



Department of Health

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Date: December 13, 2016

To: Hospitals, Diagnostic and Treatment Facilities, Local Health Departments, Long-Term Care Facilities, Clinical Laboratories

From: NYSDOH Bureau of Healthcare-Associated Infections (BHAI)

Health Advisory:
Carbapenem-resistant *Enterobacteriaceae* (CRE)

Please distribute immediately to:
Hospital Epidemiologists, Infection Preventionists, Laboratory Directors, Infectious Diseases
Physicians, Medical Directors, Nursing Directors, Risk Managers,
Administrators and Pharmacy Directors

Summary

The emergence of carbapenem resistance among *Enterobacteriaceae* in the United States represents a serious threat to public health. Wide variability exists in the incidence of these organisms identified in hospitals across New York State. Healthcare facilities should ensure awareness of the issue and appropriately implement infection prevention practices to decrease the development and spread of these organisms.

Background

The *Enterobacteriaceae* family of bacteria includes *Escherichia coli*, *Klebsiella pneumoniae*, and *Enterobacter* spp., among many others. Invasive infections with carbapenem-resistant strains are associated with mortality rates as high as 40%, and the resistance genes have the potential to spread widely. *Klebsiella pneumoniae* carbapenemase (KPC)-producing bacteria have been identified in the majority of New York State (NYS) CRE cases.

The Centers for Disease Control and Prevention (CDC) has identified carbapenemase-producing CRE in 48 states, with a number of very well-described outbreaks having occurred in this and other countries. In NYS, CRE has emerged as a serious public health threat with an estimated 2,500 cases per year identified in hospitals, not including patients who were diagnosed and treated as outpatients. While 20% of NYS hospitals have never reported a case, hospitals in the metropolitan New York City area carry a very high burden. In July 2013, the New York State Department of Health (NYSDOH) began collecting information on CRE in hospitalized patients. In 2014, 2,691 cases were reported in NYS, including approximately 354 bloodstream infections. Among those patients with CRE bloodstream infections, it is estimated that the deaths of 135 patients were attributable to the infection. (Refer to NYSDOH [Hospital-Acquired Infections Annual Reports](#)).

In 2015, reports from other states described CRE transmission associated with persistently contaminated duodenoscopes for which no breaches in reprocessing were identified.¹ In addition, more recent reports have described plasmid-mediated colistin resistance caused by the *mcr-1* gene. The presence of the *mcr-1* gene on a plasmid means that colistin resistance can be shared with other more resistant bacteria such as CRE, raising the possibility that a broad class of untreatable bacteria could develop.²

These data highlight the urgent need to intensify efforts to combat the spread of CRE and other multidrug-resistant organisms (MDROs) before the problem becomes insurmountable.

In alignment with CDC's publications, *Vital Signs: Making Health Care Safer – Stop Spread of Antibiotic Resistance*, from August 2015 and – *Protect Patients from Antibiotic Resistance*, from March 2016, NYSDOH has begun working toward a coordinated approach for CRE prevention across the state. The NYSDOH Antimicrobial Resistance/CRE Workgroup has been established with the intent of creating a statewide CRE/MDRO surveillance and response plan. The workgroup has identified strategies to enhance outbreak investigation, reporting, and response; improve surveillance; implement and evaluate epidemiologic public health practice, prevention, and control strategies; and sustain and enhance laboratory diagnostic capacity. In addition, to assist facilities with high CRE rates, NYS epidemiologists will conduct site visits as needed.

Reporting Requirements:

Despite the high incidence of CRE in NYS, few outbreaks are reported through the Nosocomial Outbreak Reporting Application (NORA). One concern is that CRE might be considered endemic in some areas, making transmission events less likely to be recognized or considered an outbreak. Although CRE is reportable by hospitals through the HAI Reporting Program, it is not currently a mandated reportable communicable disease under the New York State Sanitary Code (10NYCRR 2.10, 2.14). However, its seriousness warrants reporting through NORA (for hospitals and nursing homes) or by phone call to the local health department or NYSDOH regional epidemiologist (for other facilities and for urgent situations) when it is the first CRE isolate identified by the facility or if an outbreak or increased incidence is suspected/identified.

10NYCRR requires facilities to report suspected or confirmed communicable diseases including any unusual or emerging diseases or any outbreaks. Please refer to *Attachment A* to determine when outbreaks or increased incidence of CRE should be reported to the NYSDOH. Facilities are encouraged to, at minimum, use the NHSN definition as described in *Attachment B* to identify when an organism meets the definition of CRE.

Wadsworth Center Laboratory Support:

A report of a CRE outbreak is considered a high priority situation and will prompt an epidemiologic investigation, often with laboratory support from Wadsworth Center (WC) in Albany. WC can provide isolate identification, susceptibility testing and molecular testing for resistance mechanisms, as well as testing to determine organism relatedness, such as pulsed-field gel electrophoresis (PFGE) as needed to support investigations. WC is also building capacity as a CDC Northeast Regional Antimicrobial

Resistance Network laboratory to perform CRE colonization studies and additional testing for CRE including more comprehensive resistance gene detection and whole-genome sequencing.

Inter-facility Transfers:

The interdependence of acute care facilities and long-term care facilities in the spread and transmission of CRE has been described³. Communication between transferring and accepting facilities about a patient's CRE status is vital in order to prevent further transmission. CDC has developed an *Inter-facility Infection Control Transfer Form*. This form or any standardized paper or electronic format for transmitting infection prevention-related information should be used by facilities to improve communication: <http://www.cdc.gov/hai/pdfs/toolkits/InfectionControlTransferFormExample1.pdf>

Facility Actions:

In regions of the state with little or no CRE, such as Upstate New York, measures should be taken to limit the development and spread of any newly identified CRE cases. In these instances, the first identified CRE case within a facility should be reported to the NYSDOH regional epidemiologist in your area.

CRE containment in the high-prevalence and high-incidence regions of the state will require the implementation of prevention measures across all acute care and long-term care facilities. Concerted efforts to limit development and spread of CRE are needed. Facilities are encouraged to discuss potential strategies with other facilities in their community and to consider joining the NYSDOH workgroup.

Please ensure that your facility performs a risk assessment for CRE prevalence and incidence and implements appropriate prevention measures. Refer to the CDC *2015 CRE Toolkit: Facility Guidance for Control of Carbapenem-Resistant Enterobacteriaceae*. Updated maps of the geographically varying burden of CRE in NYS for 2015 are presented in *Attachment C*.

During suspected outbreaks or for the first identification of CRE at a facility, isolates identified as CRE should be saved and shipped to WC for verification as requested.

A list of CRE resources has been included in this mailing for your convenience (*Attachment D*). If you would like further information about the NYS initiative to prevent and contain CRE or the Antimicrobial Resistance/CRE workgroup, please contact Rosalie Giardina at 914-654-4362.

For questions or concerns regarding this advisory, please contact either the Antimicrobial Resistance/CRE Coordinator or the NYSDOH regional epidemiologist in your area:

NYSDOH Antimicrobial Resistance/CRE Coordinator:	(914) 654-4362
Central Office (Albany):	(518) 474-1142
Capital District Regional Office:	(518) 474-1142
Central New York Regional Office:	(315) 477-8166
Metropolitan Area Regional Office:	(914) 654-7149
Western Regional Office:	(716) 847-4503

References:

1. Epstein L, Hunter JC, Arwady MA, et al. New Delhi Metallo- β -Lactamase Producing Carbapenem-Resistant *Escherichia coli* Associated with Exposure to Duodenoscopes. *JAMA* 2014;312:1447-1455
2. Alert to US Healthcare Facilities: First *mcr-1* Gene in *E. coli* Bacteria found in a Human in the United States. CDC Health Alert Network (HAN). June 13, 2016. CDCHAN-00390.
3. Chitnis, AS; Caruthers, PS; Rao, AK; Lamb, J; Lurvey, R; Beau De Rochars, V; Kitchel, B; Cancio, M et al. (2012). "Outbreak of carbapenem-resistant *Enterobacteriaceae* at a long-term acute care hospital: Sustained reductions in transmission through active surveillance and targeted interventions". *Infection Control and Hospital Epidemiology* **33** (10): 984–92. [doi:10.1086/667738](https://doi.org/10.1086/667738)
4. Facility Guidance for Control of Carbapenem-resistant *Enterobacteriaceae* (CRE) – November 2015 Update CRE Toolkit. <http://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html>.

Attachment A: Title 10NYCRR

Part 2 – Communicable Diseases

(2.2) Definitions – Outbreak

Definitions shall include the following:

- (a) For public health reporting purposes, hospital-associated infections shall include an outbreak or increased incidence of disease due to microbiological agents or their toxic products occurring in patients or persons working in the hospital. Any non-reportable hospital-associated infections must be handled nonetheless by hospitals and their infection control committees.
- (b) A case is defined as a person who has been diagnosed to have a particular disease or condition. The diagnosis may be based solely on clinical judgement or solely on laboratory evidence, or on both criteria.
- (c) A suspected case is defined as a person who has been diagnosed as likely to have a particular disease or condition. The suspected diagnosis may be based solely on signs and symptoms, or solely on laboratory evidence, or both criteria.
- (d) An outbreak is defined as an increased incidence of disease above its expected or baseline level. As the number of cases which indicate the presence of an outbreak vary according to the infectious agent, size and type of population exposed, previous exposure or lack of exposure to the disease, and time and place of occurrence, the expected or baseline level of disease shall be assessed by hospitals and their infection control committees as directed in section 405.11 of this Title. While an outbreak usually involves several cases of illness (e.g., food-borne poisoning, influenza), it may consist of just one case for certain rare and/or serious diseases (e.g., botulism, measles).

Attachment B: CRE Surveillance Definition

NY hospitals are required to report CRE cases to the HAI Reporting Program following CDC's National Healthcare Safety Network (NHSN) Laboratory-Identified Event Reporting definition:

Any *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumoniae*, or *Enterobacter* spp. testing resistant to imipenem, meropenem, doripenem, or ertapenem by standard susceptibility testing methods (i.e., minimum inhibitory concentrations (MIC) of ≥ 4 mcg/mL for doripenem, imipenem and meropenem or ≥ 2 mcg/mL for ertapenem) OR by production of a carbapenemase (i.e., KPC, NDM, VIM, IMP, OXA-48) demonstrated using a recognized test (e.g., polymerase chain reaction, metallo- β -lactamase test, modified-Hodge test, Carba-NP).

(http://www.cdc.gov/nhsn/pdfs/pscmanual/12pscmetro_cdadcurrent.pdf)

Note that this definition is based on the raw MIC values prior to any additional testing or interpretation. The current Clinical and Laboratory Standards Institute (CLSI) M100-S26 breakpoints and interpretation are summarized below.

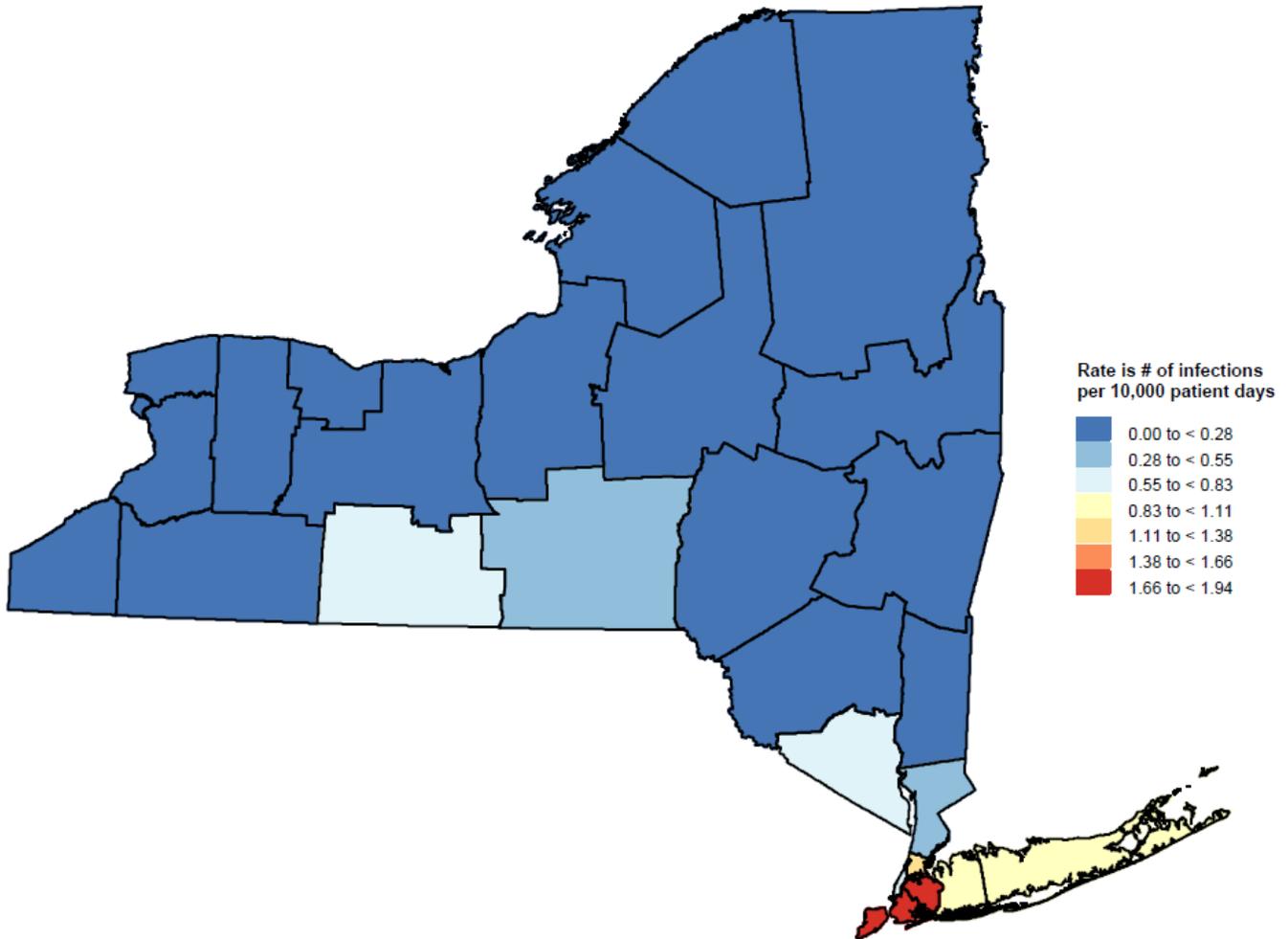
Minimum Inhibitory Concentration Breakpoints ($\mu\text{g/mL}$)			
Carbapenems	Susceptible	Intermediate	Resistant
Doripenem	≤ 1	2	≥ 4
Ertapenem	≤ 0.5	1	≥ 2
Imipenem	≤ 1	2	≥ 4
Meropenem	≤ 1	2	≥ 4

CLSI document M100-S26, Wayne, PA: Clinical and Laboratory Standards Institute: Jan 2016.

Facilities may also wish to broaden the definition to include other bacteria from the *Enterobacteriaceae* family. Additional information about choosing and implementing a CRE definition can be found at the following link: <http://www.cdc.gov/hai/organisms/cre/definition.html>.

Attachment C: Geographical Distribution of CRE, by organism, in NYS

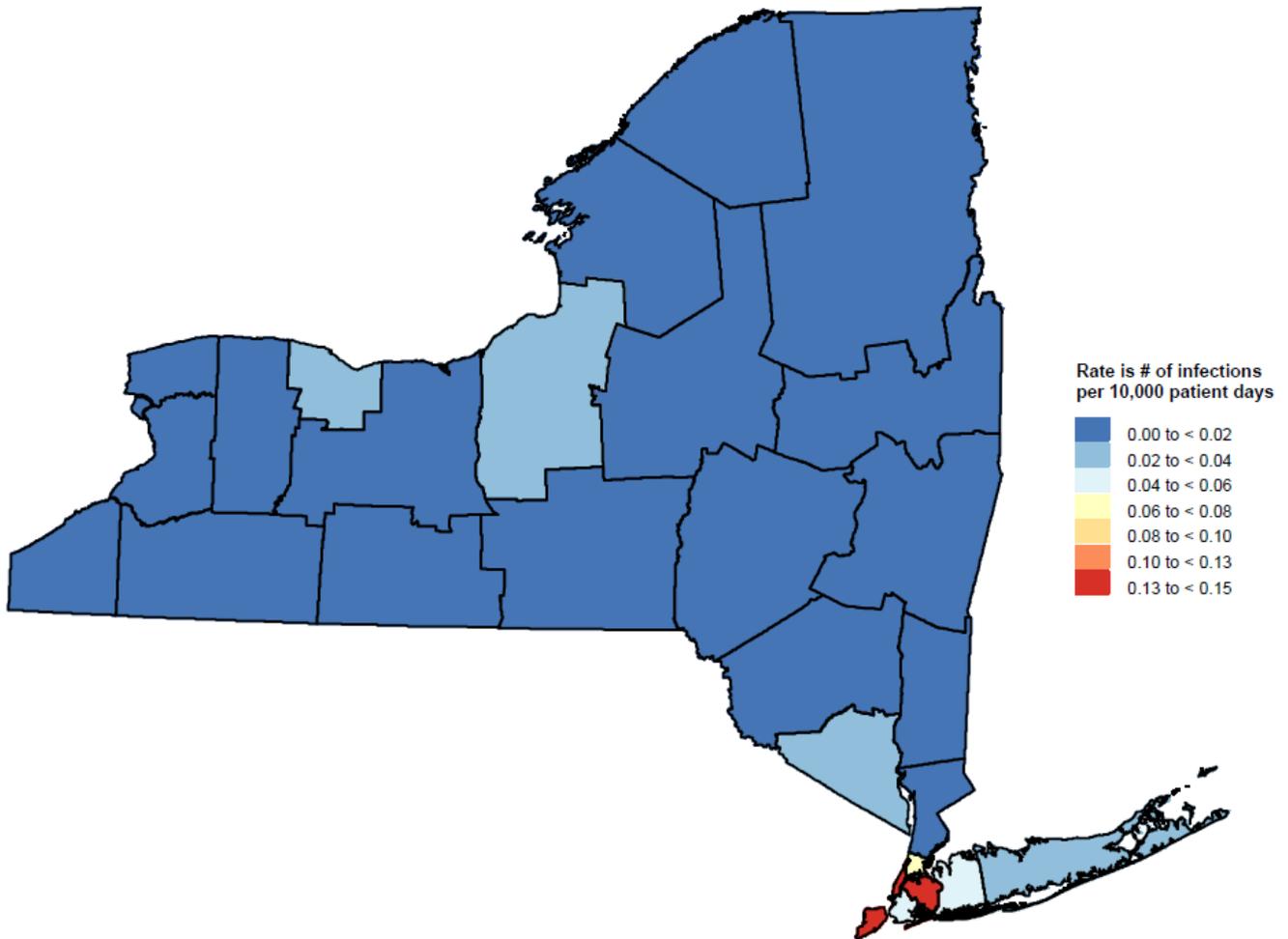
CRE-*Klebsiella* Infection/Colonization Incidence Rate NYS 2015



Inpatient data from 175 hospitals and long term acute care hospitals reported to the National Healthcare Safety Network as of October 7, 2016. This rate is the number of first infections from any body site (e.g. urine, respiratory tract, blood) per patient per hospital among those with no documented evidence of previous infection or colonization with this specific organism type at the same hospital, identified more than three days after admission to the hospital, per 10,000 patient days. Inpatient rehabilitation and psychiatric units were excluded.

Attachment C: Geographical Distribution of CRE, by organism, in NYS (continued)

CRE-*E. coli* Infection/Colonization Incidence Rate NYS 2015

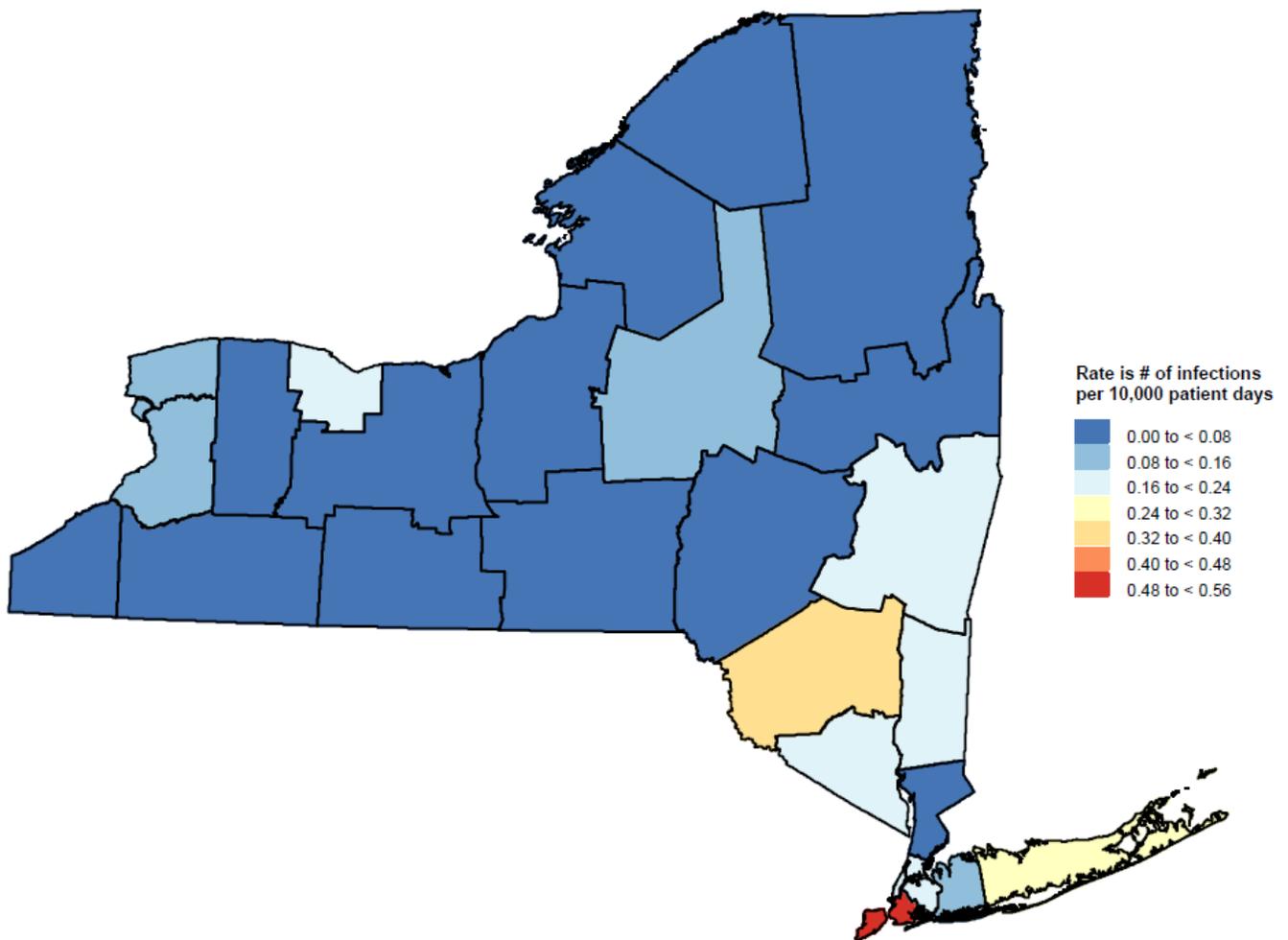


Please note that CRE-*E.coli* incidence rates are **one-tenth** that of CRE-*Klebsiella* incidence rates.

Inpatient data from 175 hospitals and long term acute care hospitals reported to the National Healthcare Safety Network as of October 7, 2016. Inpatient rehabilitation and psychiatric units were excluded.

Attachment C: Geographical Distribution of CRE, by organism, in NYS (continued)

CRE-*Enterobacter* Infection/Colonization Incidence Rate NYS 2015



Inpatient data from 175 hospitals and long term acute care hospitals reported to the National Healthcare Safety Network as of October 7, 2016. Inpatient rehabilitation and psychiatric units were excluded.

Attachment D: Resources for Carbapenem-Resistant *Enterobacteriaceae*

CENTERS FOR DISEASE CONTROL AND PREVENTION

Carbapenem-Resistant *Enterobacteriaceae* in Healthcare Settings
<http://www.cdc.gov/HAI/organisms/cre/index.html>

Facility Guidance for Control of Carbapenem-Resistant *Enterobacteriaceae* (CRE) - November 2015
Update CRE Toolkit
<http://www.cdc.gov/hai/organisms/cre/cre-toolkit/index.html>

Vital Signs: Making Healthcare Safer

Stop Infections from Lethal CRE Germs Now - March 2013
<http://www.cdc.gov/vitalsigns/hai/cre/index.html> and
<http://www.cdc.gov/vitalsigns/pdf/2013-03-vitalsigns.pdf>

Antibiotic Rx in Hospitals: Proceed with Caution – March 2014
<http://www.cdc.gov/vitalsigns/antibiotic-prescribing-practices/index.html>
<http://www.cdc.gov/vitalsigns/pdf/2014-03-vitalsigns.pdf>

Stop Spread of Antibiotic Resistance – August 2015
<http://www.cdc.gov/vitalsigns/stop-spread/index.html>
<http://www.cdc.gov/vitalsigns/pdf/2015-08-vitalsigns.pdf>

Protect Patients from Antibiotic Resistance – March 2016
<http://www.cdc.gov/vitalsigns/protect-patients/index.html>
<http://www.cdc.gov/vitalsigns/pdf/2016-03-vitalsigns.pdf>

FAQs about Choosing and Implementing a CRE Definition
<http://www.cdc.gov/hai/organisms/cre/definition.html>

CRE for Clinicians
<http://www.cdc.gov/hai/organisms/cre/cre-clinicians.html>
<http://www.cdc.gov/hai/organisms/cre/cre-clinicianFAQ.html>

Interim Duodenoscope Surveillance Protocol
<http://www.cdc.gov/hai/organisms/cre/cre-duodenoscope-surveillance-protocol.html>

FAQs on the Interim Duodenoscope Surveillance Protocol <http://www.cdc.gov/hai/organisms/cre/cre-duodenoscope-surveillance-protocol-FAQs.html>

Interim Duodenoscope Sampling Method
<http://www.cdc.gov/hai/settings/lab/lab-duodenoscope-sampling.html>

Interim Duodenoscope Culture Method
<http://www.cdc.gov/hai/settings/lab/lab-duodenoscope-culture-method.html>

Tracking CRE
<http://www.cdc.gov/hai/organisms/cre/TrackingCRE.html>

Laboratory Protocol for Detection of Carbapenem-resistant or Carbapenemase-producing *Klebsiella* spp. and *E. coli* from Rectal Swabs

http://www.cdc.gov/HAI/pdfs/labSettings/Klebsiella_or_Ecoli.pdf

National Healthcare Safety Network (NHSN)

<http://www.cdc.gov/nhsn>

<http://www.cdc.gov/nhsn/enrolled-facilities/index.html>

Surveillance for *C. difficile*, MRSA, and other Drug-resistant Infections

Acute Care Hospitals/ LTACs/ Inpatient Rehabilitation Facilities/ Inpatient Psychiatric Facilities:

http://www.cdc.gov/nhsn/pdfs/pscmanual/12pscmdro_cdadcurrent.pdf

Long Term Care Facilities, i.e. Nursing homes, Assisted Living and Residential care, Chronic care and SNFs:

http://www.cdc.gov/nhsn/pdfs/ltc/lctf-labid-event-protocol_current.pdf

Management of Multidrug-Resistant Organisms in Healthcare Settings, 2006

<http://www.cdc.gov/hicpac/pdf/MDRO/MDROGuideline2006.pdf>

ASSOCIATION FOR PROFESSIONALS IN INFECTION CONTROL AND EPIDEMIOLOGY (APIC)

CRE Home Page

<http://www.apic.org/Resources/Topic-specific-infection-prevention/cre>

Summary of State CRE Reporting Requirements

http://www.apic.org/Resource_/TinyMceFileManager/Advocacy-PDFs/CRE_ReportingRequirements_Final.pdf

Prevention Strategist articles:

Carbapenem-resistant Enterobacteriaceae: Deadly superbugs on the rise—Fall 2014

http://www.apic.org/Resource_/TinyMceFileManager/Periodical_Images/CRE.pdf

CRE in Israel

http://www.apic.org/Resource_/TinyMceFileManager/Topic-specific/CRE_outbreak_in_Israel.pdf

Webinars:

Carbapenem-resistant *Enterobacteriaceae* (CRE)

<http://webinars.apic.org/session.php?id=10780>

Comprehensive HAI Prevention: Finding and Controlling the Sources of Resistant Bacterial Transmission in the Healthcare Setting

<http://webinars.apic.org/session.php?id=5926>

AGENCY FOR HEALTHCARE RESEARCH AND QUALITY (AHRQ)

AHRQ: Carbapenem-Resistant *Enterobacteriaceae* (CRE) Control and Prevention Toolkit

<http://www.ahrq.gov/professionals/quality-patient-safety/patient-safety-resources/resources/cretoolkit/index.html>

U. S FOOD AND DRUG ADMINISTRATION (FDA) RESOURCES

FDA releases final guidance on reprocessing of reusable medical devices—The U.S. Food and Drug Administration, issued 3/12/2015

<http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm437804.htm>

Safety communication—The U.S. Food and Drug Administration, issued 2/19/2015

<http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm434871.htm>

Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling—The U.S. Food and Drug Administration, issued 3/12/2015

http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM253010.pdf?source=govdelivery&utm_medium=email&utm_source=govdelivery

Olympus validates new reprocessing instructions for model TJF-Q180V duodenoscopes--The U.S. Food and Drug Administration, issued 3/26/15

http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm439999.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

JOURNAL ARTICLES

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Ben-David D, Masarwa S, Navon-Venezia S, Mishali H, Fridental, I, Rubinovitch B, Smollan G, Carmeli Y, Schwarber, MJ, Israel Post-Acute-Care Facility carbapenem-resistant *Klebsiella pneumoniae* Working Group. Carbapenem-Resistant *Klebsiella pneumoniae* in Post-Acute-Care Facilities in Israel. ICHE 2011, 32 (9): 845-853.

Gupta N, Limbago BM, Patel JB, Kallen AJ. Carbapenem-Resistant *Enterobacteriaceae*: Epidemiology and Prevention. Clin Infect Dis. 2011, 53: 60-67.

Snitkin ES, Zelazny AM, Thomas PJ, et al. Tracking a Hospital Outbreak of Carbapenem-Resistant *Klebsiella pneumoniae* with Whole-Genome Sequencing. Science Translational Medicine. 2012;4(148):148ra116. doi:10.1126/scitranslmed.3004129.

Marchaim D, Chopra T, Bhargava A, Bogan C, Dhar S, Hayakawa K, Pogue JM, Bheemreddy S, Blunden C, Shango M, Swan J, Lephart PR, Perez F, Bonomo RA, Kaye, KS. Recent Exposure to Antimicrobials and Carbapenem-Resistant *Enterobacteriaceae*: The Role of Antimicrobial Stewardship. ICHE. 2012, 33: 817-830. doi: 10.1086/666642

Swaminathan M, Sharma S, Poliansky-Blash S, Patel G, Banach DB, Phillips M, LaBombardi VJ, Anderson KF, Kitchel B, Srinivasan A, Calfee DP. Prevalence and Risk Factors for Acquisition of Carbapenem-Resistant *Enterobacteriaceae* in the Setting of Endemicity. ICHE 2013, 34:809-817. doi:10.1086/671270

Schwaber MJ, Carmeli Y. An Ongoing National Intervention to Contain the Spread of Carbapenem-Resistant *Enterobacteriaceae*. Clin Infect Dis. (2014) 58 (5): 697-703 first published online December 4, 2013 doi:10.1093/cid/cit795

Palmore TN, Henderson DK. Managing Transmission of Carbapenem-Resistant *Enterobacteriaceae* in Healthcare Settings: A View From the Trenches. Weinstein RA, ed. Clin Infect Dis. 2013;57(11):1593-1599. doi:10.1093/cid/cit531.

Palmore TN, Henderson DK. Carbapenem-Resistant *Enterobacteriaceae*: A Call for Cultural Change. Ann Intern Med. 2014;160:567-569. doi:10.7326/M13-1910

Prasad N, Labaze G, Kopacz J, Chwa S, Platis D, Pan CX, Russo D, LaBombardi VJ, Osorio G, Pollack S, Kreiswirth BN, Chen L, Urban C, Segal-Maurer S. Asymptomatic rectal colonization with carbapenem-resistant *Enterobacteriaceae* and *Clostridium difficile* among residents of a long-term care facility in New York City. AJIC. 2016; 44 (5):525-532

<http://dx.doi.org/10.1016/j.ajic.2015.11.021>

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