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Original Article

Control of a hospital-wide outbreak of carbapenem-resistant *Acinetobacter baumannii* (CRAB) using the Israeli national carbapenem-resistant Enterobacteriaceae (CRE) guidelines as a model

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Abstract

Objective: To study the effect of implementing the Israeli national carbapenem-resistant enterobacteriaceae (CRE) guidelines on controlling a hospital-wide outbreak of *Acinetobacter baumannii* (CRAB).

Design: A before-and-after study from 2014 to 2018.

Setting: A 740-bed, secondary-care hospital in central Israel.

Intervention: Acquisition of CRAB was defined as a positive culture taken at least 48 hours after admission or a positive sample identified upon admission in a patient who had been readmitted within 30 days after discharge from our institution. The intervention included maintaining a case registry of all CRAB patients, cohorting patients under strict contact isolation, using dedicated nursing staff and equipment, rigorous cleaning, education and close monitoring of hospital staff, and involvement of hospital management.

Results: In total, 210 patients were identified with hospital-acquired CRAB: 141 before the intervention and 69 after the intervention. CRAB acquisition rates decreased by 77%, from 1.3 per 1,000 admissions before the intervention (2014–2015) to 0.3 per 1,000 admissions after the intervention (2016–2018) ($P < .001$). The decrease in acquisitions was observed hospital-wide, year by year (P for trend, <.001). In 2018, only 7 new acquisitions were detected in internal medicine wards ($P = .058$) and none in the ICUs ($P = .006$).

Conclusions: A structured intervention based on the Israeli CRE management guidelines was successful in controlling a hospital-wide CRAB outbreak.

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Carbapenem-resistant *Acinetobacter baumannii* (CRAB) is increasingly recognized as an emerging cause of healthcare-associated infections, globally.[1-3] *Acinetobacter baumannii* has been reported to cause various nosocomial infections, including sepsis, hospital-acquired and ventilator-associated pneumonia, urinary tract infection, wound infection, and postneurosurgical meningitis.[4] In most instances, isolates are resistant to the vast majority of available antibiotic agents, including carbapenems,[5] and are therefore extensively drug resistant.[6] Carbapenem resistance is usually the result of a synergistic effect of various mechanisms, but it is most widely attributed to the production of carbapenem-hydrolyzing class D β-lactamases.[7] CRAB is associated with high morbidity and mortality rates, leaving colistin the only available treatment option.[8] Although CRAB is typically an organism of low virulence, hospitalized patients are becoming ever more vulnerable to it, due to serious underlying conditions, indwelling catheters, mechanical ventilation, and increasing use of broad-spectrum antibiotics.[9] The organism's inherent ability to tolerate desiccation enables it to survive on dry surfaces for prolonged periods.[10,11] Because of this propensity to persist in the hospital environment, multiple outbreaks of CRAB have been reported, mostly in intensive care units (ICUs).[12-14]

Previous outbreak investigations have demonstrated that meticulous environmental decontamination combined with strict adherence to infection control practices is a key to successful outbreak control.[13-15] Although guidelines outline specific measures to control CRAB transmission, uncertainties concerning the optimal measures remain, especially in a hospital-wide outbreak.[16]

In our institution, we experienced an increased number of CRAB bloodstream infections in 2013. In response, we initiated documentation of infections and asymptomatic colonization due to CRAB. An increase in CRAB acquisitions was observed, starting in the ICUs and eventually spreading to almost all hospital wards. An effort to reduce CRAB acquisitions through interventions in

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each unit separately had limited success. We sought other approaches to control this outbreak and decided to adopt a successful, stricter approach used to contain carbapenem-resistant Enterobacteriaceae (CRE) in Israel. Beginning in 2006, Israel faced a nationwide outbreak of CRE. In 2007, a national strategy to contain the spread was successfully implemented,[17] including uniform requirements for screening and isolation or cohorting patients and staff. Here, we describe the CRAB outbreak and its successful management based on the national Israeli policy guidelines originally developed for CRE control.

Methods

Clinical setting

The Meir Medical Center is a 740-bed, secondary-care teaching hospital in Kfar Saba, Israel. The hospital contains medical and surgical wards, including surgical subspecialties and 2 ICUs. The number of single-patient rooms is limited to 1 or 2 in each ward. On average, during the study period (2014–2018), the hospital had 66,746 admissions annually and 238,321 patient days per year.

Case patients were those who were either colonized or infected with a CRAB isolate, as defined by an international consensus committee.[6] Acquisition of CRAB was defined as a positive culture taken at least 48 hours after admission or a positive sample identified upon admission in a patient who had been readmitted within 30 days after discharge from our institution, in patients not previously identified as carriers. Patients are routinely screened for CRAB carriage in the ICU units, upon admission and weekly thereafter, using rectal swabs. Additionally, weekly sputum cultures are obtained in mechanically ventilated patients. Patients are also screened if they shared a room with a newly discovered patient. A patient with a positive screening result was considered a carrier for the entire duration of hospitalization, and for any readmission in the subsequent 6 months. Screening strategy and compliance monitoring were similar during all phases of the intervention.

Microbiology

Acinetobacter baumannii isolates were identified by a Vitek 2 system using the AST-GN18 card (BioMerieux, France), and they were classified as multidrug resistant if they were resistant to antipseudomonal carbapenems and to all but 2 or fewer of the following antimicrobial categories: aminoglycosides, fluoroquinolones, antipseudomonal penicillins plus β-lactamase inhibitors, extended-spectrum cephalosporins, folate pathway inhibitors, polymyxin, and/or tetracyclines. Results were interpreted according to the Clinical and Laboratory Standard Institute (CLSI) criteria.[18]

The intervention

During the first phase of the intervention (2014–2015), routine infection control measures for patients with CRAB included standard and contact precautions (hand hygiene before and after patient care and use of gown and glove barrier precautions). Routine healthcare and patient education were also provided. The patient's CRAB status was clearly marked on the bed and in the electronic medical record. Terminal cleaning and disinfection were performed upon discharge, and all disposable or washable items, including curtains and linens were removed. The patients were isolated in single- or multiple-patient rooms, and there was no cohorting of patients.

The second phase of the intervention included the following components: (1) A case registry of all newly and known colonized and infected patients with CRAB was established and updated daily. (2) Case patients from the entire hospital, once identified, were placed in separate rooms or were cohorted under strict contact isolation. (3) Dedicated nursing staff was assigned in intensive care units and in the cohort departments, while entry of other staff or visitors to the cohort area was supervised. (4) Dedicated equipment was used and disposable equipment was discarded once the patient was discharged from a single-patient room or if a cohort area was no longer occupied by patients. (5) Rigorous cleaning policies of the patient's area, including any items that might have come into contact with carriers, were implemented daily and whenever the patient was transferred or discharged. (6) Timely education and status updates were held between infection control staff and unit leadership, reinforcing hand hygiene and contact isolation measures regularly. (7) Multiple proactive monitoring of healthcare worker practices were performed by infection control unit staff and representatives of the hospital management, allowing for revisions and education. (8) Enhanced care rooms in the internal medicine wards were redesigned to create more isolation options for medically complicated patients. All prevention measures were coordinated by the Infection Control Unit and the hospital management. At the end of 2016, the hospital's infection control committee decided to apply the intervention components as a standard of care.

Statistical analysis

Demographic and clinical characteristics of patients before and after the intervention were compared the χ^2 test for dichotomous variables and the Student *t* test for continuous variables, using SPSS version 25 statistical software (IBM, Armonk, NY). Acquisition rates before and after the intervention were compared, and the *P* for trend was calculated using Winpepi version 11.65 software. Because this was a quality improvement intervention, it was not subject to approval by the institutional review board, nor did it require written informed consent.

Results

Patient demographic and clinical characteristics

From January 2014 through December 2018, cultures performed for 291 patients were positive for CRAB; of these, 210 (72.2%) were defined as hospital acquired: 141 before the intervention and 69 after the intervention. Among these patients, 64% were men, and the median age was 70.5 years. The most common source of positive cultures was sputum (41.9%), and 29 patients (10%) had bacteremia. In the cohort, the screening cultures of 11.3% of these patients were positive. Positive culture for CRAB appeared an average of 16.4 ± 15.8 days after hospitalization, and more than half of these new acquisitions occurred in less than 14 days. Of the new acquisitions, 35% were identified upon readmission within a month. A total of 80 patients (38.1%) died within 30 days. The median time from positive culture to death was 14 days. Patient characteristics, including age, sex distribution, and mortality rates were similar before and after the intervention (Table 1). Notably, there was a significant decrease in the percentage of patients with prior hospitalization between the 2 periods (51% vs 10%, respectively; $P = .001$).

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Table 1. Demographic and Clinical Characteristics of Patients With Acquired Carbapenem-Resistant *Acinetobacter baumanii* (CRAB) Before and After the Intervention

Characteristic	Total (n = 210)	Before intervention (n = 141)	After intervention (n = 69)	*P* Value
Age, median y	70.5	71	70	
Sex, male, no. (%)	135 (64.3)	92 (65.2)	43 (62.3)	.68
Culture source, no. (% from cultures)				.23
Sputum	96 (45.7)	60 (42.6)	36 (52.2)	
Wound	26 (12.4)	19 (13.5)	7 (10.1)	
Urine	29 (13.8)	23 (16.3)	6 (8.7)	
Blood	25 (11.9)	19 (13.5)	6 (8.7)	
Screening	25 (11.9)	13 (9.2)	12 (17.4)	
Acquisition department, no. (%)				.009
Internal medicine	96 (45.7)	58 (41.1)	38 (55.1)	.057
Surgery	9 (4.3)	8 (5.7)	1 (1.4)	.16
Medical-surgical ICU	33 (15.7)	29 (20.6)	4 (5.8)	.006
Medical ICU	34 (16.2)	22 (15.6)	12 (17.4)	.74
Prior hospitalization, no. (%)	79 (37.6)	72 (51)	7 (10.1)	<.001
Days from admission to acquisition, mean	16.4	15.35	18.5	.18
30-day mortality, no. (%)	80 (38.1)	55 (39)	25 (36.2)	.39

Note. ICU, intensive care unit.

Outbreak control

The CRAB acquisition rates decreased by 77%, from 1.3 per 1,000 admissions before the intervention (2014–2015) to 0.3 per 1,000 admissions after the intervention (2016–2018) ($P < .001$).

After implementing the intervention in January 2016, we observed steady decreases in acquisitions all over the hospital, year by year, starting at 1.18 acquisitions per 1,000 admissions in 2014 and declining to 0.16 acquisitions per 1,000 admissions in 2018. The decrease in rates reached statistical significance in 2017 (P for trend, <.0001) (Fig. 1). A parallel decrease occurred in cases hospitalized >30 days; thus, cases defined as not hospital acquired were also observed ($P = .004$).

Most of the acquisitions occurred in the internal medicine departments and in the ICUs. In 2014, 39 acquisitions occurred in internal medicine wards and 25 occurred in ICUs. In 2018, only 7 new acquisitions were detected in internal medicine wards and none in the ICUs ($P = .058$ for internal medicine and $P = .006$ for the ICU) (Fig. 2). The average compliance for CRAB screening through both phases was 90.9%.

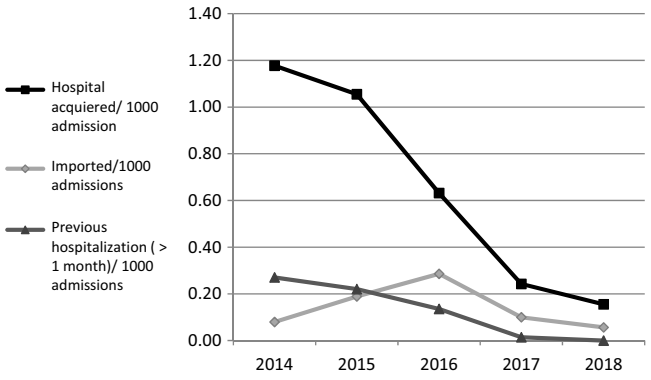

Fig. 1. Carbapenem-resistant *Acinetobacter baumanii* (CRAB) rates per 1,000 admissions 2014–2018.

Discussion

Following a hospital-wide intervention, the rate of CRAB acquisitions decreased significantly over a 3-year period, from 1.18 per 1,000 admissions to 0.16 per 1,000 admissions. After failing to control repeated secondary outbreaks all around the hospital, we decided to apply the components of the national guidelines for CRE[17] to CRAB, as well. The Israeli experience in controlling the spread of CRE is an example of the success of a coordinated, comprehensive infection control plan to reduce and contain acquisition of very resistant, fast-spreading bacteria. CRE in Israel has remained well controlled, whereas CRE has become endemic and continues to spread in many other countries.[19-21]

The key elements leading to the intervention's success were timely identification of CRAB infections and colonization, linked with effective isolation measures. Once identified, carrier patients were flagged, which enabled them to be immediately recognized through the hospital computer systems while they are hospitalized and/or upon transfer or readmission.

Notably, our definition of an acquired infection was broadly inclusive. Positive cultures upon admission were still considered to have been acquired at our hospital if the patients were readmitted within 30 days. This decision was taken based on studies showing that readmission within 30 days is a predictor for persistent carriage upon readmission for multidrug-resistant Enterobacteriaceae.[22]

With the decrease in acquisition rates, the number of readmitted patients carrying *A. baumannii* decreased accordingly. Even more importantly, parallel to the decrease in acquired cases, we witnessed a decrease in nonacquired cases, especially those

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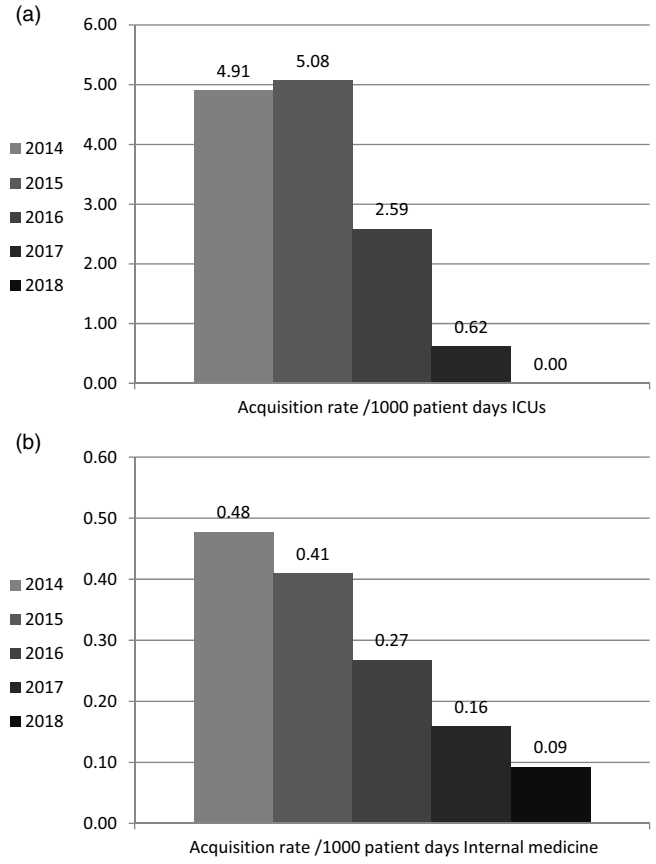

Fig. 2. Acquisition by department, 2014–2018. A. Intensive care units, B. Internal medicine wards.

readmitted after >30 days. Possible explanations for this observation are that these cases were unrecognized acquisitions at our hospital, and the intervention reduced these acquisitions as well. In support of our assumption, Marchaim et al[23] demonstrated a mean duration of *Acinetobacter* carriage of 17.5 months.

The results of the intervention might demonstrate regression to the mean, as might be exemplified in 2015 before the intervention. However, we do not think that this is the case here because the decline after the intervention persisted for >3 years, and we reached zero transmission in the ICUs in 2018. Furthermore, an increase in CRAB rates has been observed country-wide, and it continued in adjacent hospitals in 2017 and 2018.[24]

CRAB outbreaks are notoriously difficult to control, mostly due to carriage persistence[23] in parallel with the characteristic, prolonged hospitalization of carriers and survival of the bacteria in the environment. Our intervention, like others[25,26] demonstrates that, by using a multifaceted infection control program, marked reduction in CRAB acquisition, accompanied by interruption of CRAB transmission can be achieved. Such an intervention, demanding increased manpower and resources, could not have been executed without hospital and ward management support. Moreover, following the near elimination of CRAB, we decided, along with the hospital management, to keep all measures in place to avoid facing another full-blown outbreak in the future. To the best of our knowledge, this is the first report demonstrating this type of hospital-wide policy change regarding CRAB.

Successful interventions in reducing CRAB have been published previously,[25-27] but their focus was mostly in ICUs. One study from Korea described a hospital-wide intervention focusing on hand hygiene campaign and cohorting patients with CRAB.[28] They witnessed decreased CRAB acquisition but no effect on extended-spectrum β-lactamase (ESBL), *E. coli*, or *Klebsiella* rates. These investigators suggested that cohorting patients improved the ability to comply with infection control measures and had greater effect on reducing acquisition than did hand hygiene and standard precautions used for ESBL. Their observation, together with our experience with CRAB and the Israeli experience with CRE, suggest that the vertical approach, targeting a specific organism, might be the preferred way to deal with multidrug-resistant bacteria, over the horizontal approach that focuses on improving general measures such as hand hygiene and washing with chlorohexidine. This approach might be especially advantageous in places with limited single rooms and nursing resources. One potential consequence of focusing on a single multidrug-resistant organism (MDRO) is increased acquisition of other MDROs in parallel to the decrease of the target MDRO, a "squeezing the balloon" effect. This did not happen in our hospital. The infection rates of the 2 MDROs that we targeted (CRAB and CRE) are close to zero, while infections with other target MDROs, such MRSA and ESBL have remained constant, without similar decreases but without parallel increases either (data not shown).

This study has several limitations. Although CRAB isolates showed a similar pattern of antimicrobial susceptibility, suggesting that the source of the outbreak was indeed the ICU, molecular typing was not performed, which would have enabled a more thorough understanding of the evolution of the outbreak. Another limitation is that we screened for CRAB with rectal swabs only, which lowers the detection rate. This strategy was chosen to decrease workload and confusion of nursing staff, who routinely use rectal swabs for screening for other MDROs, such as CRE and VRE. Nevertheless, active surveillance is considered cost-effective and beneficial, even with lower sensitivity.[29] The study was also limited because it is likely that case finding in the period preceding the detection of the outbreak was incomplete. The study was therefore descriptive in nature. Finally, because multiple control strategies were used simultaneously, it was impossible to assess the independent contribution of each component separately.

Antibiotic stewardship has the potential to affect CRAB acquisition, as suggested by previous studies.[30] Since 1995, the hospital Infectious Diseases Unit has implemented a strict antibiotic stewardship program. There was no change in policy during the intervention.

In conclusion, this report is an example of a hospital-wide outbreak of CRAB, successfully and sustainably contained using the Israeli national CRE policy statement guidelines as a reference, leading to changes in hospital policy toward CRAB.

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References

1. Dijkshoorn L, Nemec A, Seifert H. An increasing threat in hospitals: multidrug-resistant *Acinetobacter baumannii*. *Nat Rev Microbiol* 2007;5: 939–951.
2. Karah N, Sundsfjord A, Towner K, Samuelsen O. Insights into the global molecular epidemiology of carbapenem non-susceptible clones of *Acinetobacter baumannii*. *Drug Resist Updat* 2012;15:237–247.

3. Peleg AY, Seifert H, Paterson DL. *Acinetobacter baumannii*: emergence of a successful pathogen. *Clin Microbiol Rev* 2008;21:538–582.
4. Agodi A, Voulgari E, Barchitta M, *et al.* Spread of a carbapenem- and colistin-resistant *Acinetobacter baumannii* ST2 clonal strain causing outbreaks in two Sicilian hospitals. *J Hosp Infect* 2014;86:260–266.
5. Towner KJ. *Acinetobacter*: an old friend, but a new enemy. *J Hosp Infect* 2009;73:355–363.
6. Magiorakos AP, Srinivasan A, Carey RB, *et al.* Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect* 2012;18:268–281.
7. Poirel L, Nordmann P. Carbapenem resistance in *Acinetobacter baumannii*: mechanisms and epidemiology. *Clin Microbiol Infect* 2006;12:826–836.
8. Kwon KT, Oh WS, Song JH, *et al.* Impact of imipenem resistance on mortality in patients with *Acinetobacter* bacteraemia. *J Antimicrob Chemother* 2007;59:525–530.
9. Playford EG, Craig JC, Iredell JR. Carbapenem-resistant *Acinetobacter baumannii* in intensive care unit patients: risk factors for acquisition, infection and their consequences. *J Hosp Infect* 2007;65:204–211.
10. Jawad A, Seifert H, Snelling AM, Heritage J, Hawkey PM. Survival of *Acinetobacter baumannii* on dry surfaces: comparison of outbreak and sporadic isolates. *J Clin Microbiol* 1998;36:1938–1941.
11. Kramer A, Schwebke I, Kampf G. How long do nosocomial pathogens persist on inanimate surfaces? A systematic review. *BMC Infect Dis* 2006; 6:130.
12. Bianco A, Quirino A, Giordano M, *et al.* Control of carbapenem-resistant *Acinetobacter baumannii* outbreak in an intensive care unit of a teaching hospital in southern Italy. *BMC Infect Dis* 2016;16:747.
13. Choi WS, Kim SH, Jeon EG, *et al.* Nosocomial outbreak of carbapenem-resistant *Acinetobacter baumannii* in intensive care units and successful outbreak control program. *J Korean Med Sci* 2010;25:999–1004.
14. Enfield KB, Huq NN, Gosseling MF, *et al.* Control of simultaneous outbreaks of carbapenemase-producing enterobacteriaceae and extensively drug-resistant *Acinetobacter baumannii* infection in an intensive care unit using interventions promoted in the Centers for Disease Control and Prevention 2012 carbapenemase-resistant Enterobacteriaceae toolkit. *Infect Control Hosp Epidemiol* 2014;35:810–817.
15. Gray AP, Allard R, Pare R, *et al.* Management of a hospital outbreak of extensively drug-resistant *Acinetobacter baumannii* using a multimodal intervention including daily chlorhexidine baths. *J Hosp Infect* 2016;93: 29–34.
16. Tacconelli E, Cataldo MA, Dancer SJ, *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 suppl 1:1–55.
17. Solter E, Adler A, Rubinovitch B, *et al.* Israeli national policy for carbapenem-resistant Enterobacteriaceae screening, carrier isolation and discontinuation of isolation. *Infect Control Hosp Epidemiol* 2018;39: 85–89.
18. Clinical and Laboratory Standard Institute. *Performance Standards for Antimicrobial Susceptibility Testing; Twenty-fifth Informational Supplement. CLSI Document M100-S25.* Wayne, PA: CLSI; 2015.
19. Potter RF, D'Souza AW, Dantas G. The rapid spread of carbapenem-resistant Enterobacteriaceae. *Drug Resist Updat* 2016;29:30–46.
20. van Duin D, Doi Y. The global epidemiology of carbapenemase-producing Enterobacteriaceae. *Virulence* 2017;8:460–469.
21. Yoo JH. The infinity war: how to cope with carbapenem-resistant Enterobacteriaceae. *J Korean Med Sci* 2018;33:e255.
22. Ciobotaro P, Flaks-Manov N, Oved M, *et al.* Predictors of persistent carbapenem-resistant enterobacteriaceae carriage upon readmission and score development. *Infect Control Hosp Epidemiol* 2016;37:188–196.
23. Marchaim D, Navon-Venezia S, Schwartz D, *et al.* Surveillance cultures and duration of carriage of multidrug-resistant *Acinetobacter baumannii*. *J Clin Microbiol* 2007;45:1551–1555.
24. Israeli National Center for Infection Control, Annual Report 2017, 2018. https://www.health.gov.il/UnitsOffice/HD/InfectionControl/Pages/Periodic_reports.aspx.
25. Ben-Chetrit E, Wiener-Well Y, Lesho E, *et al.* An intervention to control an ICU outbreak of carbapenem-resistant *Acinetobacter baumannii*: long-term impact for the ICU and hospital. *Crit Care* 2018;22:319.
26. Hong J, Jang OJ, Bak MH, *et al.* Management of carbapenem-resistant *Acinetobacter baumannii* epidemic in an intensive care unit using multifaceted intervention strategy. *Korean J Intern Med* 2018;33:1000–1007.
27. Garnacho-Montero J, Dimopoulos G, Poulakou G, *et al.* Task force on management and prevention of *Acinetobacter baumannii* infections in the ICU. *Intens Care Med* 2015;41:2057–2075.
28. Cho OH, Bak MH, Baek EH, Park KH, Kim S, Bae IG. Successful control of carbapenem-resistant *Acinetobacter baumannii* in a Korean university hospital: a 6-year perspective. *Am J Infect Control* 2014;42:976–979.
29. Coyle JR, Kaye KS, Taylor T, *et al.* Effectiveness and cost of implementing an active surveillance screening policy for *Acinetobacter baumannii*: a Monte Carlo simulation model. *Am J Infect Control* 2014;42:283–287.
30. Lin MF, Yang CM, Lin CH, Huang ML, Tu CC, Liou ML. Clinical features and molecular epidemiology of multidrug-resistant *Acinetobacter calcoaceticus–A. baumannii* complex in a regional teaching hospital in Taiwan. *Am J Infect Control* 2009;37:e1–e3.

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