3-29-2023

Surveillance and Stewardship: Where Infection Prevention and Antimicrobial Stewardship Intersect

Fred C. Tenover
Cepheid, ftenover1@udayton.edu

Debra A. Goff
Ohio State University - Main Campus

Open Forum Infectious Diseases

PERSPECTIVES

Surveillance and Stewardship: Where Infection Prevention and Antimicrobial Stewardship Intersect

Fred C. Tenover[1] **and Debra A. Goff**[2]

[1]Cepheid, Sunnyvale, California, USA, and [2]College of Pharmacy, The Ohio State University Wexner Medical Center, Columbus, Ohio, USA

Colonization with multidrug-resistant organisms (MDROs) is a risk factor for subsequent infection. Surveillance for MDROs, including methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci, extended-spectrum beta-lactamase-producing Enterobacterales, and carbapenemase-producing organisms, is commonly conducted in hospitals to prevent spread of MDROs, in part to reduce the potential for additional infections. Although colonization is a risk factor for infection, data on colonization with various MDROs are often not considered when selecting anti-infective therapy. There are conflicting data on the strength of the positive and negative predictive values of the colonization test results to guide therapeutic strategies. Defining therapeutic strategies for patients with complicated or drug-resistant infections or to select antimicrobial prophylaxis before performing prostate biopsies often falls under the purview of the antimicrobial stewardship team. Should colonization data, which are often present in the patient's medical record from routine infection prevention measures, be reviewed before selecting therapy for infections or for prophylaxis? In this perspective, we will explore the intersection of infection control and antimicrobial stewardship activities.

Keywords. antimicrobial agents; colonization; MRSA; multidrug resistance; VRE.

What information should antimicrobial stewardship teams consider when devising therapeutic strategies for patients with multidrug-resistant infections? Certainly, the identification of the bacterial species and the organism's antibiogram are primary considerations. For carbapenem-resistant organisms, knowing whether resistance is due to carbapenemase production versus other mechanisms has both therapeutic [1] and infection control implications [2]. Furthermore, for carbapenemase-producing Gram-negative organisms (CPOs), knowing whether the carbapenemase is a serine-based enzyme, such as a *Klebsiella pneumoniae* carbapenemase or oxacillinase-48, is critical because organisms with these enzymes may respond to newer antimicrobial agents, such as ceftazidime-avibactam and meropenem-vaborbactam. On the other hand, organisms containing metallo-beta-lactamases, such as New Delhi metallo-beta-lactamase (NDM), imipenemase (IMP), or Verona integron-mediated metallo-β-lactamase (VIM), likely will not respond to these agents [3]. For methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus faecium* (VRE), knowing the susceptibility of the isolates to agents, such as daptomycin and linezolid, may be critical for optimizing therapy [4, 5]. However, what if a neutropenic patient or solid organ transplant patient becomes septic? Are there data in the patient's medical record that should be considered before the availability of standardized antimicrobial susceptibility test results? Should colonization (ie, the presence, growth, and multiplication of a microorganism in a body site in the absence of a host response or tissue damage), with MRSA, VRE, extended-spectrum beta-lactamase (ESBL)-producing Enterobacterales, or CPO, performed as part of an infection prevention program, be considered when selecting therapeutic strategies? Using either culture or polymerase chain reaction (PCR)-based methods to detect the presence of these organisms in patients in an effort to stop their transmission to other patients in hospitals is a major effort of many infection prevention programs. In addition, although not specifically undertaken for infection prevention practices, screening for the presence of antimicrobial-resistant organisms in the gastrointestinal tract that could compromise the effectiveness of prophylactic regimens before performing prostate biopsies is becoming increasingly common. Although surveillance activities vary widely from hospital to hospital and even country to country, based on the types of patients admitted to the hospital, the philosophies of the infection prevention program, and laboratory funding to carry out surveillance activities (which, at least in the United States, are not covered by reimbursement), they are a mainstay of prevention.

Received 19 December 2022; editorial decision 24 March 2023; accepted 28 March 2023; published online 29 March 2023

Correspondence: Fred C. Tenover, PhD, Cepheid, 904 Caribbean Drive, Sunnyvale, CA, 94089 (ftenover1@udayton.edu).

Open Forum Infectious Diseases®

https://doi.org/10.1093/ofid/ofad176

Colonization with any of these organisms is a risk factor for infection, but are the positive predictive value or negative predictive value (NPV) of the surveillance methods sufficiently high to influence therapeutic strategies? In this perspective, we will consider the intersection between data already gathered for infection prevention activities or for guiding prophylaxis and the goal of optimizing antimicrobial stewardship to improve patient outcomes in the hopes that such data will be considered, if appropriate.

METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS*

One clinical situation in which colonization data are specifically used to guide antimicrobial stewardship activities is the de-escalation of vancomycin or linezolid therapy for community-acquired pneumonia and healthcare-associated pneumonia when rapid test results for MRSA on nasal specimens are negative. The recommendation, which appears in the "Diagnosis and Treatment of Adults with Community-acquired Pneumonia" guideline from the American Thoracic Society and the Infectious Diseases Society of America (ATS-IDSA), applies to pneumonia cases that are acquired outside of the hospital setting and focuses on patients in the United States who have not recently completed foreign travel and are not immunocompromised [6]. Although testing using culture methods may be used, testing the nasal swab using a rapid method is recommended to provide the information in a timely fashion, because culture results often take 24–48 hours to complete. A meta-analysis by Parente et al [7], which included data from 22 studies and 5163 patients, showed a NPV of nasal MRSA colonization testing via culture or PCR of 98.1%. The high NPV (which assumed an MRSA prevalence of 10%) supports the use of MRSA nasal screens as a tool for clinicians to rule out MRSA pneumonia and de-escalate therapy accordingly in this patient population. The ATS-IDSA guideline notes the use of a rapid method, and Parente et al [7] reported that based on their data, PCR testing was preferable due to its "improved performance" and because PCR "…can provide actionable results for discontinuation of anti-MRSA therapy within 2 hours, which may take 2 days with culture-based testing." The importance of considering the impact of disease prevalence on NPV was highlighted by Burnham et al [8] and is an important consideration when implementing surveillance testing for this indication. One advantage to using MRSA colonization data obtained by culture versus PCR or other commercial methods is that using MRSA surveillance test results to guide therapeutic decisions is considered "off-label" for commercial PCR tests. This requires the hospital laboratory to conduct an internal validation study to bring such testing in compliance for this intended use. That said, should colonization of the nares or skin with MRSA be considered when selecting therapy for patients with positive blood cultures with presumed staphylococci (ie, Gram-positive cocci in clusters) before the availability of antimicrobial susceptibility test results or data from molecular methods? It is interesting to note that a study by Sarikonda et al [9] of 164 patients in the intensive care unit (ICU) with positive MRSA nasal colonization tests showed low positive and negative predictive values for the development of bloodstream infection (BSI) and lower respiratory tract infections (LRTIs). Here, the complexities of the prevalence of MRSA colonization and disease in the population studied, the timing of the surveillance tests (ie, results from tests performed on admission vs subsequent testing during the hospital stay), and site of infection all influence the predictive value of the results. The authors concluded that nasal colonization data should not be used alone to initiate anti-MRSA therapy for patients in the ICU, because the overall sensitivity for either BSI or LRTI was only 28.7% with a negative predictive value for both of 77.6%. This confirmed other studies showing that MRSA infections often occurred in patients who were not colonized with MRSA. On the other hand, Noeldner et al [10], in a retrospective study of data from almost 2000 patients with MRSA infections other than pneumonia, concluded that "… the results of MRSA nasal PCR had a high specificity and negative predictive value for growth of MRSA in blood and bone or soft-tissue cultures". Thus, as noted in the surviving sepsis guideline [11], the issue becomes one of balancing the risk of undertreating MRSA versus the risk of overtreating MSSA for infections that fall outside of the ATS-IDSA guideline.

VANCOMYCIN-RESISTANT ENTEROCOCCI

Vancomycin-resistant enterococci containing the *vanA* gene emerged in 1988 followed by the discovery and spread of additional glycopeptide resistance determinants, including *vanB*, *vanD*, and others [12]. Soon, gastrointestinal colonization with VRE was recognized as a risk factor both for transmission of VRE among patients in the hospital and development of VRE infections, such as BSIs. Weinstock et al [13] noted that among patients undergoing hematopoietic stem cell transplantation, VRE BSI was seen by day 35 posttransplant in 34.2% of VRE-colonized patients, whereas only 1.8% of patients not colonized with VRE developed VRE BSI. They concluded that screening transplant patients for VRE was critical so that patients who became febrile in the early posttransplant period could be given antimicrobial agents with activity against VRE. In a more recent study, Kram et al [14] tested rectal swabs taken from critically ill patients for the presence of *vanA* and evaluated the impact on therapy for those patients who developed VRE BSI. The *vanA* rectal swab results showed positive and negative predictive values for VRE BSI of 85.9% and 67.5%, respectively,

when collected from the patient within 14 days of developing BSI. These data were viewed as compelling enough "… to influence antimicrobial selection and de-escalation for BSI in a mixed ICU population." The predictive values were better when the interval between detection of VRE colonization and development of BSI was shorter.

EXTENDED-SPECTRUM BETA-LACTAMASE-PRODUCING ORGANISMS

Extended-spectrum beta-lactamases emerged in Gram-negative bacilli in the early 1980s, primarily among the SHV and TEM beta-lactamase families. Currently, CTX-M beta-lactamases are much more common globally than the TEM or SHV ESBLs, although other beta-lactamases, such GES enzymes, which can be either ESBLs or carbapenemases, are emerging in many parts of the world [15]. Screening for carriage of Enterobacterales that produce ESBLs is primarily performed on stool or rectal swab specimens using chromogenic agars supplemented with antimicrobial agents. Colonized patients are typically placed in contact precautions. However, due to the high prevalence of ESBLs in many regions of the world, the high laboratory costs associated with screening, and the increased use of carbapenems in response to surveillance data, ESBL screening in hospitals, especially in the United States, is often limited to patients in the intensive care or hematology/oncology unit, if performed at all [16]. Even in ICU settings, the value of ESBL surveillance has been debated because the positive predictive value is only 40%–50%, which does not spare carbapenem use [16]. Nonetheless, as noted by Noster et al [17] and Ariza-Heredia and Chemaly [18], intestinal colonization with ESBL-producing organisms is associated both with an increased risk of developing infection with these organisms and for transmission to other patients. Thus, detection of ESBL colonization can have both antimicrobial stewardship and infection prevention implications. Mensa et al [19] note in their "Recommendations for antibiotic selection for severe nosocomial infections" that "…the knowledge of colonizing microbiota and its susceptibility pattern plays a vital role in the selection of initial empirical antibiotic treatment and, in the subsequent adjustment or de-escalation in cases where the causative microorganism of the infection has not been identified." Thus, according to this guideline, formulation of therapeutic strategies for a patient that meets the criteria for sepsis (or systemic inflammatory response syndrome [SIRS] criteria in addition to other parameters) when no etiologic agent has been identified in the first 24–48 hours should take into account surveillance culture data, such as the presence of ESBL-producing organisms from mucosal cultures. However, Ariza-Heredia and Chemaly [18] do not recommend routine surveillance for ESBLs for cancer patients who have no signs or symptoms of infection, because from their assessment of the literature, the linkage between colonization and subsequent infection and outcomes are not clear. They make an exception for outbreak situations where surveillance data are critical for guiding infection prevention activities [18]. Thus, other than agreement that patients colonized with ESBL-producing organisms should be placed in contact precautions, there is no clear consensus on the need for routine ESBL screening, on the frequency of obtaining specimens if surveillance is conducted, or on the laboratory techniques that are used to identify colonized patients. Both within and outside of the United States, the approach to ESBL screening varies from institution to institution and depends on factors such as prevalence of resistant organisms in the region, the patient populations that will undergo surveillance (eg, all patients on admission, or only patients in the intensive care unit or hematology/oncology unit), the availability of laboratory resources, and infection prevention policies.

SCREENING FOR COLONIZATION WITH ANTIMICROBIAL-RESISTANT ORGANISMS BEFORE PROSTATE BIOPSY

A parallel screening activity undertaken by many microbiology laboratories—although one that is not directly related to infection prevention activities—is screening male patients for antimicrobial-resistant organisms before undergoing transrectal, ultrasound-guided, prostate needle biopsies for diagnosis of carcinoma of the prostate. In 2012, Taylor et al [20] reported that using the results of rectal swab cultures to guide the selection of antimicrobial prophylaxis aided in preventing postoperative complications of prostate biopsies and was highly cost effective. This study set in motion numerous additional studies seeking to optimize the laboratory pathway for screening patients for resistant organisms before undergoing prostate biopsies. A recent review of data from a 9-year global study of 2 cohorts of patients undergoing prostate biopsies (one from 2010 to 2014 and the second from 2016 to 2019) noted that the rates of complications among the 1615 men increased from 6% to 11.7%. This emphasizes the need for interventions to reduce complications. Approximately 93% of patients in the study received antimicrobial prophylaxis and among those patients, approximately 74% received a fluoroquinolone [21]. The extensive use of fluoroquinolones for prophylaxis, followed by the emergence of both lower and systemic severe urinary tract infections with fluoroquinolone-resistant Gram-negative bacilli, led many laboratories to focus exclusively on this class of antimicrobial agents for their screening tests. However, screening stool specimens for any Enterobacterales species that was fluoroquinolone-resistant quickly proved to be an expensive and labor-intensive task. Thus, many laboratories instead chose a more limited approach of screening either stool or rectal swab specimens

only for ciprofloxacin-resistant *Escherichia coli* using selective agar (eg, MacConkey agar containing ciprofloxacin) to indicate the presence of resistant organisms [22]. However, when fluoroquinolone-resistant organisms were identified, additional susceptibility testing had to be done on the colonies to identify alternative antimicrobial agents for prophylaxis. This further delayed delivery of the results used for selecting a prophylaxis regimen and for performing the biopsies. Thus, some laboratories have taken a much broader approach to screening for resistant organisms using as many as 4 different selective agar media, containing either ciprofloxacin, fosfomycin, trimethoprim, or amdinocillin-amoxicillin-clavulanic acid, to identify the optimal agent for prophylaxis as rapidly as possible [23]. Although this approach is very effective in guiding selection of prophylaxis in a timely manner (all 4 media showed high sensitivity and specificity), the approach is very expensive and one that is simply untenable for many laboratories. It is important to note that the results of these tests (which may be limited to recognition of fluoroquinolone-resistant *E coli*) are typically not communicated to the infection prevention team because prostate biopsy is typically performed as an outpatient procedure. Some laboratories have combined ESBL surveillance together with screening for resistant organisms to guide biopsy prophylaxis, because they are the performed on the same specimen type. However, this does point out the complexities that sometimes arise for the laboratory in terms of what information on specimens that are collected for surveillance and screening studies, that is, outside of routine diagnostic testing, is communicated to which hospital service and for what purpose. In some institutions, surveillance culture data are communicated only to the infection prevention service to prevent the overuse of antimicrobial agents in patients who may be colonized but not infected. This helps illuminate why the intersection of antimicrobial stewardship and infection prevention activities need to be coordinated so that all services may benefit from the data generated by the microbiology laboratory.

CARBAPENEMASE-PRODUCING GRAM-NEGATIVE BACTERIA

Infections with CPO are a therapeutic challenge, especially organisms that produce metallo-carbapenemases [1, 24]. The importance of choosing the correct therapy up front is underscored by the fact that many CPOs are highly virulent clones of *K pneumoniae* [25] or *Pseudomonas aeruginosa* [26] where any delay in delivering effective therapy may be fatal. In the period between recognition of Gram-negative bacilli in the blood culture bottle and the availability of bacterial species identification and susceptibility results, which may be 72 hours or more in the absence of syndromic panel data, should colonization with CPOs be considered when selecting therapeutic strategies? Surveillance for CPO is recommended by the Centers for Disease Control and Prevention [27] to limit the spread of MDRO in hospitals but not specifically for guiding therapy. However, positive colonization data that included the type of carbapenemase produced could be valuable if the patient was colonized by CPO and harboring metallo-beta-lactamases, such as IMP, NDM, or VIM. Data specifically addressing this issue are rare; however, a study by Lapointe-Shaw et al [28] noted the cost effectiveness of screening for carbapenemase-producing Enterobacterales (CRE) both for preventing transmission in the hospital and preventing infections when the CPE prevalence levels exceeded 0.3%. In addition, Seo et al [29] reported that among 1541 hematology and hepatogastroenterology patients with liver transplantation who were colonized with a CPO, 13.4% went on to develop infection. In addition, Freire et al [30] reported that among 75 patients who had kidney transplant and were colonized by CPO, 16 (21.6%) developed infection with a CPO. They concluded that "…knowledge of CRE colonization is important to guide empirical therapy in this population…".

CONCLUSIONS

Colonization with an MDRO is a risk factor for subsequent infection, but the predictive values of positive or negative surveillance tests vary from organism to organism and with disease prevalence in the population under consideration. The data supporting de-escalation of vancomycin or linezolid for patients with community-acquired pneumonia when nasal specimens are negative for MRSA are strong and we support this use. However, basing therapy for suspected staphylococcal BSI on MRSA colonization data that may change during the course of a hospital stay has the potential of undertreating a large percentage of patients and cannot be routinely recommended. On the other hand, VRE colonization data show reasonable predictive values for BSI, at least among patients who are critically ill, especially in high prevalence populations. The literature regarding the value of surveillance for ESBL-producing organisms is mixed, with some groups advocating frequent surveillance cultures and integrating the results into their treatment guidelines for sepsis and SIRS, whereas others recommend limiting ESBL surveillance, at least among patients with cancer, to periods of outbreaks with ESBL-producing organisms. Whether it is feasible to undertake surveillance cultures for ESBL-producing organisms should be a local decision, based on resistant organism prevalence, laboratory resources, and perceived or proven benefit to patient care. On the other hand, some level of screening procedures to optimize which prophylactic antimicrobial agents should be selected for patients undergoing prostate biopsies should be undertaken by the laboratory, because the incidence of complications of these procedures is increasing. There are no direct data on the predictive value of CPO colonization for infection, especially in

patients who are immunocompromised, but such data are worth considering especially in areas where metallo-carbapenemases are common because this indicates limited options for effective therapy.

Acknowledgments

Author contributions. FCT and DAG coauthored the article.

Financial support. FCT's contributions to the article were supported by Cepheid.

Potential conflicts of interest. FCT is an employee of Cepheid; DAG has received honoraria for speaking for Cepheid. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America guidance on the treatment of extended-spectrum β-lactamase producing enterobacterales (ESBL-E), carbapenem-resistant enterobacterales (CRE), and *Pseudomonas aeruginosa* with difficult-to-treat resistance (DTR-P. aeruginosa). Clin Infect Dis **2021**; 72:e169–83.
2. Goodman KE, Simner PJ, Tamma PD, Milstone AM. Infection control implications of heterogeneous resistance mechanisms in carbapenem-resistant enterobacteriaceae (CRE). Exp Rev Anti Infect Ther **2016**; 14:95–108.
3. Tamma PD, Bergman Y, Jacobs EB, et al. Comparing the activity of novel antibiotic agents against carbapenem-resistant Enterobacterales clinical isolates. Infect Control Hosp Epidemiol Available at: https://doi.org/10.1017/ice.2022.161. Accessed 17 January 2023.
4. Rose W, Fantl M, Geriak M, Nizet V, Sakoulas G. Current paradigms of combination therapy in methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia: does it work, which combination, and for which patients? Clin Infect Dis **2021**; 73:2353–60.
5. Cheah ALY, Spelman T, Liew D, et al. Enterococcal bacteraemia: factors influencing mortality, length of stay and costs of hospitalization. Clin Microbiol Infect **2013**; 19:E181–9.
6. Metlay JP, Waterer GW, Long AC, et al. Diagnosis and treatment of adults with community-acquired pneumonia. An official clinical practice guideline of the American Thoracic Society and Infectious Diseases Society of America. Am J Respir Crit Care Med **2019**; 200:e45–67.
7. Parente DM, Cunha CB, Mylonakis E, Timbrook TT. The clinical utility of methicillin-resistant *Staphylococcus aureus* (MRSA) nasal screening to rule out MRSA pneumonia: a diagnostic meta-analysis with antimicrobial stewardship implications. Clin Infect Dis **2018**; 67:1–7.
8. Burnham JP, Kakol MK, Vazquez Guillamet MC. Methicillin-resistant *Staphylococcus aureus* nasal screening adds limited value to the choice of empiric antibiotics in community-acquired pneumonia. Clin Infect Dis **2019**; 68:1251.
9. Sarikonda KV, Micek ST, Doherty JA, Reichley RM, Warren D, Kollef MH. Methicillin-resistant *Staphylococcus aureus* nasal colonization is a poor predictor of intensive care unit-acquired methicillin-resistant Staphylococcus aureus infections requiring antibiotic treatment. Crit Care Med **2010**; 38:1991–5.
10. Noeldner HM, Bliek ZJ, Jones NE, et al. Clinical utility of methicillin-resistant *Staphylococcus aureus* nasal polymerase chain reaction (PCR) assays beyond respiratory infections. Antimicrob Steward Healthc Epidemiol **2022**; 2:e108.
11. Evans L. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. Crit Care Med **2021**; 49:e1063–143.
12. Courvalin P. Vancomycin resistance in Gram-positive cocci. Clin Infect Dis **2006**; 42: S25–34.
13. Weinstock DM, Conlon M, Iovino C, et al. Colonization, bloodstream infection, and mortality caused by vancomycin-resistant enterococcus early after allogeneic hematopoietic stem cell transplant. Biol Blood Marrow Transpl **2007**; 13:615–21.
14. Kram SJ, Kram BL, Schultheis JM, Kuhrt MM, McRae AS, Anderson DJ. VanA rectal swab screening as a predictor of subsequent vancomycin-resistant enterococcal bloodstream infection in critically ill adults. Infect Control Hosp Epidemiol **2021**; 42:411–6.
15. Castanheira M, Simner PJ, Bradford PA. Extended-spectrum β-lactamases: an update on their characteristics, epidemiology and detection. JAC Antimicrob Resist **2021**; 3:dlab092.
16. Prevel R, Boyer A, M'Zali F, et al. Is systematic fecal carriage screening of extended-spectrum beta-lactamase-producing Enterobacteriaceae still useful in intensive care unit: a systematic review. Crit Care **2019**; 23:170.
17. Noster J, Thelen P, Hamprecht A. Detection of multidrug-resistant enterobacterales-from ESBLs to carbapenemases. Antibiotics (Basel) **2021**; 10: 1140.
18. Ariza-Heredia EJ, Chemaly RF. Update on infection control practices in cancer hospitals. CA Cancer J Clin **2018**; 68:340–55.
19. Mensa J, Barberán J, Ferrer R, et al. Recommendations for antibiotic selection for severe nosocomial infections. Rev Esp Quimioter **2021**; 34: 511–24.
20. Taylor AK, Zembower TR, Nadler RB, et al. Targeted antimicrobial prophylaxis using rectal swab cultures in men undergoing transrectal ultrasound guided prostate biopsy is associated with reduced incidence of postoperative infectious complications and cost of care. J Urol **2012**; 187:1275–9.
21. Alidjanov JF, Cai T, Bartoletti R, et al. The negative aftermath of prostate biopsy: prophylaxis, complications and antimicrobial stewardship: results of the global prevalence study of infections in urology 2010–2019. World J Urol **2021**; 39:3423–32.
22. Chamberland RR. Cutting to the core of the issue: emerging strategies to reduce prostate biopsy-related infections. J Clin Microbiol **2016**; 54: 2431–5.
23. Tops SCM, Bruens M, van Mook-Vermulst S, et al. Performance validation of selective screening agars for guiding antimicrobial prophylaxis in patients undergoing prostate biopsy. J Clin Microbiol **2018**; 56:e00253-18.
24. Logan LK, Weinstein RA. The epidemiology of carbapenem-resistant Enterobacteriaceae: the impact and evolution of a global menace. J Infect Dis **2017**; 215:S28–36.
25. Peirano G, Chen L, Kreiswirth BN, Pitout JDD. Emerging antimicrobial-resistant high-risk *Klebsiella pneumoniae* clones ST307 and ST147. Antimicrob Agents Chemother **2020**; 64:e01148–20.
26. Del Barrio-Tofiño E, López-Causapé C, Oliver A. *Pseudomonas aeruginosa* epidemic high-risk clones and their association with horizontally-acquired β-lactamases: 2020 update. Int J Antimicrob Agents **2020**; 56:106196.
27. National Center for Emerging and Zoonotic Diseases. Centers for Disease Control and Prevention. CDC Facility Guidance for Control of Carbapenem-resistant Enterobacteriaceae (CRE). Centers for Disease Control and Prevention. Available at: https://stacks.cdc.gov/view/cdc/79104/cdc_79104_DS1.pdf. Accessed 11 March 2023.
28. Lapointe-Shaw L, Voruganti T, Kohler P, Thein HH, Sander B, McGeer A. Cost-effectiveness analysis of universal screening for carbapenemase-producing Enterobacteriaceae in hospital inpatients. Eur J Clin Microbiol Infect Dis **2017**; 36: 1047–55.
29. Seo H, Kim HJ, Kim MJ, et al. Comparison of clinical outcomes of patients infected with KPC- and NDM-producing Enterobacterales: a retrospective cohort study. Clin Microbiol Infect **2021**; 27: 1167.e1–8.
30. Freire MP, de Oliveira Garcia D, Lima SG, et al. Performance of two methods of carbapenem-resistant Enterobacterales surveillance on a kidney transplant ward: selective culture of and real-time PCR directly from rectal swabs. Infection **2022**; 50:1525–33.