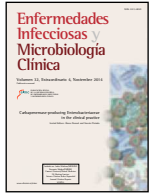




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Control strategies for carbapenemase-producing Enterobacteriaceae at different levels of the healthcare system

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ABSTRACT

Keywords:

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Hospital preparation plan

There has been a rapid increase in recent years in the incidence of infection and colonization by carbapenemase-producing Enterobacteriaceae (CPE). A number of clusters and outbreaks have been reported, some of which have been contained, providing evidence that these clusters and outbreaks can be managed effectively when the appropriate control measures are implemented. This review outlines strategies recommended to control CPE dissemination both at the healthcare facility level (acute and long-term care) and from the public health point of view.

A dedicated prepared plan should be required to prevent the spread of CPE at the hospital level. At the front line, activities should include management of patients at admission and new cases, active surveillance culturing and definition of high-risk groups. High compliance with standard precautions for all patients and full or modified contact precautions for defined categories of patients should be implemented. Long-term care facilities are areas where dissemination can also take place but more importantly they can become a reservoir as patients are admitted and released to other Health care facilities. From the public health point of view, surveillance must be tailored to identify regional spread and interfacility transmission to prevent further dissemination. Finally, a comprehensive set of activities at various levels is necessary to prevent further spread of these bacteria in the community.

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Estrategias de control de las enterobacterias productoras de carbapenemasas en diferentes niveles del sistema sanitario

RESUMEN

Palabras clave:

Enterobacterias productoras de
carbapenemasas
Control de la infección
Instituciones sanitarias
Instituciones de crónicos
Plan de preparación para el hospital

En los últimos años hemos asistido a un rápido crecimiento en la incidencia de infección y colonización por enterobacterias productoras de carbapenemasas (EPC). De los numerosos brotes y agrupamientos de casos publicados, algunos de ellos fueron controlados, lo que sugiere que cuando se implementan medidas apropiadas de control estos brotes pueden ser gestionados eficazmente. Esta revisión describe las estrategias recomendadas para controlar la diseminación de las EPC, tanto en las instituciones sanitarias (de agudos y crónicos) como desde el punto de vista de la salud pública.

Se requiere la existencia de un plan previo definido para prevenir la diseminación de las EPC a nivel hospitalario. Para la atención al paciente se debería incluir la gestión de los pacientes al ingreso y la aparición de nuevos casos, los cultivos de vigilancia activa y la definición de los grupos de alto riesgo. Debería conseguirse un alto cumplimiento, tanto de las precauciones estándar para todos los pacientes como de las precauciones de contacto para categorías definidas de pacientes. Además, las instituciones de crónicos constituyen un reservorio donde los pacientes entran y salen y donde puede ocurrir la transmisión. Desde el punto de vista de la salud pública, la vigilancia deber ser diseñada para identificar la transmisión regional y entre instituciones con el objetivo de prevenir una mayor diseminación. En conclusión, necesitamos un conjunto de actividades a diferentes niveles para prevenir una mayor diseminación de estas bacterias en nuestra población.

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Introduction

There has been a rapid increase in the incidence of infection and colonization by carbapenemase-producing Enterobacteriaceae (CPE) in Spain during the last 5 years. A number of clusters and outbreaks have been reported, some of which have been contained, providing evidence that these clusters and outbreaks can be managed effectively when appropriate control measures are implemented.¹⁻³ Evidence from around the world indicates that the rapid spread of CPE has great potential to pose a serious threat to public health and can make effective medical treatment difficult. Early detection, prevention and control of CPE is particularly important for hospitals that have had little or no experience with these organisms. For organizations that already have established or recurrent problems with the spread of these organisms, a more aggressive approach might be needed. The approach should be more rigorous for the acute setting, in which the risk of spread and its consequences are greater, given that care in non-acute settings either cannot or need not be subjected to the same stringent measures. An excellent review has been published recently concerning the broader subject of multidrug-resistant (MDR) Gram-negative bacteria focused on an acute healthcare level.⁴ This review outlines strategies recommended to control CPE dissemination at the healthcare facility level (acute and long-term care) and from the public health point of view.

Healthcare facilities

Hospital preparation plan

A dedicated, prepared plan should be required to prevent the spread of CPE.⁵ The plan should be in place before the first case is detected or if cases have already been admitted to or have occurred within the healthcare facility. Table 1 provides a checklist of actions to prevent and minimize the spread of CPE. The plan should include the following:

- *Resources and responsibilities.* Arrangements for resources should be considered so they are available to support the plan, including: a) staff to provide capacity when the ward or wards have been closed, when patients are in isolation, when cohort nursing is underway or when enhanced cleaning is required; b) the equipment to facilitate the above; c) the facilities to undertake effective patient screening and access to a laboratory that performs recommended tests and provides efficient turnaround of results; and d) a system to flag a positive result (colonization or infection) of CPE on the patient's record.

- *Staff training.* An initial training and regular updates should be in place for all healthcare personnel to enable a full understanding of the following: the plan; the potential threat of CPE; the clinical implications of such microorganisms; prudent antimicrobial prescribing; the actions required if a patient is suspected of harboring CPE; practices to prevent spread; internal and external communications with other professionals and organizations; being alert to patients at highest risk; and maintaining awareness of the changing local and international epidemiology.

- *Describe baseline data and monitor trends* to provide an understanding of CPE and other MDR organisms in hospital epidemiology. This work should be part of an ongoing activity to maintain an overview of trends in the organization. This will provide a baseline to assist in the speedy recognition of an emerging problem and to track the improvement achieved.

- *Early detection and effective infection prevention and control practices.* The plan should cover the screening of patients and patient contacts; the provision of single rooms for isolation or cohorting; standard precautions (particularly encouraging hand

Table 1

Checklist of actions to prevent and minimize the spread of CPE

Hospital checklist of actions to prevent and minimize the spread of carbapenemase-producing Enterobacteriaceae	Number of cases			
	Hospital-wide	0	1	>1
Board to make it a high priority to minimize spread and to support all infection prevention and control (IP&C) measures	X	X	X	
Prepare a dedicated management plan including IP&C measures	X			
Run awareness / training campaign for staff, particularly, but not exclusively, medical and nursing staff	X	X	X	
On admission, screen suspected cases (e.g., previously positive cases or other criteria depending on the area)	X	X	X	
Implement isolation strategy at triage/admission for suspected or recent laboratory-confirmed patients	X	X	X	
Hold regular incident management team meetings to review epidemiology and IP&C strategies, including root cause analyses where applicable		X	X	
Implement communication strategy; report as an Incident and inform Public Health Epidemiology Center if there is evidence of onward transmission				X
Ensure that any transmission becomes a top hospital priority, with leadership from board to ward				X
<i>Laboratory</i>				
Optimize and review laboratory methods to detect producers	X	X	X	
Screen by plating rectal swabs and manipulated site swabs (e.g., from skin breaks and catheter sites) onto an appropriate culture media		X	X	
<i>Infection prevention and control</i>				
It is recommended that Directors of IP&C ensure that the incident / problem is raised at the Directors level		X	X	
Implement the CPE Plan immediately, with strict adherence to standard precautions; affected patients should be isolated in a single room or cohorted adequately		X	X	
Optimize care bundles and clinical practice for indwelling devices	X	X	X	
Reinforce and optimize hand hygiene		X	X	
Minimize spread by effective routine and terminal cleaning including all hand-contact and sanitary areas (increase frequency if evidence of spread); review procedures for effective decontamination of equipment		X	X	
Designate cohort staffing depending on risk assessment, number of cases and feasibility				X
Ensure effective incident tracking via a robust surveillance system, with an incident / outbreak management team, full epidemiological investigation, maintaining line list and epidemic curve		X	X	
Prepare a readmission, discharge and transfer strategy for affected patients and contacts	X	X	X	
Plan and facilitate adequate communication to other healthcare providers	X	X	X	
<i>Screening</i>				
Screen index case and case contacts; find and isolate case immediately; determine the extent of spread; convene an outbreak control team if spread suspected; electronically flag affected patient(s) record		X	X	
Instigate weekly and discharge screening of all patient contacts (as identified) in affected units/wards for a period of 4 weeks after the last case was detected; cohort contacts if possible / feasible		X	X	

Adapted from: Public Health England 2013. Acute trust toolkit for the early detection, management and control of carbapenemase-producing Enterobacteriaceae.

hygiene with alcohol-based hand rubs and the use of personal protective equipment in line with standard precautions) and specific precautions; the safe disposal of waste and sharps; the proper use of medical devices, including their cleaning and decontamination; awareness of patient movements (such as an inpatient or a patient on medical transfer/discharge); and the management of visitors.

– *Procedures for laboratory services.* The healthcare facilities should be aware of local procedures to ensure that the following steps occur in a timely way for management of patient specimens: the transport, receipt and processing of specimens and how this will be managed over a weekend or holiday; reviewing the laboratory policies on screening, detection and referral to the reference laboratory; and the reporting of results.

– *Antimicrobial stewardship and treating infections.* The healthcare facilities should encourage the prudent use of antimicrobials, developing guidelines on antimicrobial choice when managing patients with CPE infections.

– *Planning for dealing with the first case or an increase in cases.* Plans must be in place to coordinate the response on recognition of a problem, including how the problem can be communicated rapidly to the right people; consideration of triggers for early reporting, particularly in relation to spread; rapid promotion of strict adherence to the CPE Plan; and the criteria and procedure for establishing and convening an incident/outbreak control team.

– *Effective communications.* Communications to inform and update the infection control teams (ICT) and microbiologists from neighboring hospitals with which there is regular inter-facility transfer from one unit to another and the local public health authorities is crucial. It must be ensured that no affected patient is transferred to another healthcare facility without prior communication approval and an inter-healthcare transfer form being provided. In addition, ensure no affected patient is discharged without receiving documentation concerning his or her status for future encounters with other healthcare facilities. The healthcare facility should ensure that the right people, in the right place, have the right knowledge through planning early communications within the facility; with the external laboratory; between healthcare professionals, specialist units and neighboring healthcare facilities (both hospital and non-acute care centers); with the family and/or care home to which the patient is to be discharged to provide an accurate explanation of risk in a non-acute or community setting; and to provide an opportunity for questions concerning further guidance.

– *Interventions during a suspected outbreak or cluster of cases* colonized or infected with CPE should include the following: *a)* early communication to ensure the board of directors and key senior clinical/ward staff are made aware of the case or cases; *b)* instigation of immediate control measures for early control and prevention of spread; *c)* the need to convene an ICT consisting of infection control leads, a microbiologist, an infectious disease physician, direction team representation, clinical representation, nurse manager, maintenance and cleaning service representation, a communications department and a pharmacy in charge of reviewing the list of cases (providing an epidemic curve and updates regarding microbiological investigations); the epidemiological investigations to date; current hypothesis or hypotheses for the incident, outbreak or cluster; control measures to date and effectiveness, including compliance and audit history; antimicrobial practices and compliance to policies; and staff training and awareness; *d)* leadership roles and responsibilities; *e)* frequency of meetings and reporting schedule (could change over time); *f)* action plan for ongoing investigations and control measures (including timelines); *g)* plans for maintaining and reinforcing enhanced cleaning schedule (increased frequency and terminal cleaning for rooms of affected patients); *h)* transfer and discharge arrangements for affected patients; *i)* additional expert

advice required or consideration of an external expert or peer support visit in 'difficult to control' outbreaks; and *j)* communications strategy including patients, relatives, the media, additional professionals and organizations.

Front line activities

Patient admissions. At the time of admission, *active surveillance cultures* (ASC) of unrecognized CPE carriers should be considered as a measure to prevent the introduction and transmission of CPE within the hospital because they allow an earlier detection of unrecognized colonized patients. The real impact of ASC as a single intervention to control MDR Gram-negative bacteria is unknown. A retrospective survey in 12 hospitals in Toronto found that hospitals performing rectal swab screening at admission reduced the incidence of extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae nosocomial cases by 49%.⁶ These results showed that rectal swabs at admission were useful for reducing in-hospital transmission in a non-outbreak setting. ASC of all patients on admission has been used successfully as part of multifaceted strategies to interrupt transmission of CPE in outbreak⁷ and endemic settings in intensive care units (ICUs).⁸

ASC on admission should be considered for any epidemiological settings in which patients belong to a *high-risk group*:^{5,9-11} *a)* patients transferred from a healthcare facility in any foreign country, given the strong evidence of cross-border transfer and the lack of data concerning the true prevalence of CPE in Europe and other countries; *b)* patients transferred from acute or long-term care facilities with known high CPE prevalence; *c)* patients previously colonized or infected with CPE; and *d)* patients who have had close contact with a person who has CPE, when it is known.

Rectal swab is the recommended procedure for ASC, followed by peri-anal or stool sample tests. Screening of any wounds and device-related sites (such as urinary catheter) on admission should also be considered in high-risk patients.

High-risk patients should be placed on *preemptive contact precautions* until a negative screening culture is obtained.^{5,9-11} Some mathematical models estimated the impact of ASC in MDR Gram-positive bacteria and suggested that using ASC plus preemptive contact precautions might lead to a greater reduction of transmission.¹²

New cases. Emergence of a new case of infection or colonization due to carbapenemase-producing Enterobacteriaceae (NcCPE) in a healthcare facility should be considered a key moment in CPE control. In endemic settings it constitutes a measure of efficacy of the control measures that are being taken. But early control of NcCPE in epidemic settings could be even more important, in which a faster and more efficient response against NcCPE can lead to prevention of the widespread propagation of CPE.¹¹

In addition to high-risk patient screening at admission, NcCPE can be detected from hospitalized patients' clinical or surveillance samples. Taking into account that CPE acquisition mechanisms and clinical cultures only identify one third of the total carriage rate of CPE among hospitalized patients,¹³ *epidemiologically linked contacts to any NcCPE must be screened.* This includes any inpatient who has shared a room or stayed in the room within 48 h after a non-isolated NcCPE has left it.^{5,11} Patients who have shared healthcare personnel or who have undergone the same procedures (e.g., endoscopy, bronchoscopy) without following cross-transmission prevention measures should be managed as contacts.¹⁴ ASC, such as weekly screening, has also been shown to be useful to detect previously unrecognized colonized patients during their stay in a high-risk unit.¹⁵ Other occasions to consider ASC include at discharge^{16,17} and/or just before transferring a patient to another acute or long-term healthcare facility. ASC can be discontinued 2 weeks after the last

NcCPE was detected⁵ or discharged in non-high-risk areas.¹⁴ When CPE are rare in the unit, if a case of CPE is detected, a point-prevalence survey should be considered to identify the real prevalence of unrecognized cases.^{5,11} Preemptive contact precautions (CP) for contacts pending results of screening cultures might be considered for those with CPE risk factors and/or who are admitted to high-risk units.¹¹ Surveillance of healthcare personnel or household contacts is not currently justified.⁵

Reinforcement of *hand hygiene* performance with an alcohol-based hand rub before and after all encounters with patients colonized or infected with CPE must be encouraged,¹¹ as well as implementation of CP by using gowns and gloves before entering the patient's room and removing them promptly upon leaving. There is no firm evidence regarding when CP can be discontinued.⁵ Public Health England guidelines recommend maintaining CP for the entire hospital stay.⁵ Other guidelines suggest applying CP until >1¹¹ or ≥3 screening cultures are repeatedly negative for CPE in a patient who has not received any antibiotic during the previous weeks.

NcCPEs must be housed in *single rooms* with dedicated patient care equipment, or they should at least be *cohorted together*.¹¹ Nursing staff must be instructed in performing CP, whose adherence should be audited. Diagnostic or therapeutic procedures should be carried out in the NcCPE's room. If not, they should be undertaken at the end of the working day and followed by a terminal cleaning of equipment.⁵ Furthermore, the use of invasive devices should be minimized and immediately removed when they are no longer needed.

A physical segregation of affected patient cases (cohorting of cases) or dedicated personnel exclusive to cases might occasionally be necessary, such as in very high-risk units or in uncontrolled outbreaks.^{9,11,16,17}

Regarding *patient hygiene*, although a recent randomized clinical trial demonstrated the usefulness of chlorhexidine to reduce acquisition of multiresistant organisms (particularly Gram-positives),¹⁸ there is a lack of evidence concerning the role of chlorhexidine in avoiding CPE spread. On this premise, the present recommendations are primarily based on Munoz-Price et al, who reported having controlled two CPE outbreaks by using a multifaceted bundle of control measures that included a daily bath with diluted liquid chlorhexidine (2%) or chlorhexidine-impregnated wipes for all patients admitted to an affected unit, regardless of their CPE status.^{19,20}

Oral decontamination by non-absorbable antimicrobials (e.g., gentamicin and colistin) has been proposed. Observed results have been contradictory, and emergence of antimicrobial resistance is a real drawback. This strategy could be beneficial to prevent eventual infection for selected patients colonized with CPE, such as transplant recipients or immunocompromised patients pending chemotherapy and patients who require major intestinal or oropharyngeal surgery, but their use for preventing further CPE spread remains controversial.²¹⁻²³

Given CPE are generally susceptible to the usual disinfectants, a stringent application of normal *cleaning and disinfection* schedules can eliminate CPE from the environment.⁵ Therefore, efforts should be focused on assessing the outcomes of environmental cleanliness.⁵ For this purpose, direct observation and adenosine triphosphate detection by bioluminescence-based systems or target cultures have shown usefulness.^{24,25} Daily environmental cleaning is usually performed twice a day with 1:10 sodium hypochlorite^{17,24,26} quaternary ammonium^{2,27,28} or any other low-level disinfectant. More delicate surfaces (e.g., computers and monitors) can be cleaned using an ammonium derivate¹⁶ or alcohol.¹⁷ In addition to daily cleaning, performing a terminal cleaning after an NcCPE leaves a specific area is recommended.⁵

Any NcCPE identification must be reported in a timely manner¹¹ from the laboratory to the ICT and clinical staff. Public health authorities must be also informed so they can coordinate a local and regional response, which includes alerting nearby acute and long-

term healthcare facilities. An NcCPE is also a notifiable disease in some autonomous communities.¹⁴ Reporting was traditionally based on personal communication between laboratory and ICT.²⁹ However, with the generalized use of electronic medical records, prescription programs and other information technology tools, there are a number of experiences using electronic surveillance systems (ESS) that have proven more useful than using traditional reporting methods.³⁰ Thus, healthcare facilities should endeavor to develop *CPE surveillance systems*: a) to be ESS, preferably based on web technology; b) to integrate microbiological along with demographic and pharmaceutical data; c) to generate a timely alert to ICT and public health authorities; and d) to carry out an early establishment of an NcCPE Management Plan.

NcCPEs and their contacts must be properly informed of their status as well as of the following aspects:⁵ a) the clinical significance of Enterobacteriaceae; b) the value of carbapenems as broad-spectrum antibiotics and the meaning of carbapenem resistance; c) CPE transmission mechanisms and sources for acquisition, highlighting the difficulty in assessing when and where a person acquired the bacteria; d) the importance of CP, with emphasis on good hand hygiene and avoiding touching medical devices; e) the need for isolation in a single room and the precautions that healthcare personnel and visitors should follow (primarily hand hygiene and wearing gloves and a gown), emphasizing that the quality of care will not decrease because of isolation; f) the plausible need for providing periodic samples to check CPE status, the sites from which samples are taken and that patients are promptly informed of results; g) that colonized patients go home as soon as their clinical situation allows it. Although it is probable that an NcCPE remains with CPE at discharge, it will typically clear up within approximately 6 months. During this period, no special precautions are required apart from good hand hygiene; h) the risk factors for CPE recurrence; and i) the condition of the CPE carrier is flagged in their medical and discharge reports.

Upon *discharge of the patient*, good communication with the recipient acute or long-term healthcare facilities must be ensured. The recipient facilities must be informed about patient status, and additionally about antimicrobial usage, presence of wounds and temporary or indwelling devices.⁵ Long-term facilities must be also informed about whether the transferred case is at high risk for transmission.¹¹

In addition to measures included in the CPE Management Plan, the emergence of an NcCPE in an endemic setting must lead to the following: a) reassessment of the compliance with the control measures that are being carried out; b) reinforcement of those measures that are not being adequately fulfilled; and c) rethinking the need for additional control measures.

Special risk areas. Intensive care units, hematological and burn wards are considered high-risk areas for the wide spread of any multidrug-resistant organism.

ASC of all patients on admission has been used successfully as part of multifaceted strategies to interrupt transmission of CPE in outbreak⁷ and endemic settings²⁷ in ICUs. Further, weekly screening has also been shown to be useful to detect previously unrecognized colonized patients during their stay in a high-risk unit.³¹ ASC can be discontinued 4 weeks after the last CPE was detected⁵ or discharged from high-risk units and wards.¹⁴

The Centers for Disease Control and Prevention (CDC) suggest that 2% diluted liquid chlorhexidine or 2% chlorhexidine-impregnated wipes could be used for a *daily patient bath in high-risk settings*.¹¹

Long-term care facilities

Long-term care facilities (LTCFs) have emerged as an important reservoir that could facilitate CPE transmission across different levels of healthcare facilities, both in an outbreak and in an endemic

setting.^{32,33} LTCFs present specific challenges. First, the infection control infrastructure is less stringent than that of acute care hospitals. Second, the nature of care in these facilities is of longer duration than that of acute care hospitals, making the implementation of isolation measures particularly difficult. Nevertheless, there have recently been successful experiences published regarding CPE control in these settings.³⁴ Elements of infection control independently associated with decreased risk of CPE carriage included presence of alcohol hand rubs in each room, appropriate use of gloves in the context of standard precautions and a policy of active surveillance for CPE at admission.³⁵

The available epidemiological data originate from outside Spain, where LTCFs could differ from those in our country. The recommendations to prevent CPE spread in LTCFs suggested below are based on those of the 2012 CDC guidelines for control of CPE that include "acute long-term care facilities or skilled nursing homes," excluding assisted living facilities and nursing homes. The current epidemiological situation regarding LTCFs in Spain and in Europe is less known.

CPE screening should be performed for epidemiologically linked contacts (e.g., roommates) of an NcCPE. This strategy is highly recommended in an outbreak setting or when the facility did not have patients with CPE. A point-prevalence survey might also be considered to identify the real prevalence of unrecognized cases (involving the screening of all patients in the ward).

Rectal swabs are the most recommended method for detecting CPE. Interestingly, a cross-sectional survey conducted in LTCFs in the USA found that a rectal/stool swab was the single most sensitive sample for detecting CPE carriers (88% sensitivity), and the addition of an inguinal skin swab resulted in detection of 100% of carriers.³³

Residents colonized or infected with a high risk for transmission should be placed on contact precautions: *a*) patients who are totally dependent upon healthcare personnel for their activities of daily living; *b*) patients who are ventilator-dependent; *c*) patients who are incontinent of stool; and *d*) patients who have wounds with drainage that is difficult to control.

In addition to the stringent performance of standard precautions, contact precautions might be relaxed with residents colonized or infected with low risk for transmission, but should include the use of gloves and/or gowns when contact with colonized or infected sites or body fluids is possible, this includes: *a*) patients who are able to perform hand hygiene; *b*) patients who are continent of stool; *c*) patients who are less dependent on staff for their activities of daily living; and *d*) patients without draining wounds.

Cohorting patients in a specific area or ward with dedicated staff to care for them has been demonstrated to be useful for control of CPE transmission in outbreaks.

Preemptive contact precautions might be used on high-risk patients while the high-risk conditions remain.

Patient hygiene by means of chlorhexidine baths has been shown to be useful in combination with a bundle of interventions in an outbreak in a LTCF.¹⁹

Public health

Surveillance for CPE

Public health departments should be aware of the prevalence or incidence of CPE in their area by performing some form of regional surveillance for these organisms. An epidemiological scale has been proposed to classify the nationwide expanse of the problem ranging from "no cases reported", stage 0, to "endemic situation", stage 5.³ Options for performing surveillance include making CPE a laboratory-reportable event and surveying infection preventionists and/or laboratory directors of healthcare facilities by telephone or e-mail (e.g., using an online survey).

It is recommended that CPE surveys conducted by health departments collect, at a minimum, the following facility-level data: facility demographics including location and facility name; overall frequency of CPE detection (e.g., daily, weekly, monthly); and frequency of CPE cases by timing of detection (e.g., within 48 h or greater than 48 h of admission). If surveying infection preventionists, determine whether recommended surveillance and infection prevention measures are being implemented.

E-mail reminders or phone calls to non-responders are encouraged to facilitate survey completion in a timely fashion (e.g., 1-2 weeks) and to increase response rates. Based on survey and surveillance results, prevention strategies can be tailored accordingly.

Interfacility transmission of CPE

Patients colonized or infected with CPE might seek medical care in more than one healthcare facility and serve as a reservoir that can facilitate CPE spread. 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 to different hospitals. This extensive inter-facility sharing of patients can facilitate widespread regional transmission of CPE.

Regional approach to CPE control

To prevent the emergence and further spread of CPE, a coordinated regional control effort among healthcare facilities is recommended. The implementation of such an approach was successful for reducing CPE incidence at the national level in Israel.³⁶ Given the ability of state and local health departments to interface with different types of facilities, the public health department is in a unique position to coordinate the local and regional response to multidrug-resistant organisms such as CPE 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 CPE within a given jurisdiction. Based on an initial evaluation of the prevalence or incidence of CPE, prevention strategies can be tailored to geographical regions according to the following classifications: regions without CPE, regions with few CPE-colonized or -infected patients and regions where CPE are common. In regions where there are no or few CPE-colonized or -infected patients, there might be a critical opportunity to prevent further emergence of CPE by taking an aggressive approach early in the process. For regions in which CPE have already become common, certain general prevention measures might need to be applied more broadly. However, because of the challenges associated with high CPE prevalence, further tailoring of supplemental measures for these situations is recommended.

Conflicts of interest

The authors have no conflicts of interest to declare.

References

- Sánchez-Romero I, Asensio A, Oteo J, Muñoz-Algarra M, Isidoro B, Vindel A, et al. Nosocomial outbreak of VIM producing *Klebsiella pneumoniae* isolates of multilocus sequence type 15: molecular basis, clinical risk factors, and outcome. *Antimicrob Agents Chemother.* 2012;56:420.
- Robustillo Rodela A, Díaz-Agero Pérez C, Sánchez Sagrado T, Ruiz-Garbajosa P, Pita López MJ, Monge V. Emergence and outbreak of carbapenemase-producing KPC-3 *Klebsiella pneumoniae* in Spain, September 2009 to February 2010: control measures. *Euro Surveill.* 2012;17:pii=20086.
- Grundmann H, Livermore DM, Giske CG, Canton R, Rossolini GM, Campos J, et al. Carbapenem-non-susceptible Enterobacteriaceae in Europe: conclusions from a meeting of national experts. *Euro Surveill.* 2010;15:pii=19711.

4. Tacconelli E, Cataldo MA, Dancer SJ, De Angelis G, Falcone F, Frank U, et al. ESCMID guidelines for the management of the infection control measures to reduce transmission of multidrug-resistant Gram-negative bacteria in hospitalized patients. *Clin Microbiol Infect.* 2014;**20**:S1-55.
5. Public Health England. Acute trust toolkit for the early detection, management and control of carbapenemase-producing Enterobacteriaceae. London 2013. Available at: <http://www.hpa.org.uk/Publications/InfectiousDiseases/AntimicrobialAndHealthcareAssociatedInfections/1312ToolkitforCarbapenemEnterobacteriaceae>
6. Lowe CF, Katz K, McGeer AJ, Muller MP; Toronto ESBL Working Group. Efficacy of admission screening for extended-spectrum beta-lactamase producing Enterobacteriaceae. *PLoS One.* 2013;**26**:e62678.
7. Ben-David D, Maor Y, Keller N, Regev-Yochay G, Tal I, Shachar D, 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;**31**:620-6.
8. Kochar S, Sheard T, Sharma R, Hui A, Tolentino E, Allen G, et al. Success of an infection control program to reduce the spread of carbapenem-resistant *Klebsiella pneumoniae*. *Infect Control Hosp Epidemiol.* 2009;**30**:447-52.
9. European Centre for Diseases Prevention and Control. Risk assessment on the spread of carbapenemase-producing Enterobacteriaceae (CPE) through patient transfer between healthcare facilities, with special emphasis on cross-border transfer. Stockholm: ECDC; 2011.
10. Carmeli Y, Akova M, Cornaglia G, Daikos GL, Garau J, Harbarth S, et al. Controlling the spread of carbapenemase-producing Gram-negatives: therapeutic approach and infection control. *Clin Microbiol Infect.* 2010;**16**:102-11.
11. Centers for Disease Control and Prevention (CDC) Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE). 2012 CRE Toolkit. CDC. Available at: <http://www.cdc.gov/hai/pdfs/cre/cre-guidance-508.pdf>
12. Siegel JD, Rhinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee, 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings. Available at: <http://www.cdc.gov/hicpac/pdf/isolation/isolation2007.pdf>
13. Wiener-Well Y, Rudensky B, Yinnon AM, Kopuit P, Schlesinger Y, Broide E, et al. Carriage rate of carbapenem-resistant *Klebsiella pneumoniae* in hospitalised patients during a national outbreak. *J Hosp Infect.* 2010;**74**:344-9.
14. Plan de Prevención y control frente a la infección por EPC en la Comunidad de Madrid. Madrid: Comunidad de Madrid; 2013.
15. Calfee D, Jenkins SG. Use of active surveillance cultures to detect asymptomatic colonization with carbapenem-resistant *Klebsiella pneumoniae* in intensive care unit patients. *Infect Control Hosp Epidemiol.* 2008;**29**:966-8.
16. Vergara-López S, Domínguez MC, Conejo MC, Pascual A, Rodríguez-Baño J. Wastewater drainage system as an occult reservoir in a protracted clonal outbreak due to metallo- β -lactamase-producing *Klebsiella oxytoca*. *Clin Microbiol Infect.* 2013;**19**:490-8.
17. Borer A, Eskira S, Nativ R, Sidel-Odes L, Riesenberk K, Livshiz-Riven I, et al. A multifaceted intervention strategy for eradication of a hospital-wide outbreak caused by carbapenem-resistant *Klebsiella pneumoniae* in Southern Israel. *Infect Control Hosp Epidemiol.* 2011;**32**:1158-65.
18. Climo MW, Yokoe DS, Warren DK, Perl TM, Bolon M, Herwaldt LA, et al. Effect of daily chlorhexidine bathing on hospital-acquired infection. *N Engl J Med.* 2013;**368**:533-42.
19. Muñoz-Price LS, Hayden MK, Lolans K, Won S, Calvert K, Lin M, 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;**31**:341-7.
20. Muñoz-Price LS, De La Cuesta C, Adams S, Wyckoff M, Cleary T, McCurdy SP, 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;**31**:1074-7.
21. Sidel-Odes L, Polachek H, Peled N, Riesenberk K, Schlaeffer F, Trabelsi Y, et al. A randomized, double-blind, placebo-controlled trial of selective digestive decontamination using oral gentamicin and oral polymyxin e for eradication of carbapenem-resistant *klebsiella pneumoniae* carriage. *Infect Control Hosp Epidemiol.* 2012;**33**:14-9.
22. Lübbert C, Fauchoux S, Becker-Rux D, Laudi S, Dürrbeck A, Busch T, et al. Rapid emergence of secondary resistance to gentamicin and colistin following selective digestive decontamination in patients with KPC-2-producing *Klebsiella pneumoniae*: A single-centre experience. *Int J Antimicrob Agents.* 2013;**42**:565-70.
23. Tascini C, Sbrana F, Flammini S, Tagliaferri E, Arena F, Leonildi A, et al. Oral gentamicin gut decontamination for prevention of KPC-producing *Klebsiella pneumoniae* infections: Relevance of concomitant systemic antibiotic therapy. *Antimicrob Agents Chemother.* 2014;**58**:1972-6.
24. Ciobotaro P, Oved M, Nadir E, Bardenstein R, Zimhony O. An effective intervention to limit the spread of an epidemic carbapenem-resistant *Klebsiella pneumoniae* strain in an acute care setting: from theory to practice. *Am J Infect Control.* 2011;**39**:671-7.
25. Mitchell BG, Wilson F, McGregor A, Dancer SJ. Methods to evaluate environmental cleanliness in healthcare facilities. *Healthcare Infection.* 2013;**18**:23-30.
26. Maltzou G, Giakkoupi P, Maragos A, Bolikas M, Raftopoulos V, Papahatzaki H, et al. Outbreak of infections due to KPC-2-producing *Klebsiella pneumoniae* in a hospital in Crete (Greece). *J Infect.* 2009;**58**:213-9.
27. Kochar S, Sheard T, Sharma R, Hui A, Tolentino E, Allen G, et al. Success of an infection control program to reduce the spread of carbapenem-resistant *Klebsiella pneumoniae*. *Infect Control Hosp Epidemiol.* 2009;**30**:447-52.
28. Poulou A, Voulgari E, Vrioni G, Xidopoulos G, Pliagkos A, Chatzipantazi V, et al. Imported *Klebsiella pneumoniae* carbapenemase-producing *K. pneumoniae* clones in a Greek hospital: impact of infection control measures for restraining their dissemination. *J Clin Microbiol.* 2012;**50**:2618-23.
29. López-Cerero L, Fernández-Cuenca F, Pascual A. The Microbiology laboratory in nosocomial infection surveillance and control. *Enferm Infecc Microbiol Clin.* 2013;**31**:44-51.
30. Leal J, Laupland KB. Validity of electronic surveillance systems: a systematic review. *J Hosp Infect.* 2008;**69**:220-9.
31. Calfee D, Jenkins SG. Use of active surveillance cultures to detect asymptomatic colonization with carbapenem-resistant *Klebsiella pneumoniae* in intensive care unit patients. *Infect Control Hosp Epidemiol.* 2008;**29**:966-8.
32. Prabaker K, Lin MY, McNally M, Cherabuddi K, Ahmed S, Norris A, et al. Transfer from high-acuity long-term care facilities is associated with carriage of *Klebsiella pneumoniae* carbapenemase-producing Enterobacteriaceae: a multihospital study. *Infect Control Hosp Epidemiol.* 2012;**33**:1193-9.
33. Thurlow CJ, Prabaker K, Lin MY, Lolans K, Weinstein RA, Hayden MK. Anatomic sites of patient colonization and environmental contamination with *Klebsiella pneumoniae* carbapenemase-producing Enterobacteriaceae at long-term acute care hospitals. *Infect Control Hosp Epidemiol.* 2013;**34**:56-61.
34. Schwaber MJ, Carmeli Y. An ongoing national intervention to contain the spread of carbapenem-resistant enterobacteriaceae. *Clin Infect Dis.* 2014;**58**:697-703.
35. Ben-David D, Masarwa S, Adler A, Mishali H, Carmeli Y, Schwaber MJ. A national intervention to prevent the spread of carbapenem-resistant enterobacteriaceae in Israeli post-acute care hospitals. *Infect Control Hosp Epidemiol.* 2014;**35**:802-9.
36. Schwaber MJ, Lev B, Israeli A, Solter E, Smollan G, Rubinovitch B, 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;**52**:848-55.