.

Genetic Data	Sponsor	Scope
CARD Comprehensive Antibiotic Resistance Database [link] [Jia 2017]	McMaster University	An actively curated database of AMR-related molecular sequence reference data on antibiotic resistance genes, proteins, and mutations designed to allow the development of genome analysis tools. It provides a functional resource for data curation, detection, and analysis of known resistance genes; genetic variants found in human, animal, and environmental samples; and emerging drug-resistant pathogens.
MEGARes Microbial Ecology Group Antimicrobial Resistance [link] [Lakin 2017]	Microbial Ecology Group	An AMR database and annotation structure designed to facilitate characterization of AMR genetic determinants in the context of high- throughput metagenomics studies and the analysis of large-scale ecological sequence datasets.
ResistoMap [link] [Yarygin 2017]	Russian Scientific Foundation	An online interactive tool for visualization of global data on more than 1,500 human gut metagenomes, highlighting genetic determinants conferring resistance to antibiotics, biocides, and heavy metals.
Abbreviations: AMR, antimicrobial resistance.		

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