CDC Approach to Controlling AMR: Domestic and International Projects

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ReLAVRA Meeting

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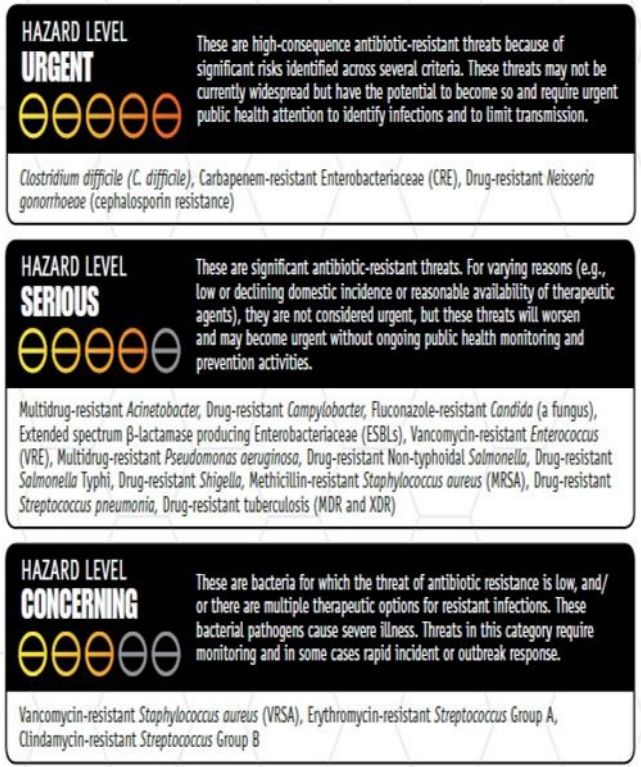
Disclosures

- None

Antibiotic Resistance in the United States

- Sickens >2 million people per year
- Kills at least 23,000 people each year
  - Plus 15,000 each year from *C. difficile*
- >$20B/year in healthcare costs
- Threatens modern medicine to lose antibiotics
  - Lose the ability to treat patients with sepsis, cancer, provide organ transplants, and save victims of burns and trauma



Success since 2016: Antibiotic Resistance Solutions Initiative

- CDC is supported by +$170M of AR funding for domestic and global activities annually.
- In the past three years, ARSI has invested $241 million to U.S. health departments to develop the domestic infrastructure to address AR.
- CDC has provided an additional nearly $110 million in research and piloting solutions to 96 public/private institutions (domestic + global), reflecting 158 applied public health research projects.
- CDC's AR Lab Network has tested more than 100,000 pathogens from public health labs across the U.S.
- CDC has shipped 140,000+ isolates to diagnostic test manufacturers, academic researchers, and pharmaceutical companies.

Emerging Resistance

- Carbapenemase-producing Gram-negative Bacilli

Carbapenem-Resistant Enterobacteriaceae (CRE)

Carbapenem-Resistant *Pseudomonas aeruginosa* (CRPA)

Carbapenem-Resistant *Acinetobacter baumannii* (CRAB)

The U.S. experience: KPC-producing CRE

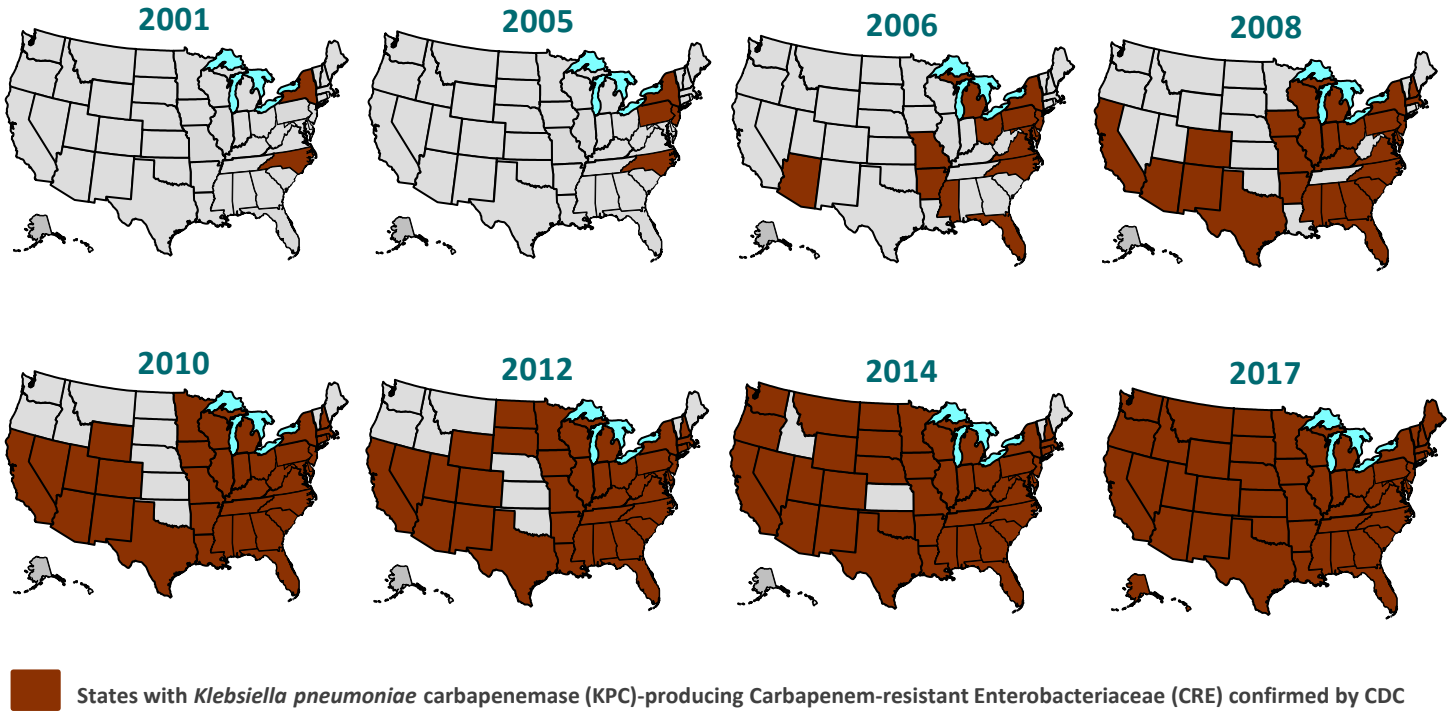
ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Apr. 2001, p. 1151–1161 Vol. 45, No. 4
0066-4804/01/$04.00+0 DOI: 10.1128/AAC.45.4.1151–1161.2001

Novel Carbapenem-Hydrolyzing β-Lactamase, KPC-1, from a Carbapenem-Resistant Strain of *Klebsiella pneumoniae*

HESNA YIGIT,[1] ANNE MARIE QUEENAN,[2] GREGORY J. ANDERSON,[1]
ANTONIO DOMENECH-SANCHEZ,[3] JAMES W. BIDDLE,[1] CHRISTINE D. STEWARD,[1]
SEBASTIAN ALBERTI,[4] KAREN BUSH,[2] AND FRED C. TENOVER[1]*

- Isolate collected in 1996 during an ICU surveillance project

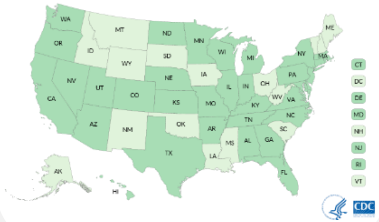
KPC-CRE found in the U.S. spread from two states in 2001 to 50 states, DC, and PR in 16 years



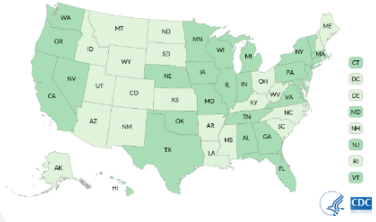
https://www.cdc.gov/hai/organisms/cre/trackingcre.html

Other carbapenemase-producing CRE (as of January 1, 2018)

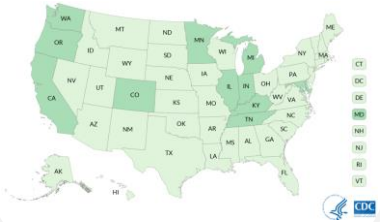
NDM
379 patients
34 states



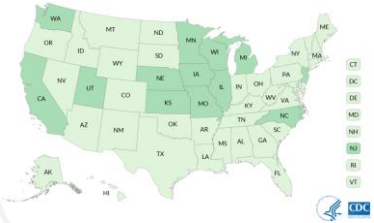
OXA-48
146 patients
27 states



VIM
57 patients
11 states



IMP
36 patients
13 states



- Other carbapenemases are less common than KPC in the U.S.
  - Some have strong regional epidemiology
  - More likely to be imported than KPC, but domestic transmission has increased

Limited ability to detect carbapenemases at US clinical laboratories

- Among 4,685 acute care hospitals reporting to US national HAI surveillance system in 2016:
  - 50% served by a lab that performed carbapenemase testing for CRE
    - 80% used phenotypic testing methods
    - 18% used molecular methods

Shugart A, et al. (2018). Hospital microbiology laboratory practices for Enterobacteriaceae: Centers for Disease Control and Prevention National Healthcare Safety Network (NHSN) annual survey, 2015 and 2016. Infection Control & Hospital Epidemiology 2018, 39, 1115–1117. doi: 10.1017/ice.2018.153

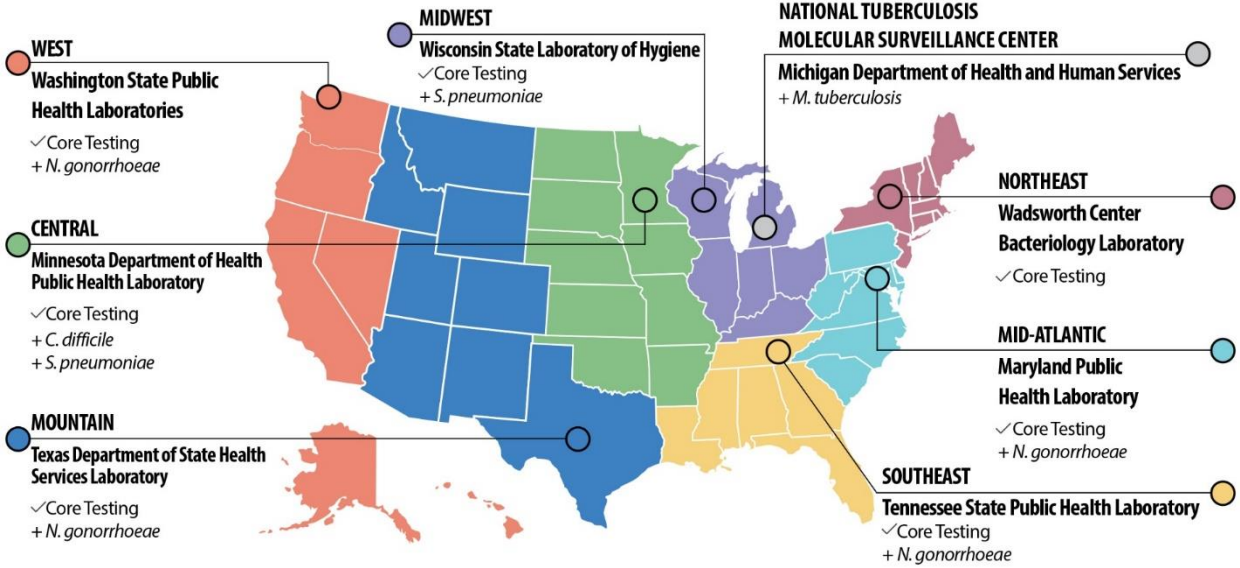
Improving detection of CP-CRE and other MDROs

Antibiotic Resistance Laboratory Network

- Core testing available to all clinical and state public health labs includes:
  - Detection of new and emerging threats, like novel carbapenemase genes
  - Expanded susceptibility testing to determine if new drugs would be effective to treat patients infected with rare resistant pathogens
  - Molecular testing to detect patients colonized with carbapenem-resistant Enterobacteriaceae
    - Significant increase in access to screening tests with rapid turnaround time

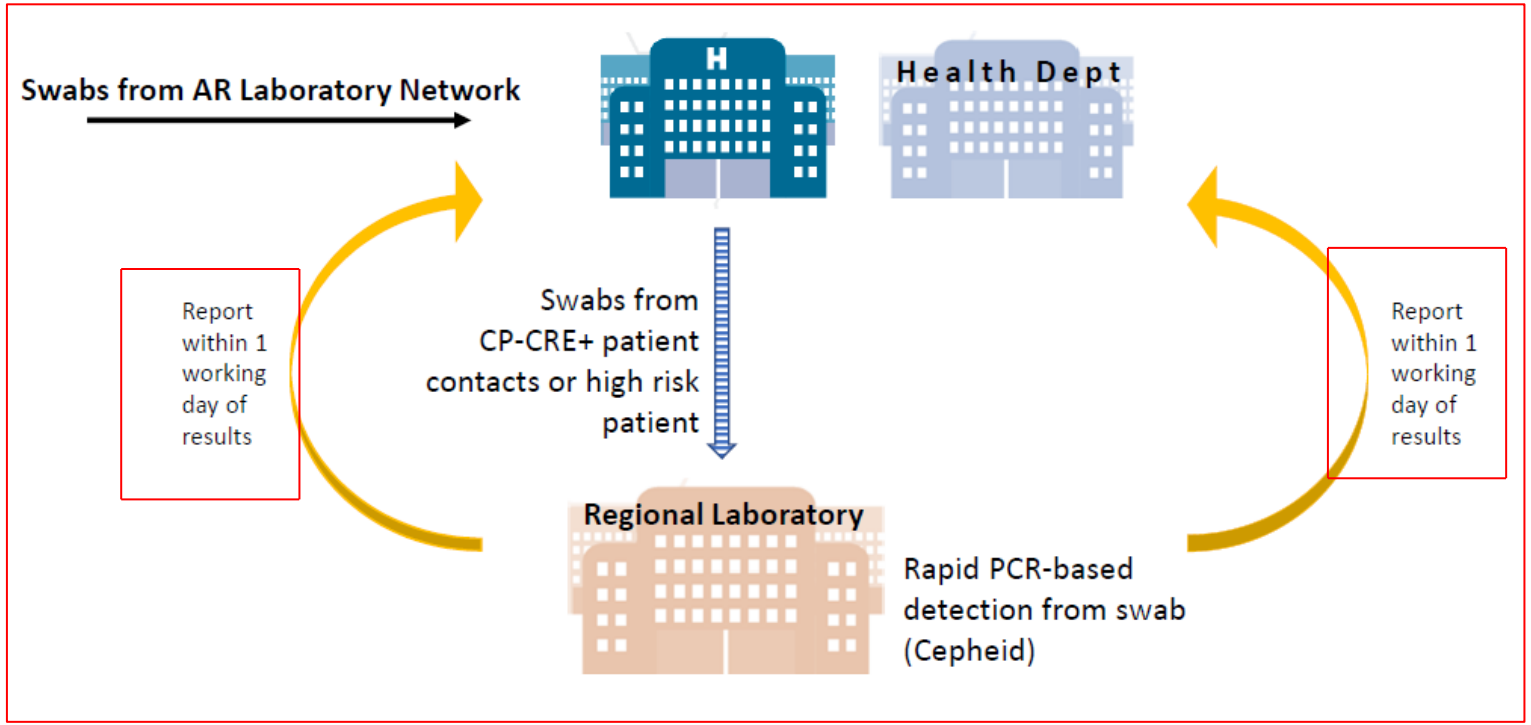
Antibiotic Resistance Laboratory Network

Nationwide lab capacity to detect AR in healthcare, food, and community. Tracks resistance to identify outbreaks faster, stop spread, and protect people.



- CDC lab expertise and coordination
- 7 regional labs
- 1 National TB Molecular Surveillance Center
- 56 state and local labs

Improving facility access to CRE screening tests



Containing emerging resistance

CDC's Containment Strategy

A systematic public health response to slow the spread of emerging AR

https://www.cdc.gov/hai/containment/guidelines.html

Containment Strategy

- Implement CDC CRE Prevention Toolkit guidance
  - Varies by facility type (acute short stay hospital vs. long term care facility, etc.)

https://www.cdc.gov/hai/organisms/cre/index.html

- Collaborate with state health department on IPC assessments and other response activities

- Notify other facilities about a patient's MDRO status if transferred

Containment Strategy

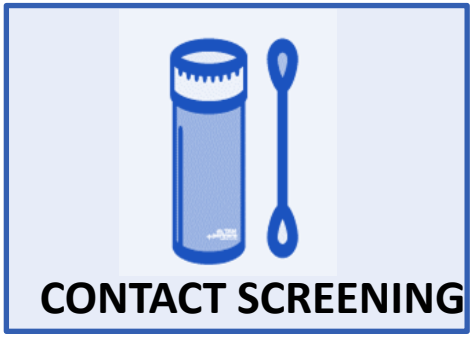
- Evaluate infection control practices at all facilities where the patient has been admitted in the prior 30 days
  - Hand hygiene, PPE, cohorting practices, environmental cleaning are priority areas
  - Use standardized assessment tools developed by CDC
    - Infection Control Assessment Response (ICAR) tools for a variety of facility types

      (https://www.cdc.gov/hai/prevent/infection-control-assessment-tools.html)
    - Acute Care Facility MDRO Control Activity Assessment Tool

      (https://www.cdc.gov/hai/pdfs/prevent/MDRO-Facility-Assessment_7_28.pdf)

Containment Strategy

- Screen healthcare contacts of the individual infected or colonized with target MDROs
  - Always: roommates
  - Sometimes: other patients in the unit
  - Rarely: household members, healthcare workers

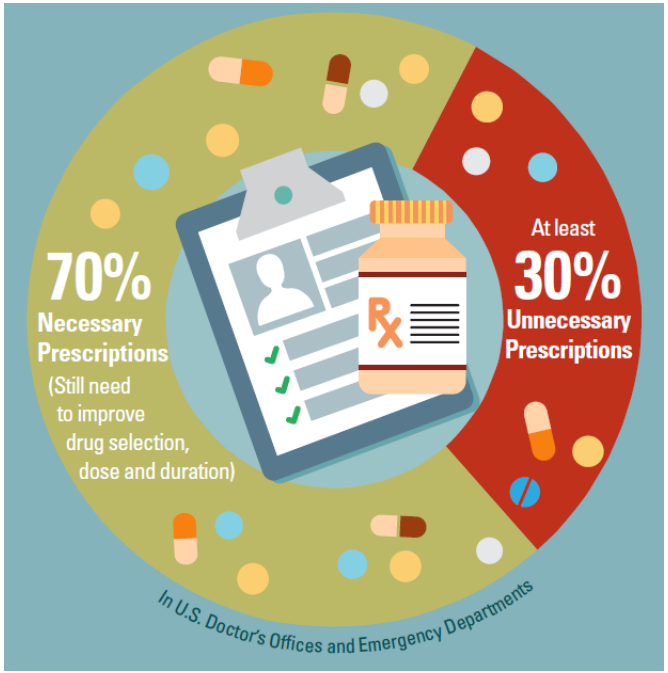


- Availability of testing:
  - Free of charge through ARLN for CP-CRE, CRPA, and *C. auris*
  - Limited to rectal swabs for carbapenemases

Antibiotic Stewardship

We are focused on all healthcare settings, including acute care, outpatient, long-term care, and nursing home facilities.

Problem: Unnecessary Prescriptions



Solution: Antibiotic Stewardship

- Every patient gets optimal antibiotic treatment
  - Antibiotics only when they are needed
  - Appropriate drug at the right time, dose and duration
- Every provider incorporates antibiotic stewardship as part of expected good clinical practices.
- Every healthcare facility implements antibiotic stewardship programs.
- All initiatives in healthcare incorporate appropriate antibiotic use (e.g., early sepsis detection).

5% Antibiotic prescribing in outpatient settings declined by 5% overall from 2011-2016.

13% Of the 5%, we've seen a 13% reduction in prescribing to children.

Improving Workforce Capacity

https://www.cdc.gov/longtermcare/training.html

CDC/STRIVE Infection Control Training

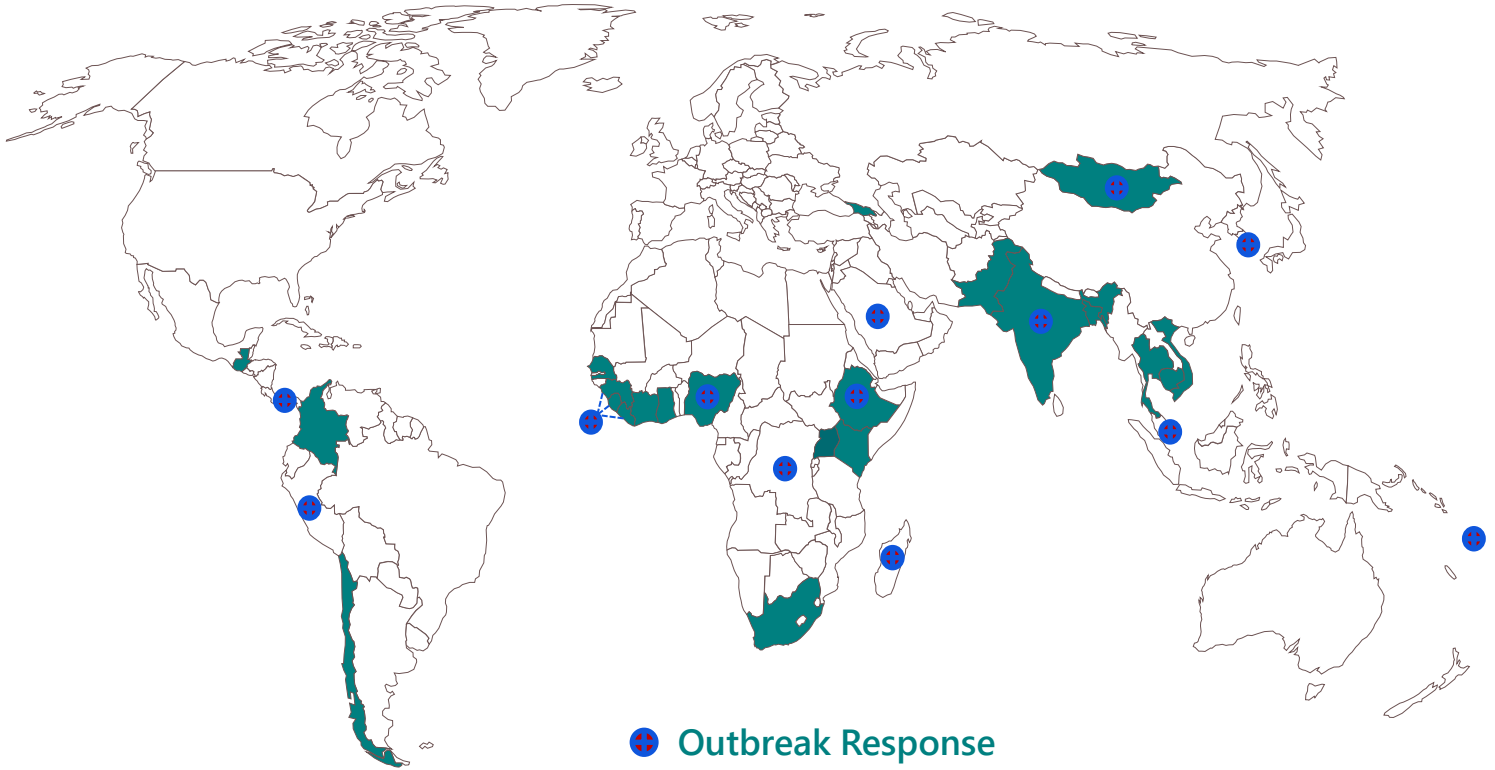
https://www.cdc.gov/infectioncontrol/training/strive.html

States Targeting Reduction in Infections via Engagement (STRIVE)

International Efforts

Overview of International Initiatives

Where we work



Our focus is on long-term programs

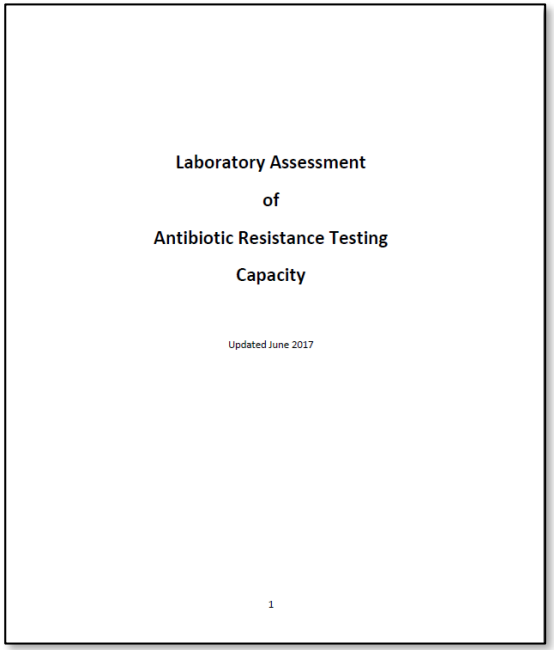
Technical Assistance Area	Countries (2015-2019)
National policies and plans	Kenya, India, Thailand, Vietnam, Pakistan, Bangladesh, Ethiopia, Tanzania, Cambodia
Lab strengthening	India, Vietnam, Kenya, Georgia, Senegal, Pakistan, Ethiopia, Tanzania
National surveillance systems	India, Vietnam, Kenya, Georgia, Thailand, Senegal, Pakistan, Bangladesh, Ethiopia, Cambodia
Workforce strengthening- IPC and stewardship	Sierra Leone, Liberia, Kenya, Vietnam, India, Nigeria, Georgia, Thailand, South Africa
Outbreak response	India, Thailand, South Africa, Fiji, Kenya, Vietnam, DRC, Liberia, Sierra Leone, Guinea, Saudi Arabia

1. Policies, Plans, Guidelines

- Global level
- National level
  - National AMR action plan
  - National AMR surveillance strategy
  - National IPC guidelines
  - National healthcare policies

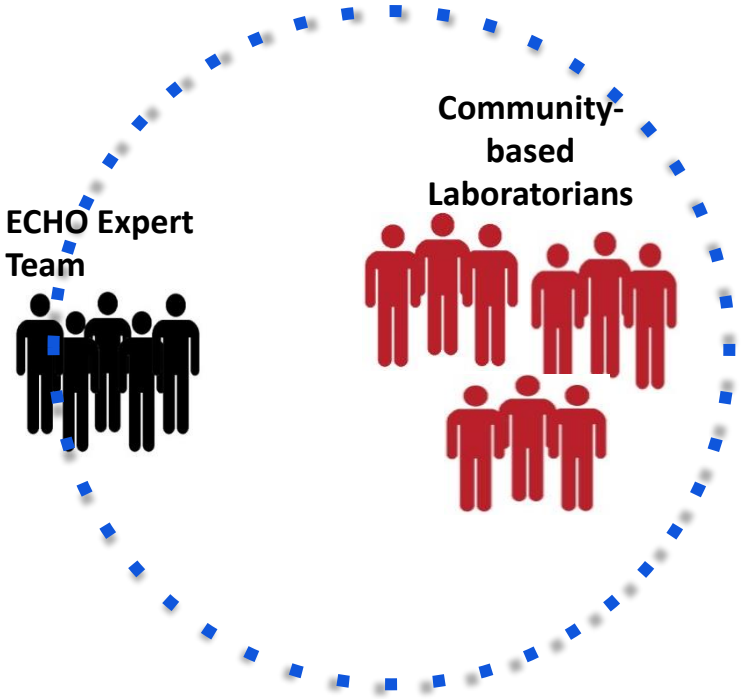
2. Lab strengthening

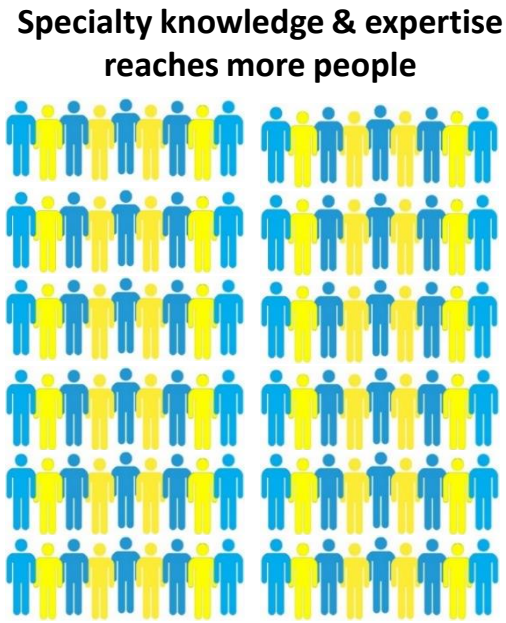
- Identify laboratories for national surveillance systems
- Assess current microbiology and AST capacity – LAARC
- Work with partners to target capacity building



AMERICAN SOCIETY FOR MICROBIOLOGY

Remote Training Program for Laboratorians

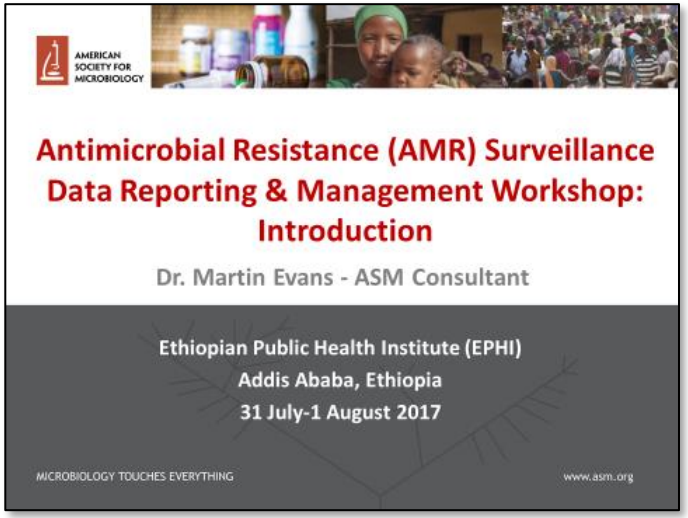




Project ECHO®

3. National Surveillance Systems

- Two main types of AMR surveillance:
  - Lab-based
  - Clinical/ healthcare
- Submission of data
  - WHONet, DHIS2, other systems
- Analysis of data

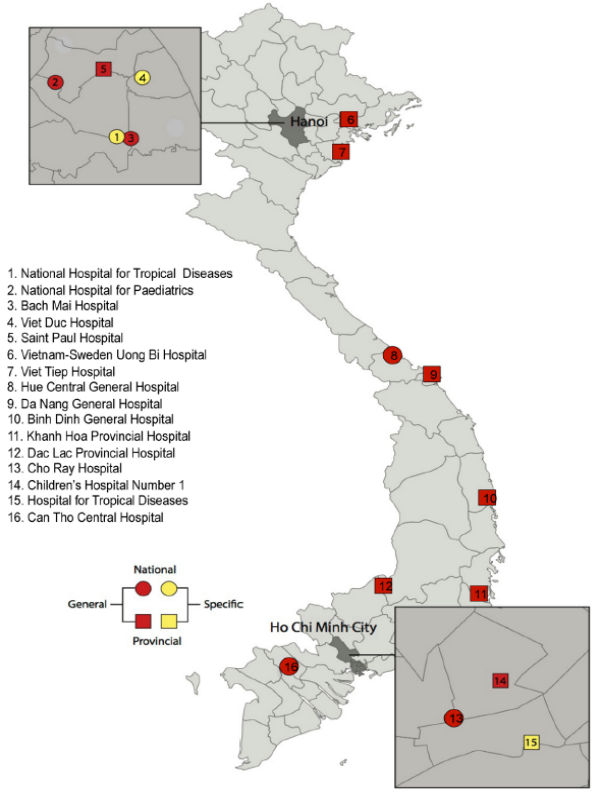


4. Improving Specimen Collection

- If specimens are not collected correctly
  - Discarded
  - Contaminated
- CDC funded Ohio State University to develop comprehensive specimen collection training http://www.ephi.gov.et/index.php/clinical-specimen-collection
  - Piloted in Ethiopia
  - Generic version to be released in 2020

Establishing an AMR Surveillance Network Among 16 Hospital Laboratories

- **Standardized AMR surveillance**
  - Reporting platform using WHONET
  - Training and practical exercises
- **Laboratory capacity building**
  - Gaps identified using IICP AMR laboratory assessment tool (LAARC)
  - ASM training and mentorship on AST and QC
- **Ongoing support for**:
  - National AMR surveillance strategy and policy
  - National microbiology guidebook



Senegal Point Prevalence Survey

- Last national PPS done in 2009 with many limitations
- IICP assisting MoH in implementing another national PPS
  - Updating the protocol with standard definitions adapted for Senegal
  - Piloting the protocol in one hospital
- Planning for national data collection in November

Protocol training in St. Louis Hospital

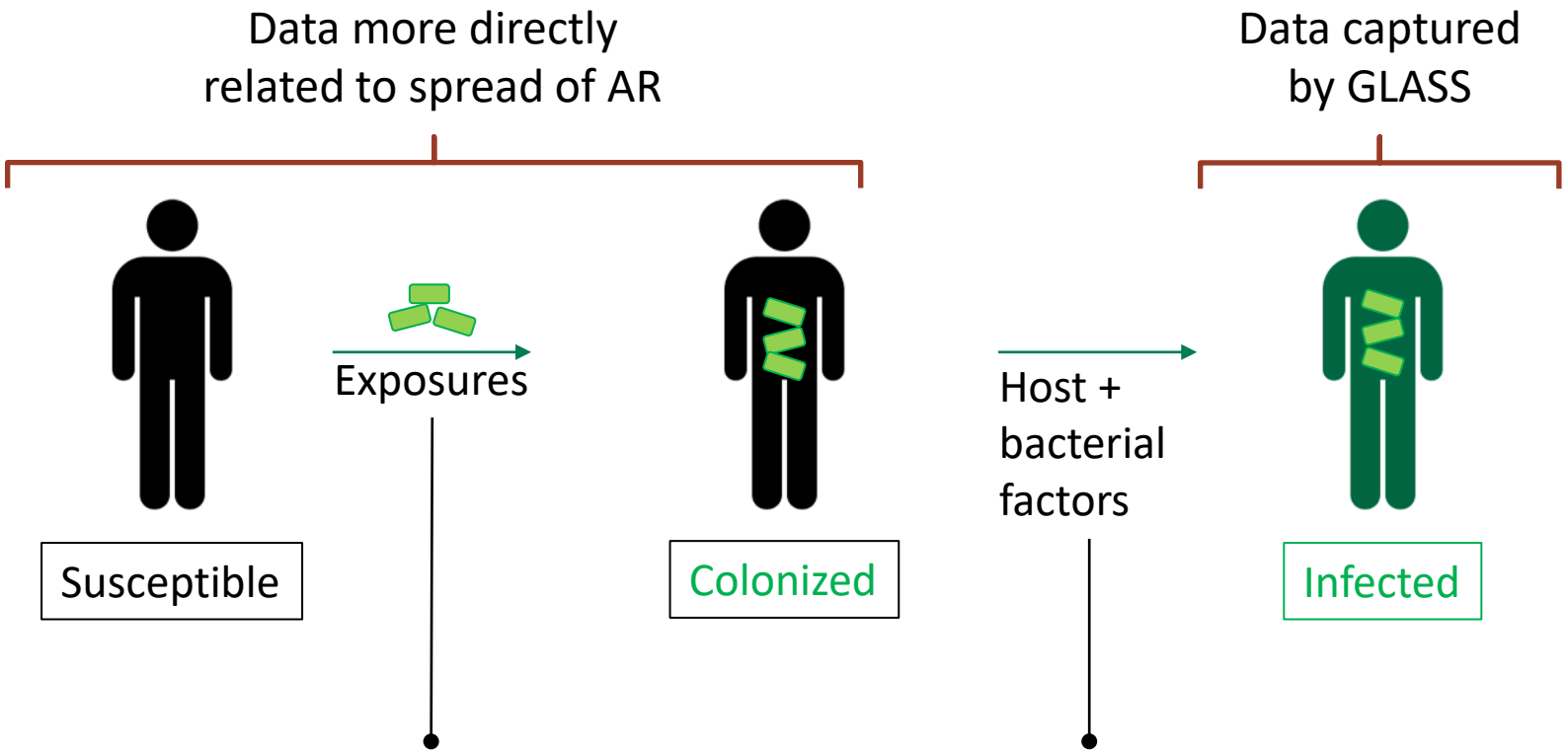
Assisting data collectors applying definitions

Colonization with AR bacteria in hospitals and communities

Limitations with current global AR surveillance

- IICP supports implementation of WHO Global Antimicrobial Resistance Surveillance System (GLASS) in low- and middle-income countries (LMICs)
  - Facility-based reporting of antimicrobial resistance (AR) in priority pathogens isolated from clinical specimens

- Experience suggests several problems to GLASS framework in LMICs
  - Culturing often reserved those who have failed empiric therapy
  - Focus on priority pathogens isolated from clinical specimens might not correctly inform transmission risks


Data more directly related to spread of AR
Data captured by GLASS
Exposures
Host + bacterial factors
Susceptible
Colonized
Infected
• Contact with other colonized or infected persons
• Ingestion of contaminated food or water
• Contact with contaminated surfaces
• Invasive medical device use
• Virulence genes

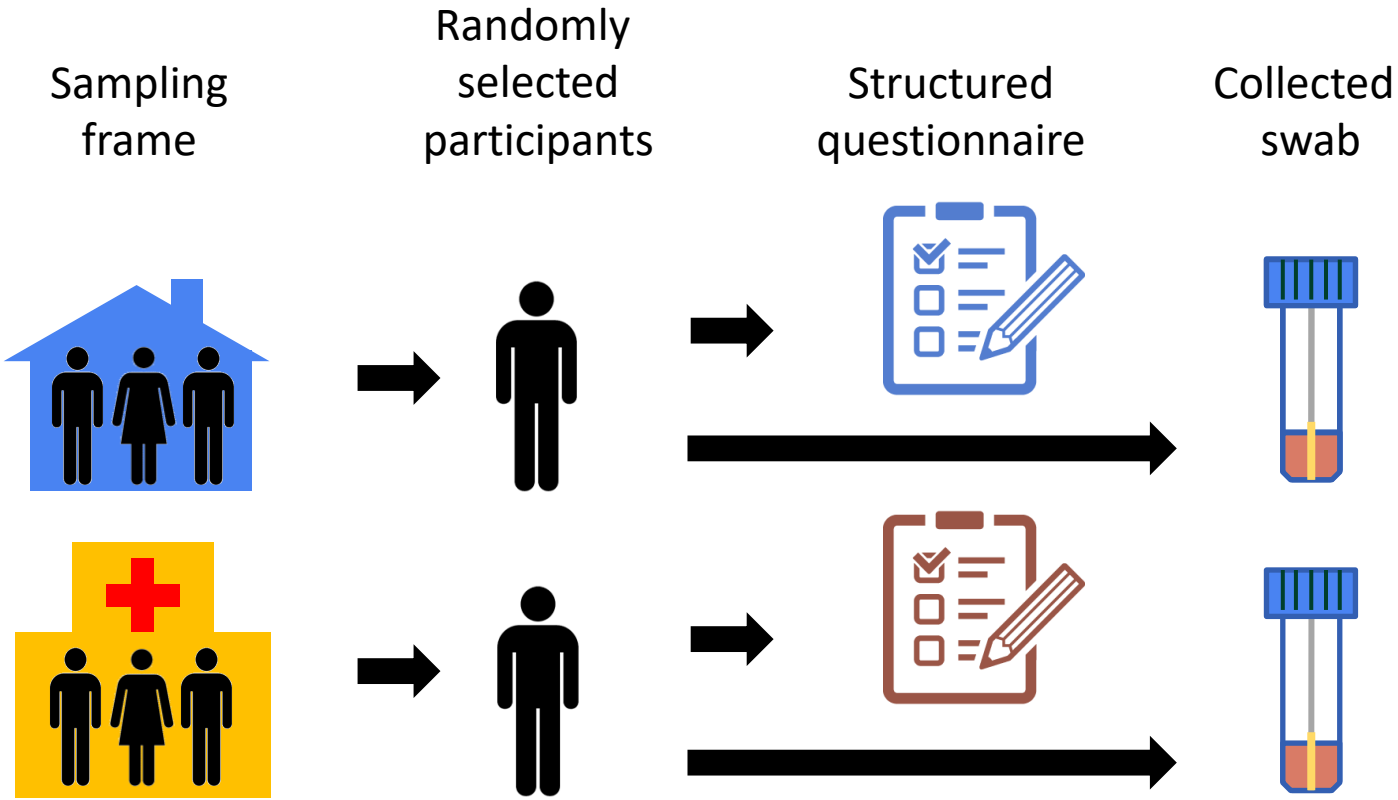
Survey to measure colonization with AR bacteria

- Title: Antimicrobial Resistance in Communities and Hospitals (ARCH)

- Design goals
  - Leverage existing population-based sampling frames
  - Use simple tests to detect colonization at household and hospital levels
  - Administer questionnaires to assess risk factors for colonization
  - Create an archive of isolates for future whole genome sequencing

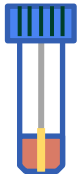
- Target bacteria: CRE, ESBLE, MRSA, ColRE

Field approach

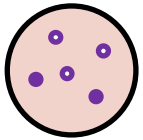


Laboratory approach

Collected swab



Selective media

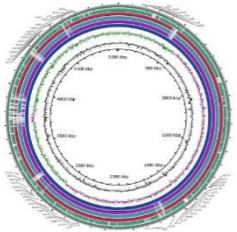


Confirmatory ID/AST

Invasive isolates

Archive

Whole genome sequences



Genomic characterization

Summary

- Diverse activities in many parts of the world
- Implementation projects and research
- Long term investments and short-term outbreak support
- Work with countries with cooperative agreements and Technical Assistance

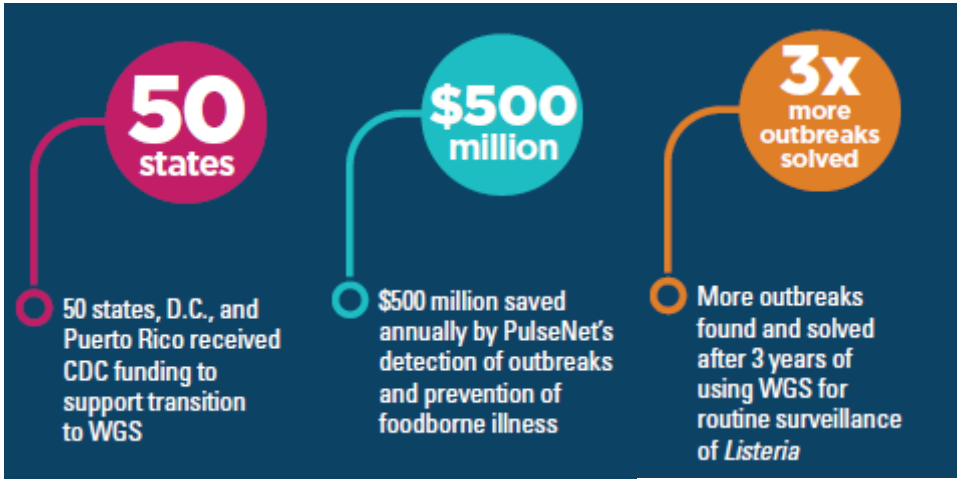
For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Site criteria

- Population of at least 10,000 individuals
- Access to sampling frame for population-based surveys
  - Demographic and health surveys (USAID)
  - Multiple indicator cluster surveys (UNICEF)
  - Local population-based surveillance platforms
- At least one hospital in the geographic area of the sampling frame
- Access to a bacteriology laboratory
  - Isolation and identification
  - Antimicrobial susceptibility testing
  - Long-term archiving

Resistant Infections from Food: Whole Genome Sequencing

Rapidly identifying and responding to drug-resistant foodborne bacteria and outbreaks by using whole genome sequencing (WGS) and increasing lab testing nationwide.



- This year, the PulseNet national laboratory network is transitioning from PFGE to WGS.
- This change will allow foodborne illnesses to be detected more effectively.
- Following the successful AMD pilot, the AR Solutions Initiative funding allowed for WGS to be scaled up nationwide.

Accelerating & Implementing Innovative Solutions

With Industry Partners

- **Via the CDC & FDA AR Isolate Bank:**
  - Support for development of new diagnostic tests and antibiotics
  - CRE isolates for proof-of-concept testing for a new rapid diagnostic test

With Academics & Healthcare

- **Making public CDC's sequencing data** from resistant germs to spur innovation and research
- **Discovering** effective interventions across healthcare, food, and the environment
- **Piloting** evidence-based strategies to detect, respond, and prevent spread
- **Scaling up** solutions in the U.S. and globally to maximize public health impact

Summary

- Antibiotic resistance can spread very rapidly - slowing the spread is easier if the problem is still small
- Containing the spread of unusual resistance requires access to adequate microbiology reference laboratory testing capacity
- Improved detection of unusual resistance, in conjunction with rigorous implementation and assessment of infection control practices and screening to identify colonized patients, can contain its spread
- Improving capacity of healthcare workers and antibiotic stewardship are vital parts of controlling AMR