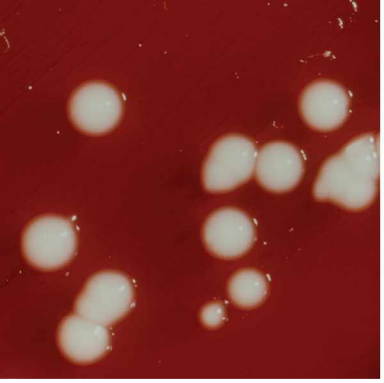
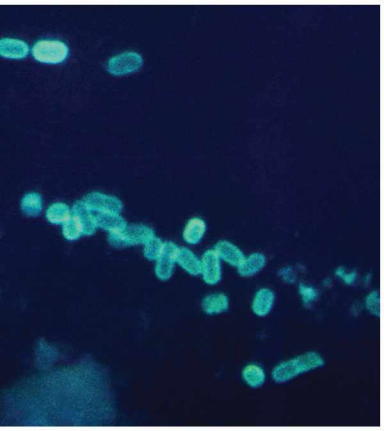
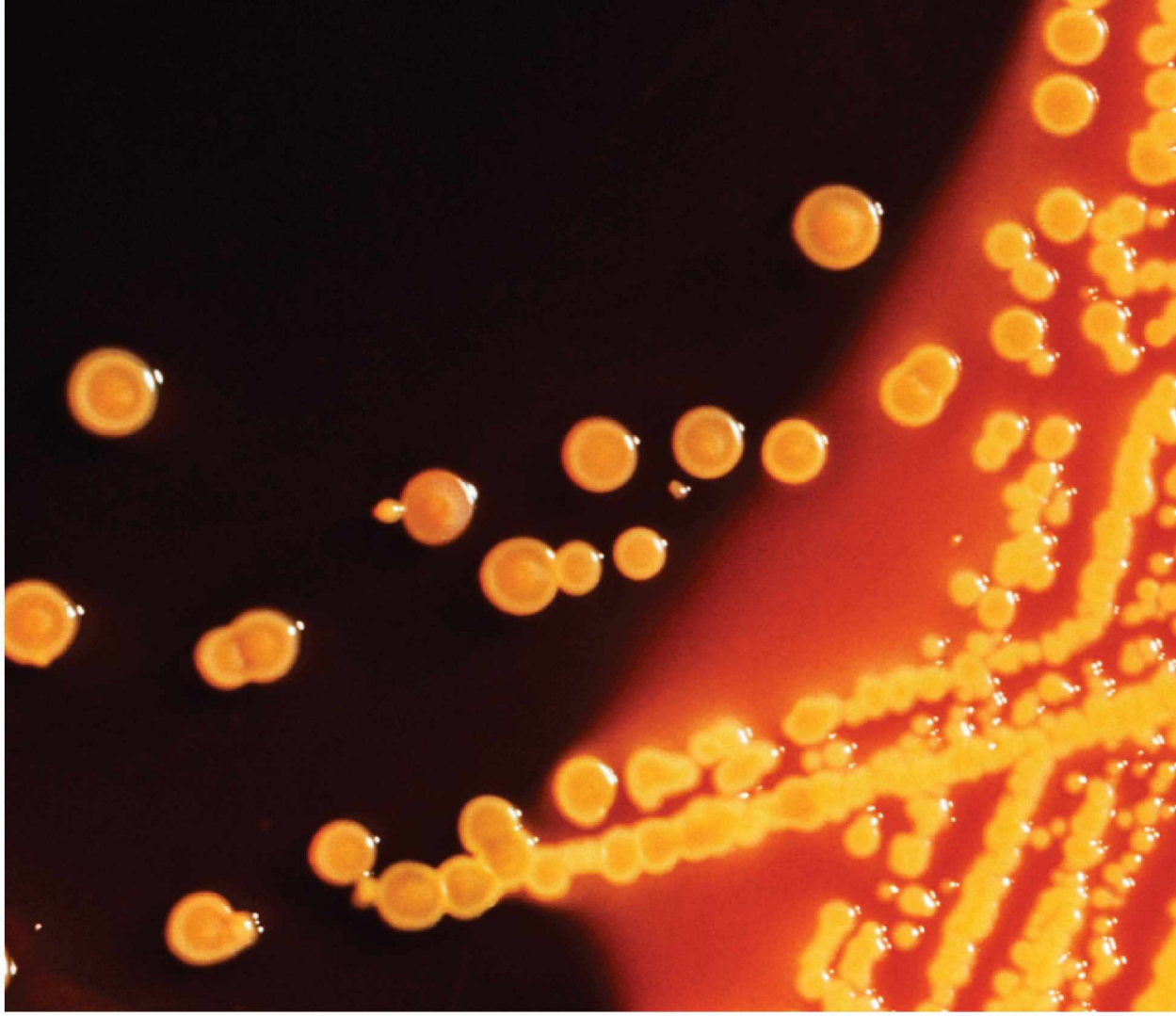






Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE)

2012 CRE Toolkit

National Center for Emerging and Zoonotic Infectious Diseases
Division of Healthcare Quality Promotion

Guidance for Control of Carbapenem-resistant Enterobacteriaceae

This document contains two parts. Part 1 contains recommendations for healthcare facilities and is intended to expand upon the March 2009 "Guidance for Control of Carbapenem-Resistant or Carbapenemase-Producing Enterobacteriaceae in Acute-Care Facilities." Part 2 reviews the role of public health authorities in the control of carbapenem-resistant Enterobacteriaceae.

Unless otherwise specified, healthcare facilities refer to all acute care hospitals and any long-term care facility that cares for patients who remain overnight and regularly require medical or nursing care (e.g., maintenance of indwelling devices, intravenous injections, wound care, etc.). This would include all long-term acute care hospitals and skilled nursing homes (including certain rehabilitation facilities), but would generally exclude assisted living facilities and nursing homes that do not provide more than basic medical care. In addition, this toolkit is not intended for use in ambulatory care facilities.

Background

The emergence and dissemination of carbapenem resistance among Enterobacteriaceae in the United States represent a serious threat to public health. These organisms are associated with high mortality rates and have the potential to spread widely. Decreasing the impact of these organisms will require a coordinated effort involving all stakeholders including healthcare facilities and providers, public health, and industry. This document expands on the 2009 Centers for Disease Control and Prevention (CDC) and Healthcare Infection Control Practices Advisory Committee (HICPAC) recommendations and will continue to evolve as new information becomes available.

The approach to controlling transmission of these organisms in healthcare facilities includes the following:

- Recognizing these organisms as epidemiologically important
- Understanding the prevalence in their region
- Identifying colonized and infected patients when present in the facility
- Implementing regional and facility-based interventions designed to stop the transmission of these organisms

Carbapenem-resistant Enterobacteriaceae (CRE) appear to have been uncommon in the United States before 1992. However, carbapenemase-producing Enterobacteriaceae, most commonly producing *Klebsiella pneumoniae* carbapenemase (KPC), have disseminated widely throughout the United States since being first reported in 2001. Despite the spread of KPC-producing Enterobacteriaceae, the current U.S. distribution of CRE appears to be heterogeneous; these organisms are commonly isolated from patients in some parts of the United States, but they are not regularly found in patients from other regions. Even in areas where CRE are found they may be more common in some healthcare settings, such as long-term acute care, than they are in others.

In addition to KPC-producing Enterobacteriaceae, several different metallo-β-lactamase-producing strains have been identified in the United States since 2009. These include the New Delhi metallo-β-lactamase (NDM), Verona integron-encoded metallo-β-lactamase (VIM), and the imipenemase (IMP) metallo-β-lactamase. These enzymes are more common in other areas of the world and in the United States have generally been found among patients who received medical care in countries where these organisms are known to be present.

CRE are epidemiologically important for several reasons:

- CRE have been associated with high mortality rates (up to 40 to 50% in some studies).
- In addition to β-lactam/carbapenem resistance, CRE often carry genes that confer high levels of resistance to many other antimicrobials, often leaving very limited therapeutic options. "Pan-resistant" KPC-producing strains have been reported.
- CRE have spread throughout many parts of the United States and have the potential to spread more widely.

Definitions

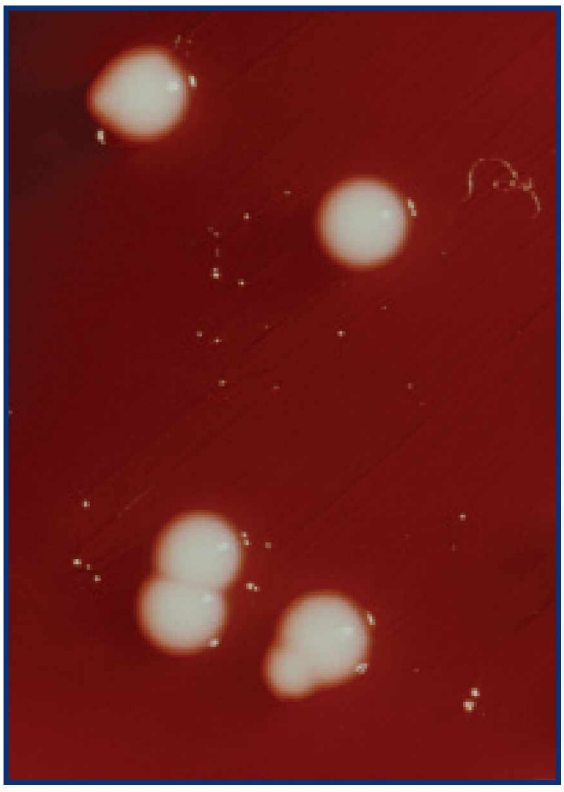
CDC has developed the following interim surveillance definition for CRE. CRE are defined as Enterobacteriaceae that are:

- Nonsusceptible to one of the following carbapenems: doripenem, meropenem, or imipenem AND
- Resistant to all of the following third-generation cephalosporins that were tested: ceftriaxone, cefotaxime, and ceftazidime. (Note: All three of these antimicrobials are recommended as part of the primary or secondary susceptibility panels for Enterobacteriaceae)
- *Klebsiella species* and *Escherichia coli* that meet the CRE definition are a priority for detection and containment in all settings; however, other Enterobacteriaceae (e.g., *Enterobacter* species) might also be important in some regions.
- For bacteria that have intrinsic imipenem nonsusceptibility (i.e., *Morganella morganii, Proteus* spp., *Providencia* spp.), requiring nonsusceptibility to carbapenems other than imipenem as part of the definition might increase specificity.
- This CRE surveillance definition is based upon the current (M100-S22 2012) Clinical and Laboratory Standards Institute (CLSI) interpretative criteria (breakpoints) for carbapenem susceptibility among Enterobacteriaceae (Appendix A); if the older CLSI breakpoints (pre-dating M100-S20 U) are being used to determine carbapenem susceptibility, consideration should be given to including ertapenem in the CRE definition to increase sensitivity.

Definitions for CRE are complicated by a number of factors including the diversity of the genera. Another important challenge to developing a standardized definition of CRE is a recent (mid-2010) change in the Clinical and Laboratory Standards Institute (CLSI) interpretative criteria (breakpoints) for determining susceptibility to carbapenems among Enterobacteriaceae. These new recommendations lowered the breakpoints and removed the requirement for testing for carbapenemase (e.g., modified Hodge Test) to determine susceptibility. These breakpoints were further modified in January 2012 (M100-S22).

Changes in the breakpoints are shown in Appendix A. Although the use of the current CLSI breakpoints offers laboratories a simpler and more straightforward approach to identifying CRE, adoption may be delayed by the fact that the U.S. Food and Drug Administration has not yet approved all of these breakpoints and some automated susceptibility panels currently do not include dilutions low enough to allow for application of the lower breakpoints.

Since most carbapenem resistance mediated by carbapenemases in the United States is found among *Klebsiella* spp. and *E. coli*, individual facilities or public health authorities might choose to apply the CRE surveillance definition only to these specific Enterobacteriaceae.



Klebsiella pneumonia

Part 1: Facility-level CRE Prevention

Surveillance

Inpatient facilities should have an awareness of whether or not CRE (at least *E. coli* and *Klebsiella* spp.) have ever been cultured from patients admitted to their facility and, if so, whether these positive cultures were collected within 48 hours of admission.

If CRE have been present, facilities should also determine:

- If there is evidence of intra-facility transmission
- Which wards/units are most affected

Facilities that do not have this information should consider performing an evaluation to quantify the clinical incidence of these organisms, such as a review of archived lab results to determine the number and/or proportion of Enterobacteriaceae that meet the CRE definition over a pre-specified time period (e.g., 6 to 12 months). In addition, facilities should consider collecting information on the basic epidemiology of patients colonized or infected with these organisms in order to understand common characteristics of these individuals. This might include patient demographics, dates of admission, outcomes, medications, and common exposures (e.g., wards, surgery, procedures, etc).

Facility-level Prevention Strategies

The following briefly summarizes an approach to preventing CRE transmission in healthcare settings. For a more in-depth review, please refer to the CDC HICPAC guidelines "Management of Multidrug-Resistant Organisms in Healthcare Settings, 2006" (http://www.cdc.gov/hicpac/mdro/mdro_toc.html).

Core Measures for All Acute and Long-term Care Facilities

There are 8 core measures facilities should follow.

1. Hand Hygiene

Hand hygiene is a primary part of preventing multidrug-resistant organism (MDRO) transmission. Facilities should ensure that healthcare personnel are familiar with proper hand hygiene technique as well as its rationale. Efforts should be made to promote staff ownership of hand hygiene using techniques like developing local (e.g., unit) hand hygiene champions. It is not enough to have policies that require hand hygiene; hand hygiene adherence should be monitored and adherence rates should be fed directly back to front line staff. Immediate feedback should be provided to staff who miss opportunities for hand hygiene. In addition, facilities should ensure access to adequate hand hygiene stations (i.e., clean sinks and/or alcohol-

based hand rubs) and ensure they are well stocked with supplies (e.g. towels, soap, etc.) and clear of clutter. Further information on hand hygiene is available at www.cdc.gov/handhygiene/. This intervention is applicable to both acute and long-term care settings.

2. Contact Precautions

Patients in acute care settings who are colonized or infected with CRE should be placed on Contact Precautions. Systems should be in place to identify patients with a history of CRE colonization or infection at admission so that they can be placed on Contact Precautions if not known to be free of colonization. In addition, clinical laboratories should have an established protocol for notifying clinical and/or infection prevention personnel when CRE are identified from clinical or surveillance cultures.

There is not enough information for a firm recommendation about when to discontinue Contact Precautions among infected patients; however, CRE colonization in some patients identified during CDC investigations has been prolonged (> 6 months). If surveillance cultures are used to decide if a patient remains colonized, more than one culture should be collected in an attempt to improve sensitivity. One recent study found that among rectal CRE carriers, predictors of rectal CRE carriage at a future healthcare encounter included exposure to antimicrobials (especially fluoroquinolones), admission from another healthcare facility, and less than 3 months' elapsed time since their first positive CRE test.

The probability of being CRE positive at the next encounter increased to 50% if one predictor was present. Presence of ongoing risk factors for carriage such as these should be considered before discontinuing use of Contact Precautions in these patients. The presence of CRE infection or colonization alone should not preclude transfer of a patient from one facility to another (e.g., acute care to long-term care). Facilities should ensure that Contact Precautions are used correctly by staff caring for all patients with epidemiologically important MDROs including CRE.

Proper use of Contact Precautions includes:

- Performing hand hygiene before donning a gown and gloves
- Donning gown and gloves before entering the affected patient's room
- Removing the gown and gloves and performing hand hygiene prior to exiting the affected patient's room

Ensuring healthcare personnel (HCP) are educated about the proper use and rationale for Contact Precautions is an important part of this process. In addition, facilities should ensure that there is a process to monitor and improve HCP adherence to Contact Precautions. This might include conducting periodic surveillance on the use of Contact Precautions and providing feedback to frontline staff about these results.

Preemptive Contact Precautions, often in conjunction with surveillance cultures, might be used on patients transferred from high-risk settings (see supplemental interventions) pending results of screening cultures. Examples include transferred patients from hospitals in countries or areas in the United States where CRE are common or patients transferred from facilities known to have outbreaks or clusters of CRE colonized or infected patients.

In long-term care settings, Contact Precautions are still indicated for residents infected or colonized with CRE; however, these might be modified to fit the inherent differences between acute and long-term care facilities. Contact Precautions should be used for residents with CRE who are at higher risk for transmission, including patients who are totally dependent upon HCP for their activities of daily living, are ventilator-dependent, are incontinent of stool, or have wounds with drainage that is difficult to control. For other residents who are able to perform hand hygiene, are continent of stool, are less dependent on staff for their activities of daily living, and are without draining wounds, the requirement for Contact Precautions might be relaxed. However, in these situations Standard Precautions should still be observed, including the use of gloves and/or gowns when contact with colonized/infected sites or body fluids is possible.

3. Healthcare Personnel Education

HCP in all settings who care for patients with MDROs, including CRE, should be educated about preventing transmission of these organisms. At a minimum this should include information on the proper use of Contact Precautions and hand hygiene. This intervention is applicable to both acute and long-term care settings.

4. Use of Devices

Use of devices (e.g., central venous catheters, endotracheal tubes, urinary catheters) puts patients at risk for device-associated infections and minimizing device use is an important part of the effort to decrease the incidence of these infections. Additionally, device use has been associated with carbapenem resistance among Enterobacteriaceae. Therefore, minimizing device use in all healthcare settings should be part of the effort to decrease the prevalence of all MDROs including CRE. In acute and long-term care settings, device use should be reviewed regularly to ensure they are still required and devices should be discontinued promptly when no longer needed. For more information on preventing device-associated infection including appropriate use of devices please see www.cdc.gov/hicpac/BSI/BSI-guidelines-2011.html and www.cdc.gov/hicpac/cauti/002_cauti_toc.html.

5. Patient and Staff Cohorting

When available, patients colonized or infected with CRE should be housed in single patient rooms and if not available these patients should be cohorted together. In addition, consideration should be given to cohorting patients with CRE in specific areas (e.g., units or wards), even if in single patient rooms, and to using dedicated staff to care for them. This recommendation applies to both acute and long-term care settings. Preference for single rooms should be given to patients at highest risk for transmission such as patients with incontinence, medical devices, or wounds with uncontrolled drainage.

6. Laboratory Notification

Laboratories should have protocols in place that facilitate the rapid notification of appropriate clinical and infection prevention staff whenever CRE are identified from clinical specimens to ensure timely implementation of control measures. This is true for both facilities with on-site laboratories and those sending cultures off-site and is applicable to acute and long-term care settings.

7. Antimicrobial Stewardship

Antimicrobial stewardship is another primary part of MDRO control. Although the role of this activity specifically for CRE has not been well studied, multiple antimicrobial classes have been shown to be a risk for CRE colonization and/or infection. Further, restricting use of carbapenems has been associated with a lower incidence of carbapenem-resistant *Pseudomonas aeruginosa* in one ecological analysis. As part of an antimicrobial stewardship program designed to minimize transmission of MDROs, facilities should work to ensure that 1) antimicrobials are used for appropriate indications and duration and 2) that the narrowest spectrum antimicrobial that is appropriate for the specific clinical scenario is used. For more information on antimicrobial stewardship in healthcare settings please see http://www.cdc.gov/getsmart/healthcare. This intervention is applicable to both acute and long-term care settings.

8. CRE Screening

Screening is used to identify unrecognized CRE colonization among epidemiologically-linked contacts of known CRE colonized or infected patients as clinical cultures will usually identify only a fraction of all patients with CRE. Generally, this screening has involved stool, rectal, or peri-rectal cultures and sometimes cultures of wounds or urine (if a urinary catheter is present). A laboratory protocol for evaluating rectal or peri-rectal swabs for CRE is available at http://www.cdc.gov/hai/pdfs/labsettings/Klebsiella_or_E_coli.pdf; however, it is important to note that this procedure has only been validated for *E. coli* and *Klebsiella* spp. CRE screening of epidemiologically linked patients is a primary prevention strategy for all healthcare facilities; however, it is particularly important for healthcare facilities with CRE outbreaks or facilities that do not or only rarely admit patients with CRE infection or colonization. This intervention is applicable to both acute and long-term care settings.

CRE screening might include:

- Point prevalence surveys:
  Point prevalence surveys might be an effective way for facilities to rapidly evaluate the prevalence of CRE in particular wards/units. This could be useful in a situation where a review of clinical cultures using laboratory records identifies unreported CRE patients in certain wards/units. A point prevalence survey is generally conducted by screening all patients in that ward/unit. Point prevalence surveys might be done only once if few or no additional CRE colonized patients are identified or might be done serially if colonization is more widespread or to follow the effect of an intervention.

- Screening of epidemiologically linked patients:
  If previously unrecognized CRE carriers are identified, screening of patient contacts could be conducted to identify transmission instead of a wider point prevalence survey. Those patients considered contacts may vary from setting to setting; however, they usually include roommates of the unrecognized CRE patients as well as patients who might have shared HCP.

Supplemental Measures for Healthcare Facilities with CRE Transmission

These additional measures should be considered when baseline core prevention practices are not effective in reducing CRE incidence.

Active Surveillance Testing

This process involves culturing patients who might not be epidemiologically linked to known CRE patients but who meet certain pre-specified criteria. This could include everyone admitted to the facility, pre-specified high-risk patients (e.g., those admitted from long-term care facilities), and/or patients admitted to high-risk settings (e.g., intensive care units [ICUs]). Active surveillance testing has been used in control efforts for several MDROs including CRE; however, the exact contribution of this practice to decreases in CRE is not known.

As described above, active surveillance testing is based on the finding that clinical cultures will identify only a minority of those patients colonized with CRE; unrecognized colonized patients might not be on Contact Precautions and are a potential source for CRE transmission. If done, surveillance testing could be focused on patients admitted to certain high-risk settings (e.g., ICUs, long-term acute care) or could target specific patients (i.e., patients with risk factors, patients admitted from high-risk settings like long-term acute care or transferred from areas with high CRE

prevalence). This testing is generally done at admission but can also be done periodically during admission (e.g., weekly). Patients identified as positive by this surveillance testing should be treated as colonized (i.e., placed on Contact Precautions, etc.). In some situations (e.g., patients admitted from high-risk settings) patients might be placed in preemptive Contact Precautions until surveillance testing is found to be negative.

As with screening of epidemiologically linked CRE contacts, the use of active surveillance testing to control CRE is applicable to both acute and long-term care settings.

Chlorhexidine Bathing

Chlorhexidine bathing has been used successfully to prevent certain types of healthcare-associated infections (e.g., bloodstream infections) and to decrease colonization with specific MDROs, primarily in ICUs. For CRE, it has been used as part of a multifaceted intervention to reduce the prevalence of CRE during an outbreak in a long-term acute care facility. During chlorhexidine bathing, diluted liquid chlorhexidine (2%) or 2% chlorhexidine-impregnated wipes are used to bathe patients (usually daily) while in high-risk settings (e.g., ICUs). The chlorhexidine is usually not used above the jaw line or on open wounds. When chlorhexidine bathing is used for a particular patient population or in a particular setting, it is usually applied to all patients regardless of CRE colonization status.

In long-term care settings this type of an intervention might be used on targeted high-risk residents (e.g., residents that are totally dependent upon healthcare personnel for activities of daily living, are ventilator-dependent, are incontinent of stool, or have wounds whose drainage is difficult to control) or high-risk settings (e.g., ventilator unit). In addition, chlorhexidine bathing might be less frequent in long-term care depending on the facility's usual bathing protocol.

Recommendations for Facilities with No or Rare CRE

Experience with other MDROs suggests that it might be most effective to intervene on emerging MDROs when they first are recognized in a facility before they become common. For this reason facilities that rarely (e.g., < 1 per month) or never have patients admitted who are colonized or infected with CRE should be aggressive about controlling these organisms when they are identified. An example of one approach to CRE control in these settings is shown in Appendix B.

In addition, if a facility without previous CRE performs a review of archived clinical laboratory results for CRE and identifies previously unrecognized CRE-colonized or -infected patients, the facility should consider point prevalence surveys of high-risk units to further clarify the CRE prevalence. If additional CRE colonized patients are identified, facilities should also follow the approach in Appendix B. Facilities without CRE that receive patients that are transferred from facilities known to have CRE colonized or infected patients could also consider screening those patients for CRE at admission and placing them in preemptive Contact Precautions pending the result of surveillance cultures.

Summary Of Prevention Strategies For Acute And Long-Term Care Facilities

Core Measures for All Acute and Long-term Care Facilities

1. Hand hygiene

- Promote hand hygiene
- Monitor hand hygiene adherence and provide feedback
- Ensure access to hand hygiene stations

2. Contact Precautions

Acute care

- Place CRE colonized or infected patients on Contact Precautions (CP)
    - Preemptive CP might be used for patients transferred from high-risk settings
- Educate healthcare personnel about CP
- Monitor CP adherence and provide feedback
- No recommendation can be made for discontinuation of CP
- Develop lab protocols for notifying clinicians and IP about potential CRE

Long-term care

- Place CRE colonized or infected residents that are high-risk for transmission on CP (as described in text); for patients at lower risk for transmission use Standard Precautions for most situations

3. Patient and staff cohorting

- When available cohort CRE colonized or infected patients and the staff that care for them even if patients are housed in single rooms
- If the number of single patient rooms is limited, reserve these rooms for patients with highest risk for transmission (e.g., incontinence)

4. Minimize use of invasive devices

5. Promote antimicrobial stewardship

6. Screening

- Screen patient with epidemiologic links to unrecognized CRE colonized or infected patients and/or conduct point prevalence surveys of units containing unrecognized CRE patients

Supplemental Measures for Healthcare Facilities with CRE Transmission

1. Conduct active surveillance testing

- Screen high-risk patients at admission or at admission and periodically during their facility stay for CRE. Preemptive CP can be used while results of admission surveillance testing are pending
- Consider screening patients transferred from facilities known to have CRE at admission

2. Chlorhexidine bathing

- Bathe patients with 2% chlorhexidine

Public Health Engagement

Inter-facility Transmission of CRE

Patients colonized or infected with CRE may seek medical care in more than one hospital and serve as a reservoir that can facilitate the spread of CRE from one facility to another. With the pressure to reduce length of stay in acute care hospitals, patients who require complex medical treatment are often transferred to long-term care facilities (e.g., long-term acute care hospitals and skilled nursing homes) to complete their treatment. These patients frequently require readmission either to the same or different hospitals. This extensive inter-facility sharing of patients across the continuum of care has the potential to facilitate widespread regional transmission of CRE.

Regional Approach to CRE Control

To prevent the emergence and further spread of CRE, a coordinated regional control effort among healthcare facilities is recommended. The implementation of such an approach was successful in controlling vancomycin-resistant enterococci in the Siouxland region of the United States and for reducing CRE incidence at the national level in Israel. Given the ability of state and local health departments to interface with different types of facilities, public health is in a unique position to coordinate the local and regional response to MDROs, like CRE, by providing situational awareness within their jurisdiction and facilitating the implementation of appropriate control measures.

The optimal public health response will vary depending on the prevalence of CRE within a given jurisdiction. Based on an initial evaluation of the prevalence or incidence of CRE, prevention strategies can be tailored for geographical regions according to the following classifications: regions without CRE, regions with few CRE colonized- or infected-patients, and regions where CRE are common. (Although there is no standard definition for the latter two categories, some criteria that can be considered to determine a region's classification are provided below.) In regions where there are no or few CRE colonized- or infected-patients, there may be a critical opportunity to prevent further emergence of CRE by taking an aggressive approach early in the process. For regions where CRE have already become common, certain general prevention measures may need to be applied more broadly as outlined in the respective section. However, because of the challenges associated with high CRE prevalence, it is recommended that further tailoring of supplemental measures be determined in consultation with CDC and in accordance with the 2006 CDC HICPAC "Guidelines for Management of Multidrug-Resistant Organisms in Healthcare Settings" (http://www.cdc.gov/hicpac/pdf/guidelines/MDROGuideline2006.pdf).

For this document, a region could represent part of a state, a whole state, or even multiple states. In some regions, patients may be shared between facilities located in different jurisdictions and/or states. Ideally for MDRO control, state health departments would take the lead and coordinate with local health departments. However, depending on the region targeted, prevention strategies may also require coordination between states.

Regional Surveillance for CRE

Health departments should understand the prevalence or incidence of CRE in their jurisdiction by performing some form of regional surveillance for these organisms. As described above, the interim CDC surveillance definition for CRE is Enterobacteriaceae that are nonsusceptible to one of the carbapenems and resistant to all of the third-generation cephalosporins that were tested. At a minimum, initial surveillance efforts should focus on key organisms (i.e., *K. pneumoniae, E. coli*, and *Enterobacter* spp. that meet the CRE definition).

Options for performing surveillance include making CRE a laboratory-reportable event or surveying Infection Preventionists and/or laboratory directors of healthcare facilities by telephone or email (e.g., using online survey). An example of a survey for Infection Preventionists in acute care and long-term acute care hospitals can be found in Appendix C; this survey could also be modified for use in other long-term care facilities.

It is recommended that CRE surveys conducted by health departments collect, at a minimum, the following facility-level data:

- Facility demographics including location and facility name if possible
- Overall frequency of CRE detection (e.g., daily, weekly, monthly, etc.)
- Frequency of CRE cases by timing of detection (e.g., within 48 hours or greater than 48 hours of admission)
- If surveying Infection Preventionists, determine whether recommended surveillance and infection prevention measures are being implemented, as outlined in Part 1

Email reminders or phone calls to non-responders are encouraged to facilitate survey completion in a timely fashion (e.g., 1-2 weeks) and increase response rates. Based on survey/surveillance results, prevention strategies can be tailored accordingly as outlined below and in the algorithms provided in appendix D.

Regional Prevention Strategies

Regions with No CRE Identified

Regional Surveillance and Feedback of Results

In regions that have no identified CRE colonized- or infected-patients, it is recommended that health departments take an aggressive approach to future CRE detection, such as making CRE a reportable event (e.g., laboratory reportable) to ensure that CRE are recognized when they occur. If CRE reporting is not feasible, health departments should periodically survey healthcare facilities for the presence of CRE and provide feedback to increase awareness. The frequency of surveillance may depend on the prevalence of CRE in neighboring areas or jurisdictions. For example, in an area where nearby locations have known CRE colonized- or infected-patients, quarterly or even monthly surveillance may be reasonable. To maintain an understanding of CRE prevalence in surrounding regions, neighboring health departments should consider establishing a mechanism for communicating updates with one another about the level of CRE activity within their respective jurisdictions.

Education of Healthcare Facilities

Health departments should also increase awareness among healthcare facilities about the public health importance of CRE, recommended prevention measures, and the importance of timely recognition of any CRE colonized- or infected-patients. This could include targeted education of Infection Preventionists and other healthcare personnel and could take place at conferences, training sessions, or through webinars or newsletters.

Regions with Few CRE Identified

The prevention strategies described in this section apply to regions where the majority of healthcare facilities do not regularly have patients with CRE admitted. This would include regions where several facilities may have identified CRE colonized- or infected-patients on an infrequent basis (e.g., monthly basis or greater), as well as regions where some facilities may have several CRE colonized- or infected-patients but are surrounded by facilities with only a few or none. In these situations, health departments should still take an aggressive approach to contain CRE. This may require working more closely with specific healthcare facilities and targeting prevention efforts to certain parts of the region. Regions with few CRE are also most in need of increased situational awareness across all facilities regarding which facilities are being most impacted by CRE.

Regional Surveillance and Feedback of Results: Targeted Prevention

Health departments should consider making CRE a reportable event (e.g., laboratory reportable) to track CRE rates within their jurisdiction for the purposes of identifying new cases and assessing the efficacy of infection prevention measures. If this is not feasible, health departments should still continue to periodically survey acute and long-term care facilities for the presence of CRE.

CRE surveillance results should be shared with facilities (e.g., via newsletters, emails, or presentations at regional conferences), including facility administrators, in order to provide awareness of the current regional situation with respect to CRE; knowing which facilities have CRE colonized- or infected-patients may be one of the most important benefits of a coordinated regional approach to CRE control, allowing nearby facilities to take appropriate action. For example, patients admitted from facilities that have CRE could be placed preemptively on Contact Precautions pending surveillance culture results. Even if facility identifiers cannot be revealed, health departments can provide feedback of results stratified by facility type or by geographical distribution. Knowing which parts of the region have CRE can allow nearby facilities to intensify CRE prevention efforts (e.g., using supplemental measures) in consultation with the health department.

Implementation of Prevention Measures

In all facilities, health departments should ensure that core prevention measures (e.g., hand hygiene, Contact Precautions, patient and staff cohorting) are being implemented accordingly. Particularly in facilities that have CRE, it is recommended that health departments work closely with the infection prevention personnel to review and improve facility adherence to recommended practices. This may involve ongoing communication with infection prevention personnel, conducting site visits where feasible, providing in-service training, and engaging the facility directors and/or administrators in discussions about the importance of CRE prevention.

In facilities without CRE, health departments should take steps to ensure that a plan is in place in the event that a CRE colonized- or infected-patient is identified. Additionally, health departments should work closely with individual facilities that have not identified CRE to determine appropriate supplemental interventions. These measures may include targeting active surveillance testing and preemptive Contact Precautions to patients admitted from facilities with ongoing transmission of CRE (e.g., CRE detection on at least a weekly basis or in a CRE outbreak situation). If facility identifiers cannot be disclosed, targeted use of active surveillance testing and preemptive Contact Precautions can be guided by the local epidemiology of CRE. Specifically, in facilities without CRE but located in areas where CRE are present, active surveillance testing and preemptive Contact Precautions could be applied to the following patients: (a) those admitted from long-term care facilities (e.g., long-term acute care hospitals), where there may be a large reservoir of CRE colonized- or infected-patients as a result of inter-facility patient sharing and longer length of stay and/or (b) those with potential risk factors for CRE (e.g., patients with open wounds, presence of indwelling devices, and/or high antimicrobial usage).

In facilities with known CRE, health departments should promote implementation of surveillance measures to identify additional cases in order to prevent further intra-facility CRE transmission. These interventions may include screening patients with epidemiologic links to previously unrecognized cases and conducting periodic point prevalence surveys in high-risk settings (e.g., ICUs). Health departments should also promote inter-facility communication as described in the following section. As needed, health departments should consult with CDC and/or regional experts for additional guidance.

Inter-facility Communication

To reduce inter-facility transmission of all MDROs, all facilities should be encouraged to routinely complete inter-facility transfer forms whenever a patient is transferred to another facility; this becomes especially important when a patient with known CRE colonization or infection is to be transferred to another facility. The form should indicate whether the patient has ever been colonized and/or infected with CRE and other MDROs (if available, the dates and results of any relevant clinical and/or surveillance cultures should be provided) and whether the patient has any open wounds and/or indwelling devices. In addition, if the patient is currently being given antimicrobials, information should be included describing why the patient is receiving them and how much longer treatment is required. An example of an inter-facility transfer form developed by CDC is available for facilities to use (http://www.cdc.gov/HAI/toolkits/InterfacilityTransferCommunicationForm11-2010.pdf)

Education of Healthcare Facilities

Education for healthcare facility staff about CRE and recommended surveillance and prevention measures should continue to be provided as described above. This might be especially important for facilities that have not detected CRE in order to increase their vigilance.

Regions Where CRE are Common

In general, CRE are considered common in regions where the majority of healthcare facilities have identified cases, and these facilities regularly have CRE colonized- or infected-patients admitted (e.g., CRE detected at least weekly).

Whereas a targeted approach to prevention may be successful in regions with few CRE cases, limited experiences indicate that a broad, public health approach is required when CRE are common. The national implementation of a centrally-coordinated intervention in Israel succeeded in containing CRE. Their success was attributed in part to the creation of a task force dedicated to ensuring that all hospitals complied with national CRE guidelines. Based on Israel's experience and the 2006 CDC HICPAC "Guidelines for Management of Multidrug-Resistant Organisms in Healthcare Settings" (http://www.cdc.gov/hicpac/pdf/guidelines/MDROGuideline2006.pdf), the following prevention measures are recommended for regions where CRE are common:

Dedicated Personnel

To effectively coordinate infection prevention across the region, health departments should have dedicated personnel assigned to this task. Ideally, these personnel should have an adequate understanding of CRE/MDRO prevention practices. As needed, a health department-led advisory panel consisting of experienced professionals in infection prevention and clinical microbiology can be established to provide additional technical support to facilities.

Engagement of Healthcare Facilities

As an initial step to engaging all facilities in the region, health departments should first communicate to appropriate personnel the CRE prevalence within the region and the importance of a regional approach to prevention. This may involve discussions with the facility directors and/or administrators in addition to the infection prevention personnel. The purpose of these discussions is to convey the urgency of the situation and to obtain facility leadership support to prioritize CRE prevention.

Reinforcement of Core Prevention Measures

Health departments should review current infection control policies and practices related to CRE at all acute and long-term care facilities within the region. At a minimum, all facilities should be implementing the core measures for CRE prevention (e.g., hand hygiene, Contact Precautions, patient and staff cohorting). To reinforce best practices, targeted education and in-service training may need to be provided to individual facilities.

Implementation of Supplemental Measures

Additional measures to be implemented by facilities should be determined in close consultation with the health department and in accordance with the interventions summarized in Part 1 of this document and the Tier 2 recommendations of the 2006 CDC HICPAC Guidelines for Management of Multidrug-resistant Organisms in Healthcare Settings (http://www.cdc.gov/hicpac/pdf/guidelines/MDROGuideline2006.pdf). These interventions may include performing active surveillance testing and/or chlorhexidine bathing.

Assessing Facility Compliance to Prevention Measures

Health departments should periodically assess for facility compliance to recommended practices (e.g., on a monthly basis). This may be based on reporting by facility Infection Preventionists or assessed through site visits to individual facilities if feasible. Depending on compliance rates, additional educational outreach, such as in-service trainings and webinars, may need to be provided to individual facilities. To increase staff adherence, performance feedback should be shared with facility directors and/or administrators. Health departments can also consider providing feedback of aggregate compliance data stratified by facility type and/or by geographical distribution, so that individual facilities can compare their performance with others.

Inter-facility Communication

As described previously, an inter-facility transfer form should be completed whenever a patient is being transferred to another facility. This should indicate the CRE status of the patient and the presence of open wounds and indwelling devices and antimicrobial usage.

Regional Surveillance and Feedback of Results

Health departments should continue to perform periodic regional surveillance to assess efficacy of infection prevention measures and to feedback results to facilities. Although it may not be practical to make every CRE case reportable in a region where CRE are common, certain events to consider making reportable could be an increase in CRE rate above baseline or CRE cases with unique features (e.g., all fatalities or healthy patients with fatal outcome).

Appendix A: Previous and Current Clinical and Laboratory Standards Institute Interpretive Criteria for Carbapenems and Enterobacteriaceae

Agent	Previous Breakpoints (M100-S19) MIC (µg/mL)			Current Breakpoints (M100-S22) MIC (µg/mL)		
	Susceptible	Intermediate	Resistant	Susceptible	Intermediate	Resistant
Doripenem	-	-	-	≤1	2	≤4
Ertapenem	≤2	4	≥8	≤0.5	1	≥2
Imipenem	≤4	8	≥16	≤1	2	≥4
Meropenem	≤4	8	≥16	≤1	2	≥4

Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing; Twenty Second Informational Supplement (January 2012). CLSI document M100-S22. Wayne, Pennsylvania, 2012.

Appendix B: General Approach to Carbapenem-resistant Enterobacteriaceae (CRE) Control in Facilities that Rarely or Have Not Identified CRE

New CRE-colonized or CRE-infected patient identified

↓

- Notify appropriate personnel (i.e., clinical staff, infection prevention staff)
- Notify public health if indicated

↓

- Place patient on Contact Precautions in single room (if available)
- Reinforce hand hygiene and use of Contact Precautions on affected ward/unit
- Educate healthcare personnel about preventing CRE transmission

↓

- Screen epidemiologically-linked patient contacts (e.g., roommates) for CRE with at least stool, rectal, or peri-rectal cultures and/or consider point prevalence survey of affected unit
- Consider preemptive Contact Precautions of these patients pending results of screening cultures

↓

- If screening cultures or further clinical cultures identify additional CRE-colonized or -infected patients, consider additional surveillance cultures of contacts or point prevalence surveys of affected units (if not already done)
- Consider cohorting patients and staff

↓

- Ensure if patient transferred within the facility that precautions are continued
- Ensure if patient transferred to another facility CRE information is shared with accepting facility

Appendix C: Example of a Survey for Infection Preventionists

Instructions for Administering Survey for Carbapenem-resistant Enterobacteriaceae (CRE)

Given the increasing incidence of CRE in parts of the United States and the potential for widespread dissemination, health departments are encouraged to assess the incidence of CRE within their jurisdictions to guide response efforts. To facilitate this activity, the attached survey has been designed to be used by health departments to determine: 1) the frequency of CRE colonized- or infected patients identified, 2) the type of surveillance conducted, and 3) the infection control measures implemented to prevent transmission.

It is recommended that health departments administer this survey by telephone to infection prevention personnel of all acute care hospitals and long-term acute care hospitals within their jurisdictions; this survey could also be modified for use in other long-term care facilities. The survey consists of 7 questions and will take approximately 5 minutes to complete.

Survey of Healthcare Facilities for Carbapenem-resistant Enterobacteriaceae (CRE)

1. Does the microbiology laboratory that performs cultures for your facility have an established system for alerting infection prevention staff in a timely manner (i.e., within 24 hrs) whenever a carbapenem-resistant Enterobacteriaceae isolate is identified?

☐ Yes ☐ No

2. In the past 12 months, have any CRE infected- or colonized-patients been present in your facility?

☐ Yes ☐ No

If YES,

a. In general, how often do you identify CRE infected- or colonized-patients from clinical cultures?

☐ Daily ☐ Weekly ☐ Monthly ☐ Biannually ☐ Yearly

b. Specifically, how often are CRE infected- or -colonized patients identified from clinical cultures collected in the following categories:

i. From cultures collected before or within 48 hours of admission (i.e., transfers or community-onset)?

☐ Daily ☐ Weekly ☐ Monthly ☐ Biannually ☐ Yearly ☐ Not Identified

ii. From cultures collected after 48 hours of admission (i.e., hospital-onset)?

☐ Daily ☐ Weekly ☐ Monthly ☐ Biannually ☐ Yearly ☐ Not Identified

3. If CRE cases have not been identified or have only rarely been identified (i.e., 0-3 cases per quarter), has your facility ever reviewed 6 to 12 months of microbiology records to detect any previously unrecognized CRE cases?

☐ Yes ☐ No

If YES, did your review identify any previously unrecognized CRE cases?

☐ Yes ☐ No

4. Has your facility ever conducted a point prevalence survey (single round of active surveillance cultures) for CRE in high-risk units (e.g., units where previously unrecognized cases were identified, ICU, and units with high antimicrobial utility)?

☐ Yes ☐ No

If YES, did your facility identify any unrecognized CRE?

☐ Yes ☐ No

5. If a CRE case is identified, does your facility conduct active surveillance testing of patients with epidemiologic links to the CRE case (e.g., patients in same unit or who were provided care by same healthcare personnel)?

☐ Yes ☐ No

6. If a patient infected or colonized with CRE is identified, which of the following measures are implemented (check all that apply):

a. Place on Contact Pecautions ☐ Yes ☐ No

b. Place in single-patient rooms when possible ☐ Yes ☐ No

c. Other:_____

_____

7. In your opinion, does your facility consider CRE to be an epidemiologically important multidrug-resistant organism for which specific infection control practices are indicated to eliminate transmission?

☐ Strongly Agree ☐ Agree ☐ Neither ☐ Disagree ☐ Strongly Disagree

Regions With No CRE Identified

In regions without known CRE, the emphasis should be on regional surveillance for CRE and education of healthcare personnel (e.g., infection prevention staff) to increase awareness.

Recommended Health Department Action

I. Regional Surveillance and Feedback

A.

Make CRE laboratory-reportable

OR

Survey all IPs or lab directors by phone or email (refer to Appendix C for an example of an IP survey)

B.

- If no CRE cases are identified:
  - Feedback results to IPs and/or lab directors
  - Promote facility-level CRE guidance[1]
- If CRE cases are identified:
  - For regions with few CRE identified, refer to appropriate algorithm
  - For regions where CRE are common, refer to the appropriate algorithm

C.

Repeat survey/surveillance at least quarterly if CRE are present in neighboring jurisdictions; otherwise, repeat at least every 6 months

II. Education of All Healthcare Facilities[2]

- Explain importance of CRE and provide updates on national and/or neighboring regional prevalence and epidemiology
- Review recommended surveillance and prevention measures[1]
- Increase vigilance for CRE detection

1. Refer to Part 1: Facility-Level Recommendations
2. Refers to all acute care hospitals and long-term care facilities that provide medical or nursing care (e.g., long-term acute care hospitals and skilled nursing facilities). Refer to the text for more details.

Regions with Few CRE Identified

In regions where CRE have been identified but cases remain uncommon, an aggressive approach to prevention is needed to prevent further transmission and widespread emergence of CRE. This will require increased prevention efforts targeting select facilities in the region where CRE are found.

Recommended Health Department Action

I. Regional Surveillance and Feedback

A.

Make CRE laboratory-reportable

OR

Survey all IPs or lab directors by phone or email (refer to Appendix C for an example of an IP survey)

B.

Feedback results to IPs and/or lab directors and to facility administrators (e.g., director) by email or letter

- Strongly consider providing facility identifiers; if not feasible, stratify results by geographic area and/or by facility type (acute vs. long-term care)
- Engage Hospital Association, Quality Improvement Organizations, and other relevant partners as needed to facilitate communication with facility leadership
- Provide facility-level CRE guidance[1]

C.

Repeat CRE surveillance and feedback at least quarterly

II. Infection Prevention

For facilities without CRE but located in areas of the region where CRE are present:

- Engage facility administrators to prioritize CRE prevention
- Ensure a CRE control plan is in place
- Reinforce core prevention measures
- Guide implementation of active surveillance testing and preemptive Contact Precautions for
    - Patients admitted from facilities with ongoing CRE transmission
    - Patients admitted from long-term care facilities (e.g., long-term acute care hospitals) or with CRE risk factors (e.g., open wounds, indwelling devices, high antimicrobial use)

Algorithm Continued for Regions with Few CRE Identified:

For facilities with CRE:

- Engage facility administrators to prioritize CRE prevention
- Review infection prevention practices to ensure core prevention measures are in place
- Provide in-service training (as needed)
- Ensure CRE screening is in place and guide implementation of supplemental measures[1]
- If CRE rates do not decrease, consult CDC and/or regional experts for additional guidance

III. Inter-facility Communication

Ensure facilities with known CRE complete an inter-facility transfer form when transferring patients (indicate CRE status of patient, presence of open wounds/devices, antimicrobial use and ength of therapy)[2]

IV. Education of All Healthcare Facilities[3]

- Explain importance of CRE and provide updates on regional prevalence and epidemiology
- Review recommended surveillance and prevention measures[1]
- Increase vigilance for CRE detection

1. Refer to Part 1: Facility-Level Recommendations
2. http://www.cdc.gov/HAI/toolkits/InterfacilityTransferCommunicationForm11-2010.pdf
3. Includes all acute care facilities and long-term care facilities that provide medical or nursing care (e.g, long-term acute care hospitals and skilled nursing facilities). Refer to the text for more details.

CRE containment in high-prevalent regions will require the implementation of core and supplemental prevention measures across all acute care and long-term care facilities that provide medical or nursing care (e.g., long-term acute care hospitals and skilled nursing facilities).

Recommended Health Department Action

I. Dedicated Personnel to Engage Healthcare Facilities

- Assign specific personnel to this task
- Form advisory panel if additional technical support is needed
- Engage all facility administrators (e.g., director) and IP personnel early in process
  - Engage Hospital Association, QIOs, and other relevant partners as needed to facilitate communication with facility leadership

II. Regional Surveillance and Feedback

A.

Perform steps for CRE surveillance and feedback of results to IPs and/or lab directors and facility administrators as outlined for regions with few CRE identified

- Ensure that urgency of situation is appropriately conveyed to facility leadership

B.

Determine if certain CRE events should be made reportable (e.g., fatalities)

C.

Repeat CRE surveillance and feedback at least quarterly

III. Infection Prevention

A.

Reinforce core prevention measures in all facilities

- Work closely with IPs to review practices
- Provide in-service training

B.

Consider supplemental measures in all facilities[1,2]

- Active surveillance testing and preemptive Contact Precautions for
  - Patients admitted from facilities with ongoing CRE transmission or high CRE prevalence
  - Patients admitted from long-term care facilities (e.g., long-term acute care hospitals) or with CRE risk factors (e.g., open wounds, indwelling devices, high antimicrobial use)
  - Patients being admitted to high-risk units (e.g., ICUs)
- Chlorhexidine bathing on high-risk patients

C.

Assess Compliance to Prevention Measures

- At least monthly assessment (e.g., report from IPs)
- Share performance measures with facility administrators
- As needed, provide additional in-service training

IV. Inter-facility Communication

Ensure facilities with CRE cases complete an inter-facility transfer form (indicate CRE status, presence of open wounds/devices, antimicrobial use and length of therapy)[3]

V. Assess Efficacy of Infection Prevention Measures

If CRE rates do not decrease,

- Intensify efforts in select facilities as needed
- Implement additional interventions in consultation with CDC and/or regional experts and in accordance with CDC HICPAC MDRO guidelines[2]

1. Refer to Part 1: Facility-Level Recommendations
2. http://www.cdc.gov/ncidod/dhqp/pdf/ar/MDROGuideline2006.pdf
3. http://www.cdc.gov/HAI/toolkits/InterfacilityTransferCommunicationForm11-2010.pdf

Selected References

Ben-David D, Maor Y, Keller N, et al. Potential role of active surveillance in the control of a hospital-wide outbreak of carbapenem-resistant *Klebsiella pneumoniae* infection. Infect Control Hosp Epidemiol 2010 Jun;31(6):620-6.

Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing; Twenty Second Informational Supplement (January 2012). CLSI document M100-S22. Wayne, Pennsylvania, 2012.

Kochar S, Sheard T, Sharma R, et al. Success of an infection control program to reduce the spread of carbapenem-resistant *Klebsiella pneumoniae*. Infect Control Hosp Epidemiol 2009 May;30(5):447-52.

Munoz-Price LS, De La Cuesta C, Adams S, et al. Successful eradication of a monoclonal strain of *Klebsiella pneumoniae* during a *K. pneumoniae* carbapenemase-producing *K. pneumoniae* outbreak in a surgical intensive care unit in Miami, Florida. Infect Control Hosp Epidemiol 2010 Oct;31(10):1074-7.

Munoz-Price LS, Hayden MK, Lolans K, et al. Successful control of an outbreak of *Klebsiella pneumoniae* carbapenemase-producing *K. pneumoniae* at a long-term acute care hospital. Infect Control Hosp Epidemiol 2010 Apr;31(4):341-7.

Ostrowsky BE, Trick WE, Sohn AH, et al. Control of vancomycin-resistant *enterococcus* in health care facilities in a region. N Engl J Med 2001;344(19):1427-33.

Schechner V, Kotlovsky T, Tarabeia J, et al. Predictors of rectal carriage of carbapenem-resistant Enterobacteriaceae (CRE) among patients with known CRE carriage at their next hospital encounter. Infect Control Hosp Epidemiol 2011 May;32(5):497-503.

Patel G, Huprikar S, Factor SH, Jenkins SG, Calfee DP. Outcomes of carbapenem-resistant *Klebsiella pneumoniae* infection and the impact of antimicrobial and adjunctive therapies. Infect Control Hosp Epidemiol 2008 Dec;29(12):1099-106.

Schwaber MJ, Klarfeld-Lidji S, Navon-Venezia S, Schwartz D, Leavitt A, Carmeli Y. Predictors of carbapenem-resistant *Klebsiella pneumoniae* acquisition among hospitalized adults and effect of acquisition on mortality. Antimicrob Agents Chemother 2008 Mar;52(3):1028-33.

Schwaber MJ, Lev B, Israeli A, et al. Containment of a Country-wide Outbreak of Carbapenem-resistant *Klebsiella pneumoniae* in Israeli Hospitals via a Nationally Implemented Intervention. Clin Infect Dis 2011 Feb 11.