

Antimicrobial Resistance

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Objectives

- ❑ Define the problem of antibiotic resistance
- ❑ Explain the national strategy to combat antibiotic resistance

Estimated minimum number of illnesses and deaths caused annually by antibiotic resistance*:

At least



*bacteria and fungus included in this report

CARBAPENEM-RESISTANT ENTEROBACTERIACEAE

9,000 DRUG-RESISTANT INFECTIONS PER YEAR
600 DEATHS

THREAT LEVEL: URGENT (5 yellow circles)

⚠️ CRE HAVE BECOME RESISTANT TO ALL OR NEARLY ALL AVAILABLE ANTIBIOTICS ⚠️

DRUG-RESISTANT NEISSERIA GONORRHOEAE

246,000 DRUG-RESISTANT GONORRHEA INFECTIONS
820,000 GONOCOCCAL INFECTIONS PER YEAR

THREAT LEVEL: URGENT (5 yellow circles)

CLOSTRIDIUM DIFFICILE

250,000 INFECTIONS PER YEAR
14,000 DEATHS
\$1,000,000,000 IN EXCESS MEDICAL COSTS PER YEAR

THREAT LEVEL: URGENT (5 yellow circles)

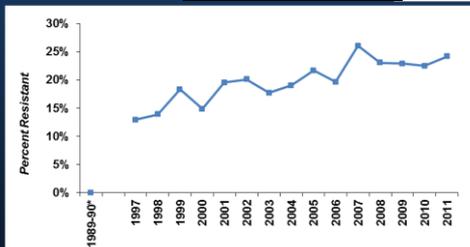
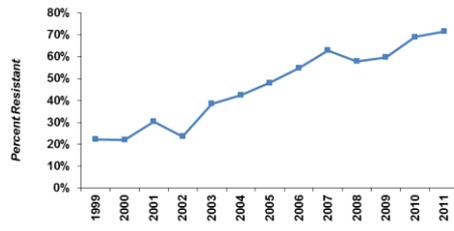
Carbapenem-resistant *Enterobacteriaceae* (CRE)



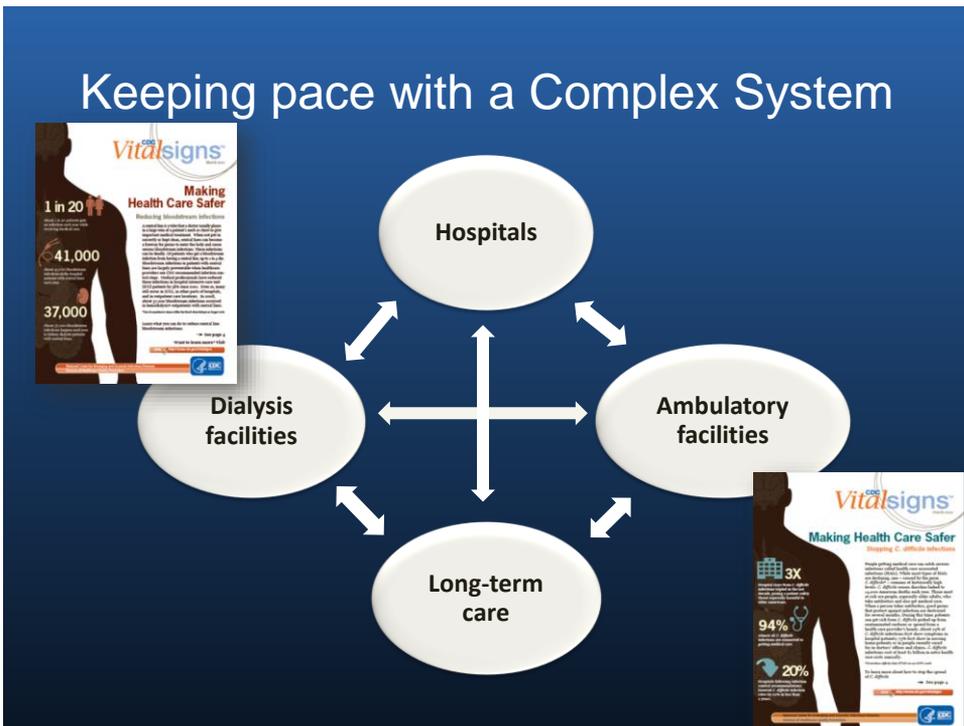
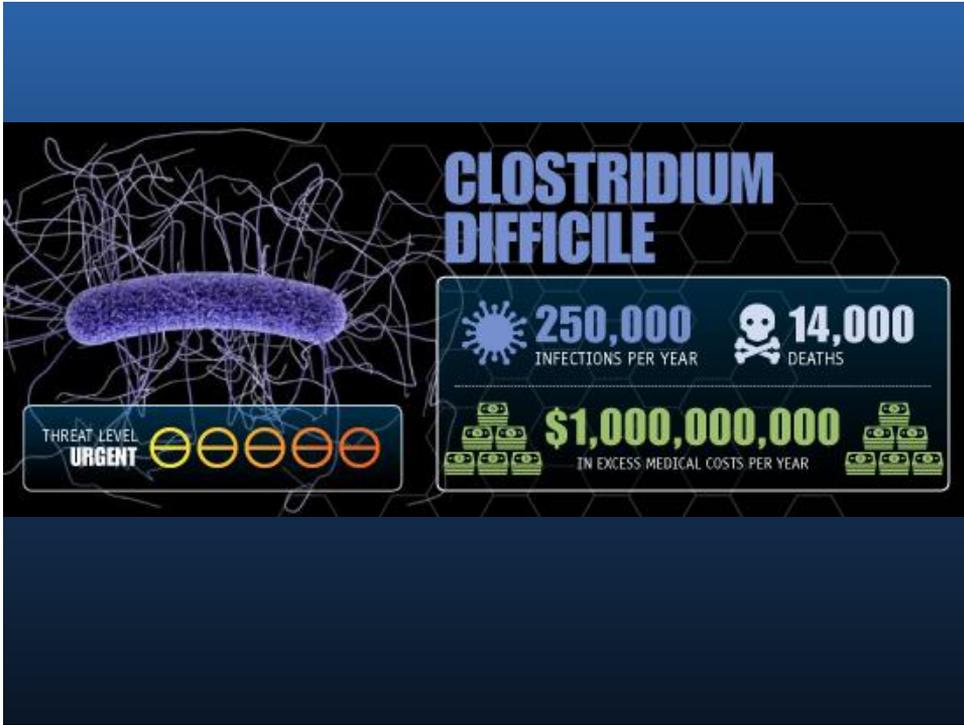
- CRE affects patients across the spectrum of healthcare
- CRE is found across US
 - one state in 2001, now in at least 38 states
- Common form of CRE is resistant to nearly untreatable

Enteric diseases becoming increasingly resistant to antibiotics

Salmonella
resistance/
partial resistance to
ciprofloxacin



Campylobacter
resistance to
ciprofloxacin



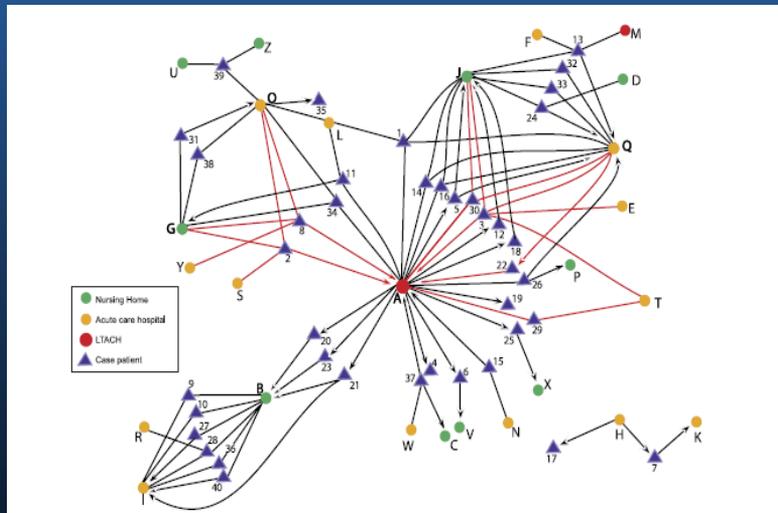
State HAI/AR Prevention Programs: Detect, Prevent, Respond



<http://www.cdc.gov/drugresistance/solutions-initiative>
<http://www.cdc.gov/vitalsigns/stop-spread>

- Expand the core capacity in all 50 states to detect, respond to, protect against HAI/AR threats
- Across all healthcare settings, networks of facilities in up to 25 states working with health departments to:
 - Prevent infections
 - Improve prescribing

Regional control of Carbapemen-resistant Enterobacteriaceae (CRE)



Won S, Munoz-Price S, Lolans K, Hota B, Weinstein R, Hayden M. for the Centers for Disease Control Prevention Epicenter Program. Rapid and Regional Spread of *Klebsiella pneumoniae* Carbapenemased CID 2011;53: 532-540

CDC's Healthcare-associated Infections-Antibiotic Resistance Leadership: Looking Forward

Detect & Respond

- Regional Lab
- Population-based Surveillance (EIP)
- NHSN



Prevent

- State AR Prevention (Protect) Programs
- Stewardship



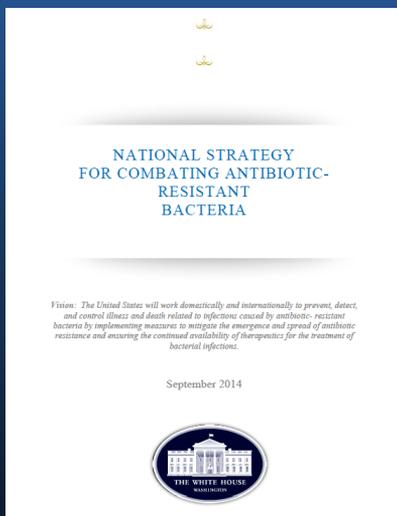
Innovate

- Microbiome
- Academic Partnerships (Prevention Epicenters)



- Comprehensive Tracking
- Rapid Detection
- Faster Outbreak Response
- Insights for Research Innovation
- Better Patient Care
- Improved Prescribing

National Strategy to Combat Antibiotic Resistant Bacteria, September 2014 – 5 Goals



1. Slow the Emergence of Resistant Bacteria and Prevent the Spread of Resistant Infections
2. Strengthen National One-Health Surveillance Efforts to Combat Resistance
3. Advance Development and Use of Rapid and Innovative Diagnostic Tests for Identification and Characterization of Resistant Bacteria
4. Accelerate Research to Develop New Antibiotics and Alternative Therapeutics, and Vaccines
5. Improve International Collaboration and Capacities for Disease Prevention and Surveillance and Antibiotic Research and Development

White House Forum on Antibiotic Stewardship

- Active Partnership outreach
- Brought together more than 100 leading organizations representing interests in both human and animal health
- Human health partners included:
 - Healthcare facilities
 - Healthcare providers
 - Insurance providers
 - Consumer and patient advocates
 - Industry- pharmaceutical, diagnostic, information technology



Timely Data + Effective Policies → Impact

- **National Healthcare Safety Network (NHSN)**
 - Web-based system for US hospitals to send healthcare outcomes data to CDC and State health departments
- **US Centers for Medicare and Medicaid Services (CMS)**
 - National healthcare reimbursement policies require hospitals to send data to CDC
 - Payment is now adjusted based on data reported to NHSN
- **Non-punitive opportunities + resources for improvement**
 - Technical assistance from CDC and State health departments
 - CMS-supported Quality Improvement Networks
 - Accreditation Organizations

Data for Action:



Nationwide Coverage
with CMS Reporting Requirements:

- Acute care hospitals
- Long-term acute care hospitals
- Inpatient rehabilitation facilities
- Outpatient dialysis facilities

State mandates can add additional requirements

2007

491 facilities enrolled
44% had 201-500 beds

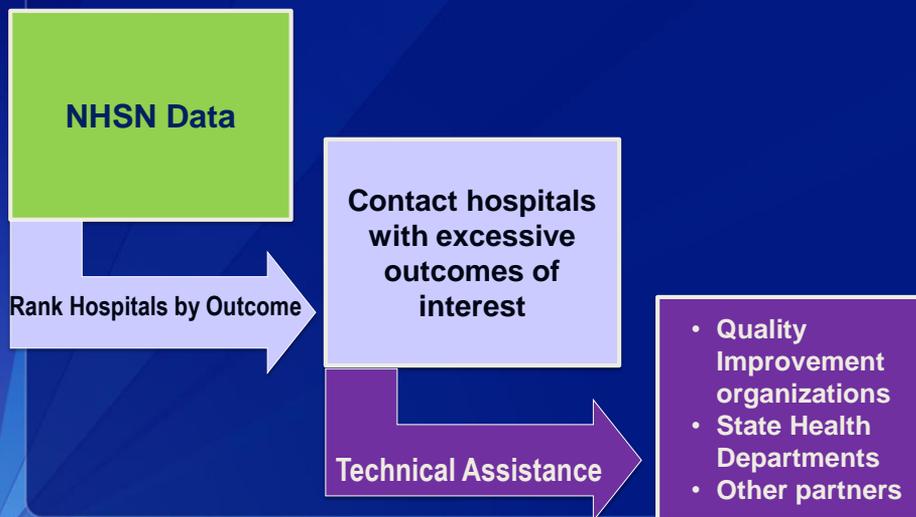
2008

2,003 facilities enrolled
19 States using NHSN for
mandatory reporting

2016

>18,000 facilities enrolled
33 states using NHSN for
mandatory reporting

Data for Action: Targeted Assessment for Prevention (TAP)



Increasing Transparency: CDC data for State and Federal initiatives

Medicare.gov | Hospital Compare
The Official U.S. Government Site for Medicare

Healthcare Associated Infections - details

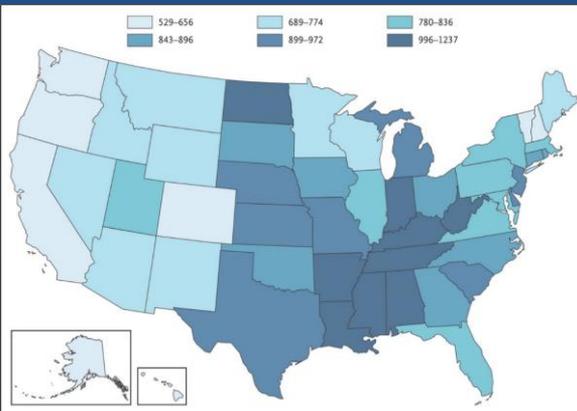
Table of 6 Central line-associated blood stream infections (CLABSI)

	No. of Infections Reported (N)	Central Line Days (CLD) ¹	Predicted No. Infections (E)	Standardized Infection Ratio (SIR) ² (A/R)	Evaluate
GEORGE WASHINGTON LINV HOSPITAL	20	6983	15,230	1.313	No Differs than U.S. National Benchmark
CHILDREN'S HOSPITAL NMC	Not Available	Not Available	Not Available	Not Available ³	Not Available
MEDSTAR GEORGETOWN UNIVERSITY HOSPITAL	13	9769	24,425	0.532	Better than the U.S. National Benchmark

Standardized infection ratio (SIR) national benchmark = 1.
Lower SIRs are better. A score of (0) – meaning no CLABSIs – is best.

Improving Use of antibiotics in the US

Outpatient Antibiotic Prescriptions per 1000 Persons of All Ages According to State, 2010



- At least **one-third** of antibiotics used in inpatient settings are unnecessary or inappropriately prescribed
- At least **one-third** of antibiotics prescribed in outpatient settings are unnecessary and misuse is common
- Doctors in some hospitals prescribed 3 times as many antibiotics as doctors in other hospitals

Hicks LA et al. N Engl J Med 2013;368:1461-1462.

Antimicrobial Use Data

- Data from:
 - Critical care - medical and surgical critical care units
 - Ward - medical and surgical wards
 - Specialty care area – e.g., oncology, dialysis
 - Facility-wide – All inpatient locations
- Numerator: Antimicrobial days (days of therapy)
 - 86 antimicrobials collected – includes antibacterial, antifungal, and anti-influenza agents
 - Agents are sub-stratified by route of administration: intravenous (IV), intramuscular (IM), digestive (oral), and respiratory (inhaled)
- Denominators:
 - Days Present - number of patients present for any portion of each day of a calendar month in specific unit or in any inpatient location (facility-wide)
 - Admissions - number of patients admitted to the facility (facility-wide calculation only)

Rate Table for Facility-Wide AU

National Healthcare Safety Network
Rate Table - Most Recent Month of AU Data - Antimicrobial Utilization Rates for FACWIDEIN
Rate per 1,000 Days Present
 As of: February 23, 2015 at 1:44 PM
 Date Range: All AU_RATES1MONTHFACWIDEIN

Facility Org ID=13860

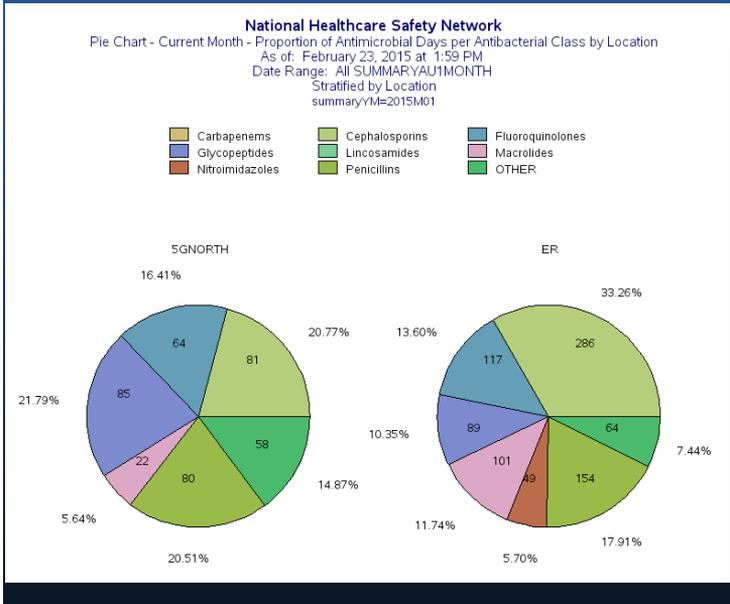
Summary Year/Month	Antimicrobial Category	Antimicrobial Class	Antimicrobial Days	Days Present	Rate per 1000 Days Present
2015M01	Antibacterial	-- All --	1626	2177	746.899
2015M01	Antibacterial	Aminoglycosides	22	2177	10.106
2015M01	Antibacterial	Carbapenems	101	2177	46.394
2015M01	Antibacterial	Cephalosporins	337	2177	154.8
2015M01	Antibacterial	Fluoroquinolones	244	2177	112.081
2015M01	Antibacterial	Folate pathway inhibitors	32	2177	14.699
2015M01	Antibacterial	Folate pathway inhibitors/Sulfonamides	0	2177	0

Sample rate table for all submitted AU data by FacWideIN (all inpatient locations reporting AU data)

- Generates a rate of utilization per 1,000 days present for each antimicrobial class for all inpatient locations combined
- Report includes separate rates for each antimicrobial class for each month of data submitted

*Data for example only

AU Data - Pie Chart by Location

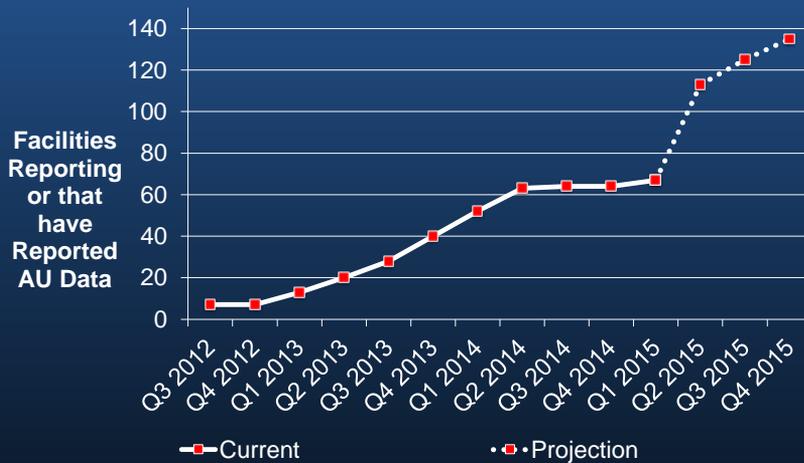


Sample pie chart by location

Shows proportion of antimicrobial days per antibacterial class

*Data for example only

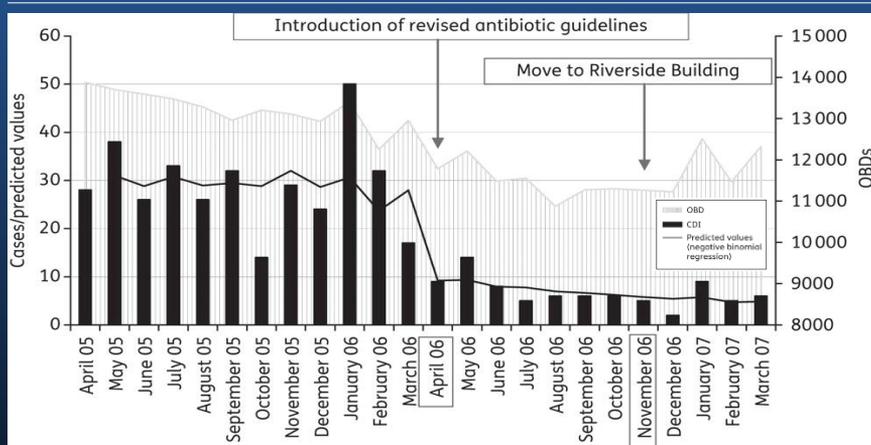
Quarterly AU Data Submissions to NHSN - Current and Projected as of April 2015



Antibiotic stewardship is an effective strategy to prevent AMR

Facility benefits	Antibiotic best practices	Antibiotic stewardship programs are a “win-win”
<ul style="list-style-type: none"> • Decrease antibiotic resistance • Decrease <i>C. difficile</i> infections • Decrease costs • Improve patient outcomes 	<ol style="list-style-type: none"> 1. Ensure all orders have dose, duration, and indications 2. Get cultures before starting antibiotics 3. Take an “antibiotic timeout,” reassessing antibiotics after 48-72 hours 	<ul style="list-style-type: none"> • A University of Maryland study showed one antibiotic stewardship program saved \$17M over 8 years • Antibiotic stewardship helps improve patient care and shorten hospital stays

C. diff infections declined sharply after revision of antibiotics guidelines University Hospital Lewisham, London, 2005-07



Source: Talpaert et al. *J. Antimicrob Chemother* 2011;66: 2168-74.

CDC's Seven Core Elements for Antibiotic Stewardship Programs

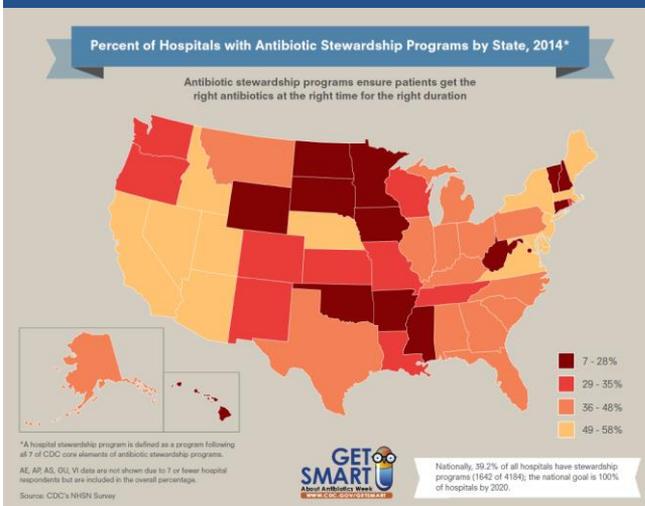


Hospital guidelines published March 2014;
Nursing Home guidelines published Sept. 2015

- **Leadership commitment:** commitment to safe and appropriate antibiotic use
- **Accountability:** physician, nursing and pharmacy leads to support antibiotic stewardship activities
- **Drug expertise:** access to pharmacists or other staff with experience or training in antibiotic stewardship
- **Action:** implement practices to improve antibiotic use
- **Tracking:** monitor antibiotic use and stewardship improvements in your facility
- **Reporting:** provide regular feedback on antibiotic use and resistance to facility staff
- **Education:** provide resources to facility staff, patients, and families about antibiotic resistance and opportunities for improving antibiotic use

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Stewardship in Hospitals



- In 2014, only 39.2% of US acute care hospitals report having antibiotic stewardship programs incorporating all seven CDC Core Elements for Hospital Antibiotic Stewardship Programs
- State specific percentages for hospitals with antibiotic stewardship programs are included in CDC's Prevention Status Report

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Partners Promoting Use of Stewardship in Hospitals and Nursing Homes

- **The Pew Charitable Trusts** Antibiotic Resistance Project: expanding the use of effective **stewardship programs** to ensure antibiotics are used only when needed and prescribed at the proper dose for the right duration
- **The Joint Commission**: inclusion of antibiotic stewardship programs and activities in **accreditation criteria**
- **National Quality Forum**: recently released Antibiotic Stewardship in Acute Care: A Practical Playbook, a **implementation guide** for the core elements
- **CMS Conditions of Participation**: recently proposed inclusion of antibiotic stewardship programs as part of **COP requirements** for nursing homes and acute care and critical access hospitals



Health Insurers Promoting Use of CDC's Seven Core Elements for Stewardship

- Anthem and Blue Cross/Blue Shield Quality-In-Sights® Hospital Incentive Program (Q-HIP®)
 - National hospital quality and **value-based payment** initiative
 - Introduced **metric** to reward hospitals for implementing the core measures described in the CDC CRE Toolkit
 - Developed a measure focused on **implementation** of comprehensive Antibiotic Stewardship program meeting CDC's Seven Core Elements
- HealthCore, subsidiary of Anthem
 - **Measuring antibiotic use** as key piece of antibiotic stewardship

Healthcare Effectiveness Data and Information Set

- National Committee on Quality Assurance's Healthcare Effectiveness Data and Information Set (**HEDIS**) measures are used by more than 90% of U.S. health plans to measure performance
- 3 measures are relevant to using antibiotics appropriately in the outpatient setting (all goals of 100%):
 - Appropriate treatment for **children with upper respiratory infections**
 - In 2014, overall performance for commercial plans: **85-87%**
 - Appropriate testing for **children with pharyngitis**
 - In 2014, overall performance for commercial plans: **80-82%**
 - Avoidance of antibiotic treatment in **adults with acute bronchitis**
 - In 2014, overall performance for commercial plans: **26-28%**
- There is a need to feedback performance to providers and to incentivize improved performance through linking to quality-based payments

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Emerging Infections Program

- Network of state and local health departments, academic institutions, other federal agencies, public health and clinical laboratories, infection preventionists, and healthcare providers
- **Population-base surveillance for:**
 - Invasive bacterial disease
 - Foodborne disease
 - Laboratory confirmed influenza-related hospitalizations and influenza vaccine effectiveness
 - **HAI-Community Interface projects**
- EIP supports epidemiologic studies to explore risk factors, spectrum of disease, and guide prevention strategies.

Emerging Infections Program HAI-Community Interface



Multi-Drug Resistant
Gram-Negative
Bacteria

MRSA

Clostridium difficile

HAI & Antimicrobial
Use Point Prevalence
Survey

Measuring Scope and Magnitude Characterizing New Epidemiology

ORIGINAL CONTRIBUTION



Invasive Methicillin-Resistant *Staphylococcus aureus* Infections in the United States

R. Monica Kloos, DDS, MPH
Melissa A. Morrison, MPH
Jedie Nalle, MPH
Susan Petit, MPH
Ken Gorbman, MD, MPH
Susan Ray, MD

The first estimate of
MRSA disease burden
drives a new national
focus on prevention
efforts.

**USA 300
MRSA causing
healthcare-
associated
infections**

TABLE 2. Epidemiologic characteristics of invasive MRSA isolates, according to PFGE type

PFGE type	No. (%)	No. (%) in indicated epidemiologic class			
		HO	HACO	CA	UNK*
USA100	1,063 (53.6)	306 (28.8)	669 (62.9)	83 (7.8)	5 (0.5)
USA200	15 (0.8)	6 (40)	9 (60)	0 (0)	0 (0)
USA300	627 (31.6)	76 (12.1)	293 (46.7)	246 (39.2)	12 (1.9)
USA400	6 (0.3)	0 (0)	3 (50)	3 (50)	0 (0)
USA500	79 (3.7)	11 (14.9)	57 (77)	6 (8.1)	0 (0)
USA600	14 (0.7)	6 (42.9)	6 (42.9)	2 (14.3)	0 (0)
USA700	8 (0.4)	2 (25)	3 (37.5)	3 (37.5)	0 (0)
USA800	38 (1.9)	6 (15.8)	25 (65.8)	6 (15.8)	1 (2.6)
USA1000	16 (0.8)	1 (6.2)	10 (62.5)	5 (31.2)	0 (0)
USA1100	8 (0.4)	2 (25)	4 (50)	2 (25)	0 (0)
Iberian	36 (1.8)	8 (22.2)	20 (55.6)	8 (22.2)	0 (0)
Novel type ^a	11 (0.6)	4 (36.4)	7 (63.6)	0 (0)	0 (0)
EMRSA15	4 (0.2)	2 (50)	1 (25)	1 (25)	0 (0)
Group D	2 (0.1)	0 (0)	1 (50)	1 (50)	0 (0)
Nontypable	1 (0.1)	0 (0)	0 (0)	1 (100)	0 (0)
Not done	61 (3.1)	17 (27.9)	32 (52.5)	12 (19.7)	0 (0)
Total	1,984	447 (22.5)	1,140 (57.5)	379 (19.1)	18 (0.9)

* UNK, unknown.

National Burden of Disease estimates (Adults) of Invasive MRSA Infection by Subgroup (2009)

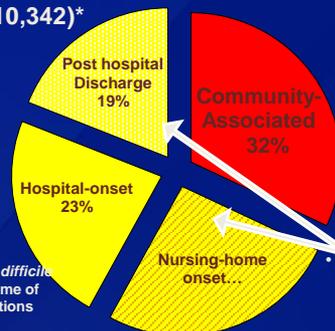
Population	Estimated No. Infections	Estimated Population	No. per 100,000
U.S. adults	76,392	232,458,000	32.9
18-64 years	38,420	192,888,000	19.9
≥65 years	37,972	39,571,000	96.0
Private household resident	41,941	227,371,000	18.4
Long Term Care resident	15,281	1,402,000	1,090
Chronic hemodialysis	10,772	370,000	2,909

66% of invasive MRSA (non-dialysis patients) cases admitted from home were in hospital during the previous 12 weeks; making vaccination at hospital discharge among high risk discharges a viable vaccine administration window – especially if protection is anticipated to be transient

Fagan, IDWeek 2012; Dantes, JAMA Internal Medicine 2013

Clostridium difficile: EIP Data to Assist Development of New Interventions (e.g., vaccine)

CDI Cases (N=10,342)*



Distribution of *Clostridium difficile* Infections by Location at Time of Diagnosis, Emerging Infections Program, 2010

- 82% have had at least one outpatient healthcare exposure in the 12 weeks prior to symptoms onset; understanding these settings can inform vaccine trials

- 45% of all CDI occurs in post-discharge setting or in nursing homes, making these populations important consideration for primary prevention through vaccine

Enrolling "high risk" patients at discharge decreases estimated no. to enroll and decreases cost of a clinical trial

CDC, MMWR March 9, 2012 / 61:157-162

* EIP Sites: California, Colorado, Connecticut, Georgia, Minnesota, New York, Oregon, and Tennessee

EIP Point Prevalence Antibiotic Use Survey “Infections” Treated with Antibiotics

Clinician-Defined Therapeutic Site*	Patients (N=4278)
	No. (%)
Lower respiratory infection	1480 (36)
Urinary tract infection	955 (22)
Skin and soft tissue infection	688 (16)
Gastrointestinal infection	537 (13)
Undetermined infection site (empiric therapy)	364 (9)
Bloodstream infection	401 (9)
Intraabdominal infection	178 (4)
Ears, eyes, nose, throat, mouth infection	183 (4)
All other sites	287 (7)

Infections where new diagnostics will have
the greatest impact in antibiotic use

Preliminary data, subject to change

Public Health & Clinical Laboratory data

Complementary roles:

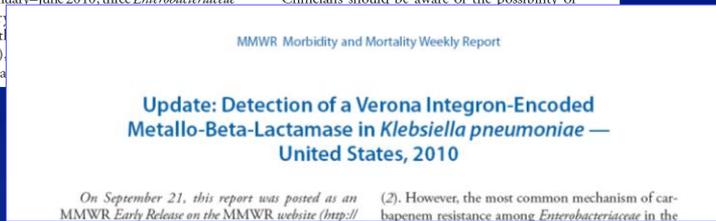
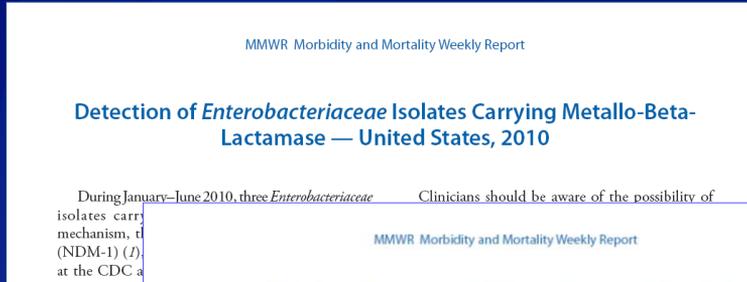
- Clinical - testing for patient-care decisions and contributing to regional and national data
- State Public Health - testing to inform both clinical and local public health decision-making (e.g., outbreak identification)
- CDC - reference testing, esoteric testing, providing national data for local, regional & national interventions



Accurate, reliable laboratory data are essential for AMR control.

Detection of New CRE

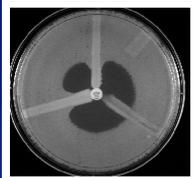
- ❑ Reference laboratory identification of new CRE
- ❑ Guidance for laboratory detection of CRE



New Carbapenemase Tests

- ❑ In response to CRE, CDC evaluated assays to detect carbapenemase production for inclusion in CLSI documents.

Modified Hodge Test



CarbaNP



Next



Progressively improving diagnostic test performance

Collaboration for New Diagnostics and Treatments

CDC's Surveillance Programs and Reference Laboratories:

- ❑ Identify clinical situations where diagnostics and treatments are most needed
- ❑ Evaluate and validate new diagnostics for the most important antibiotic resistant threats and new threats
- ❑ Assess impact of implementation
- ❑ Provide industry and researchers with a unique collections of well-characterized antibiotic threat isolates

CDC Isolate Bank- Launched July 2015

[CDC](#) > [Antibiotic / Antimicrobial Resistance](#) > [AR Bank](#)

Overview



Overview of AR Isolate Bank

The AR Isolate Bank is a centralized repository of microbial pathogen assembled by CDC in collaboration with the Food and Drug Administration to advance development of diagnostic devices and antimicrobial drug products.

[National Action Plan for Combating Antibiotic-Resistant Bacteria](#) [PDF - 63 Pages] by advancing the development of diagnostic tests to identify and characterize resistant bacteria, and by accelerating research and development for new antibiotics. See more information on CDC's efforts to combat antibiotic-resistant bacteria on CDC's [Antibiotic Resistance Solutions Initiative](#) page.



Goal: Provide documented organisms of interest to industry and academic partners to support research and development in new diagnostic technology and antibiotic development.

Currently Available Panels (Nov 2015)

- Enterobacteriaceae Carbapenem Breakpoint
- Gram Negative Carbapenemase Detection
- Enterobacteriaceae Carbapenemase Diversity
- Vancomycin Intermediate *Staphylococcus aureus* (VISA)

The screenshot shows the CDC website interface for the Resistance Bank. The main heading is 'Antibiotic / Antimicrobial Resistance'. Below this, there are several panels listed, including 'Enterobacteriaceae Carbapenemase Diversity Panel'. A table of isolates is displayed, showing the following data:

Bank #	Species	Carbapenem Susceptibility	IG Dn
1112	<i>Klebsiella pneumoniae</i>	Resistant	KF
1113	<i>Klebsiella pneumoniae</i>	Resistant	KF
1114	<i>Escherichia coli</i>	Resistant	KF
1115	<i>Klebsiella pneumoniae</i>	Resistant	KF
1116	<i>Citrobacter freundii</i>	Resistant	KF
1117	<i>Klebsiella pneumoniae</i>	Resistant	KF

www.cdc.gov/DrugResistance/Resistance-Bank

CDC Collaborations Beyond Data Sharing....

- Prevention implementation networks**
 - state, regional, healthcare-community networks
 - Academic centers, healthcare systems
- Communication strategies to change the “norm”**
 - Campaigns
 - Targeted publications
- Expansion of partnerships**
 - Federal partners
 - State and local public health organizations
 - Professional organizations
 - Healthcare systems
 - Private industry
 - Consumers

Estimated minimum number of illnesses and deaths caused annually by antibiotic resistance*:

At least



**bacteria and fungus included in this report*

Implications of antimicrobial resistance

- ~30,000 motor vehicle accidents/year
- ~450,000 burn injuries/year
- ~1.6 million new cancer diagnoses/year
- ~2.3 million trauma hospital admissions/year

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The time for action is now.

Post Assessment Questions

1. One of the common forms of CRE is resistant to nearly all antibiotics?
(True or False)
2. At least **one-third** of antibiotics used in inpatient settings are unnecessary or inappropriately prescribed (True or False)?

Post Assessment Questions

3. The benefits of antibiotic stewardship include:
- A. Decreased antibiotic resistance
 - B. Decreased *C.difficile* infections
 - C. Decreased costs
 - D. Improved patient outcomes
 - E. All of the above



Thank you

For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333
Telephone, 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
E-mail: cdcinfo@cdc.gov Web: www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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