

A Multifaceted Intervention to Reduce Pandrug-Resistant *Acinetobacter baumannii* Colonization and Infection in 3 Intensive Care Units in a Thai Tertiary Care Center: A 3-Year Study

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Background. We sought to determine the long-term effect of a multifaceted infection-control intervention to reduce the incidence of pandrug-resistant *Acinetobacter baumannii* infection in a Thai tertiary care center.

Methods. A 3-year, prospective, controlled, quasi-experimental study was conducted in medical intensive care, surgical intensive care, and coronary care units for a 1-year period before intervention (period 1), a 1-year period after intervention (period 2), and a 1-year follow-up period (period 3). The interventions in period 2 included strictly implementing contact isolation precautions and appropriate hand hygiene, active surveillance, cohorting patients who were colonized or infected with pandrug-resistant *A. baumannii*, and environmental cleaning with 1:100 sodium hypochlorite solution. All interventions were continued in period 3, but environmental cleaning solutions were changed to detergent and phenolic agents.

Results. Before the intervention, the rate of pandrug-resistant *A. baumannii* colonization and/or infection was 3.6 cases per 1000 patient-days. After the intervention, the rate of pandrug-resistant *A. baumannii* colonization and/or infection decreased by 66% in period 2 (to 1.2 cases per 1000 patient-days; $P < .001$) and by 76% in period 3 (to 0.85 cases per 1000 patient-days; $P < .001$). The monthly hospital antibiotic cost of treating pandrug-resistant *A. baumannii* colonization and/or infection and the hospitalization cost for each patient in the intervention units were also reduced by 36%–42% ($P < .001$) and 25%–36% ($P < .001$), respectively, during periods 2 and 3.

Conclusions. A multifaceted intervention featuring active surveillance and environmental cleaning resulted in sustained reductions in the rate of pandrug-resistant *A. baumannii* colonization and infection, the cost of antibiotic therapy, and the cost of hospitalization among intensive care unit patients in a developing country.

Pandrug-resistant (PDR) *Acinetobacter baumannii* has emerged as an important cause of both endemic nosocomial infections and epidemic outbreaks [1–4]. In Thailand, PDR *A. baumannii* has become an important cause of nosocomial infection, especially in intensive care units (ICUs) [5]. Outbreak investigations demonstrate that the main modes of transmission are environmental contamination and hand carriage by health

care workers (HCWs) [6–8]. Risk factors for PDR *A. baumannii* include use of broad-spectrum antibiotics, prolonged hospitalization, receipt of mechanical ventilation, being hospitalized in a trauma ICU, and the use of pulsatile lavage wound irrigation [9–14]. Therefore, strict infection-control measures and the rational use of antibiotics are crucial to prevent the spread of PDR *A. baumannii* [2, 8]. Although infection-control interventions to prevent PDR *A. baumannii* transmission during an outbreak have been reported [15], no study has evaluated the long-term impact of infection-control interventions designed to limit PDR *A. baumannii* infection and colonization.

At Thammasat University Hospital, from 1 January 2005 through 31 December 2005, an increase in the rate of PDR *A. baumannii* infection and colonization

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was identified in the medical ICU (MICU), surgical ICU (SICU) and coronary care unit (CCU) (to 3.6 cases per 1000 patient-days). Although the increase was not statistically significant, this represented a 42% increase in the rate of PDR *A. baumannii* infection and colonization, compared with the rate during the previous 12 months (2.1 cases per 1000 patient-days; $P = .10$). During this period (1 January 2005 through 31 December 2005), cultures of samples obtained from respiratory equipment and intravenous and other fluid solutions failed to identify a common source of infection. We sought to determine the long-term effect of multifaceted infection-control interventions, featuring active surveillance cultures (ASCs) and environmental cleaning, to prevent transmission of PDR *A. baumannii*.

PATIENTS AND METHODS

Setting and patients. Thammasat University Hospital is a 500-bed university hospital located in central Thailand. There are 3 ICUs, each of which has 8 beds. These are the MICU, SICU, and CCU, each of which has ~450 admissions per year. These ICUs are multibed open wards in which multidisciplinary teams provide patient care. There are ~35 HCWs caring for patients in each unit. Nurses and respiratory therapists do not rotate between ICUs. The same infectious disease consultant (IDC) evaluated patients in these units in all study periods. The estimated patient-to-nurse ratio in the ICUs was 2:1. The study population consisted of all consecutive patients admitted to the 3 ICUs from 1 January 2005 through 31 December 2007. The study consisted of a 12-month baseline observation period (1 January 2005–31 December 2005; period 1), followed by a 12-month intervention period (1 January 2006–31 December 2006; period 2) and a 12-month follow-up period (1 January 2007–31 December 2007; period 3). The intervention was performed in the MICU, SICU, and CCU. During the study period, basic infection-control measures, including hand hygiene and contact precautions, were standard practice to prevent nosocomial transmission of drug-resistant microorganisms in this hospital. An antibiotic-control program was established in this hospital in July 2004 for 4 major classes of antibiotics (third-generation cephalosporins, β -lactam/ β -lactamase inhibitors, glycopeptides, and carbapenems) [16]. The antibiotic-control program did not change during the study [17]. No other protocols aimed at influencing the rates of PDR *A. baumannii* were introduced during the study. The medical and nursing leadership of each unit and the patient-to-nurse ratios in the ICUs remained constant during the study period.

Definition and data collection. PDR *A. baumannii* was defined as an *A. baumannii* isolate that was resistant to all currently available systemic antibiotics, including cephalosporins, aztreonam, carbapenems, aminoglycosides, fluoroquinolones, and sulbactam (except polymyxin B). Bacterial isolation and antimicrobial susceptibility testing were performed in ac-

cordance with Clinical and Laboratory Standards Institute methodology [18]. Nosocomial infection was defined using Centers for Disease Control and Prevention definitions [19]. Nosocomial acquisition of PDR *A. baumannii* was defined as detection of this microorganism by ASC >48 h after ICU admission, following a negative ASC result obtained at ICU admission. Case patients were defined as patients with nosocomial colonization and/or infection due to PDR *A. baumannii* identified by clinical cultures >48 h after admission to the study ICUs. Sustained reduction was defined as a persistent reduction in any measured outcomes of interest. The antibiotic use density for inpatients was recorded as the total number of grams of the drug, and the value was converted into defined daily doses per 1000 patient-days, in accordance with the recommendations of the World Health Organization [20]. Data on the number of patient admissions and patient-days were supplied by the hospital's medical records database system.

In all units, PDR *A. baumannii* colonization and infection rates were prospectively tracked by the same infection-control specialist (ICS) throughout the study and were expressed as cases of PDR *A. baumannii* colonization and infection per 1000 patient-days. The data collected included patient demographic characteristics, underlying diseases, severity of illness (measured by Acute Physiology and Chronic Health Evaluation II [APACHE-II] score), the occurrence of PDR *A. baumannii* colonization and/or infection, compliance with infection-control processes (e.g., ASC and environmental cleaning), cost of antibiotics to treat PDR *A. baumannii* infection, and the cost of hospitalization. The use of antibiotics to treat PDR *A. baumannii* colonization and infection was determined by chart reviews conducted by an IDC after excluding other possible indications. The antibiotic use categories were modified from Kunin et al. [21] and were strictly observed using a checklist [16, 17]. Costs, rather than charges, were used for each patient. The cost accounting database uses a set-down allocation method to calculate costs, which include indirect, direct, and fixed costs. All patient charge codes received during the hospitalizations were recorded, and the departmental cost for each charge code was calculated on the basis of each department's actual cost components multiplied by the charges for that code, divided by the total departmental charges. Costs were summed across each department to provide total hospital costs for each hospitalization. Only hospital-associated costs were included in analysis; physician costs were not included. Antibiotic costs were calculated on the basis of the actual dosage given to the patients and were based on the purchase price to the institution, without administration costs. All costs were converted to US dollars at an exchange rate of 35 Thai baht to 1 US dollar.

Program design. During period 1 (1 January 2005–30 November 2005), an intervention team collected and analyzed baseline data; no specific intervention was performed and no

routine environmental cultures were obtained, apart from basic infection-control measures. From 1 December 2005 through 31 December 2005, feedback of baseline data was given to nursing staff and physicians in all ICUs by the intervention team, and an action plan was developed. During period 2, infection-control measures included: (1) implementation of enhanced contact isolation precautions (i.e., strict adherence to hand hygiene protocol before and after patient care and donning of gowns and gloves before patient care), (2) ASCs for PDR *A. baumannii*, (3) cohorting patients with PDR *A. baumannii* in a single section of the unit, and (4) environmental cleaning with 1:100 sodium hypochlorite solution. Similar infection-control measures were continued during period 3. Hand hygiene was promoted during periods 2 and 3 using educational sessions (performed every 4 months), posters to encourage hand hygiene with alcohol gel, and monthly feedback of handwashing compliance and PDR *A. baumannii* colonization and infection rates. Environmental cleaning with 1:100 sodium hypochlorite solution was performed on bed rails, sinks, overbed tables, infusion pumps, and surrounding counter tops. Daily environmental cleaning with 1:100 sodium hypochlorite solution was performed during the first 6 months of period 2 and was replaced by cleaning with detergent and phenolic agents (for surface contaminated with body fluid and/or blood) until the end of period 3. Because the optimum anatomical site to screen for PDR *A. baumannii* carriage is not known, ASCs for PDR *A. baumannii* were performed using surveillance cultures of tracheal aspirates and rectal swabs (if culture of tracheal aspirate specimens had negative results) on day 0, day 7, and every week until discharge from the ICU for all patients who were admitted to the intervention units. Contact isolation was employed for all patients with results positive for PDR *A. baumannii* (identified either by ASC or clinical culture) and for patients who had been recently discharged from the ICU who had culture results positive for PDR *A. baumannii* until there was evidence of clearance (defined as 3 culture-negative specimens obtained from sites from which culture-positive specimens had previously been obtained). All basic infection-control measures (i.e., adherence to hand hygiene before and after patient care and donning of gowns and gloves before patient care) were continuously monitored using standardized observation forms during period 3. All patients in these ICUs were intubated. The intervention team included a representative from the hospital administration, an IDC, a clinical microbiologist, ICU attending physicians and chief nurses from intervention units, 2 ICSs, and a hospital epidemiologist.

Monitoring adherence to infection-control measures. Adherence to infection-control measures was prospectively monitored in all units by the same ICS throughout the study. The ICS observed housekeepers cleaning beds throughout the study, including on weekends and/or on the night shift. We

noted whether environmental sites (e.g., bed rails, over-bed tables, infusion pumps, clean countertops, and soiled countertops) were cleaned and recorded the results as “cleaned (during observation),” “not cleaned (during observation),” “not applicable” (i.e., item not present), or “not observed.” Per week, the fraction of items scored as “cleaned” and “not cleaned” was calculated. Hand hygiene observations were made by the same ICS in each unit at various times of day. Hand hygiene observations began when a HCW entered the intervention unit and was observed in an activity that involved contact with a patient or their environment and ended when that HCW completed the activity. Monitored variables included hand hygiene (with soap and water or with alcohol gel) before and after contact with the patient or environment, plus donning gowns and gloves for interacting with patients who were in contact isolation.

Statistical analysis. Categorical variables were compared using the χ^2 test or Fisher’s exact test, as appropriate. Normally distributed continuous variables were expressed as means (\pm SDs). Student’s *t* test was used to compare continuous variables. Trend analysis was performed to evaluate the overall pattern of changes on outcomes of interest over time using interrupted time series, with segmented regression analysis performed using SPSS, version 12.0 (SPSS). All tests were 2-tailed. $P < .05$ was considered to be statistically significant.

RESULTS

Patient demographic characteristics. There were 4071 patients enrolled during the entire study period (1363 patients in the MICU, 1462 in the SICU, and 1246 in the CCU). The mean age of the patients was 51 years (range, 15–89 years). The patient characteristics, underlying diseases, APACHE-II score, duration of hospital stay, number of admissions per unit, and number of patients who were placed on contact isolation are summarized in table 1. There were no significant differences in patient characteristics between the study periods.

Active surveillance and antimicrobial use. A total of 6965 tracheal aspirate cultures and rectal swab cultures were obtained at ICU admission in all intervention units. Ninety-five percent of the patients’ medical records (2578 of 2714 patients) had documentation of ASCs being ordered (in all cases, within 4 h after ICU admission). Eighty-eight percent of patients admitted to the intervention units (2388 of 2714 patients) had >1 ASC performed (326 [12%] did not have an ASC performed because of a hospital stay <24 h in duration), and 1927 (71%) had >1 ASC performed. Daily proportions of patients in the intervention units who were colonized with PDR *A. baumannii* ranged from 4% to 50%. The mean colonization pressure (\pm SD) decreased during the 3 study periods, from 0.36 ± 0.18 patients per day in period 1 to 0.24 ± 0.12 patients per day in period 2 ($P < .001$) and 0.12 ± 0.05 patients per day in

Table 1. Characteristics of patients with pandrug-resistant *Acinetobacter baumannii* infection and colonization in intervention intensive care units, by study period.

Characteristic	Period 1 (n = 1357)	Period 2 (n = 1273)	Period 3 (n = 1441)
Age, mean years ± SD	51 ± 9	53 ± 8.4	50 ± 9.1
Female sex	650 (48)	606 (48)	700 (49)
Source of patient			
Home	814 (60)	738 (58)	879 (61)
Other unit in the hospital	339 (25)	331 (26)	331 (23)
Transfer from outside hospital	204 (15)	204 (16)	231 (16)
Underlying disease			
Cardiovascular disease	204 (15)	216 (17)	231 (16)
Gastrointestinal disease	366 (27)	356 (28)	365 (25)
Diabetes	475 (35)	344 (27)	490 (34)
Cerebrovascular disease	204 (15)	178 (14)	202 (14)
Immunocompromised state	244 (18)	204 (16)	259 (18)
Malignancy	136 (10)	102 (8)	159 (11)
Source of <i>Acinetobacter baumannii</i> infection and colonization			
Bloodstream	14/53 (26)	4/17 (24)	3/13 (23)
Urinary tract	4/53 (8)	1/17 (6)	1/13 (8)
Pulmonary	31/53 (58)	11/17 (65)	8/13 (62)
Other ^a	4/53 (8)	1/17 (6)	1/13 (8)
Admission rate, mean no. of patients admitted per day	3.7	3.5	3.9
APACHE-II score, mean score ± SD	17 ± 5	17 ± 4	18 ± 5
Total no. of patient-days	14,650	14,456	15,410
Daily occupancy, mean patient-days ± SD ^b	20.2 ± 1.4	21 ± 2.4	20 ± 2.4
Duration of hospital stay, mean days ± SD	10.4 ± 4.7	11.5 ± 3.5	10.6 ± 3.5
Patients with contact isolation, mean no. of patients per day ± SD ^c	8.8 ± 1.9	5.5 ± 2.1 ^d	3.8 ± 1.2 ^d

NOTE. Data are no. (%) of patients, unless otherwise indicated. Period 1 was the baseline period (1 January 2005 through 31 December 2005), period 2 was the intervention period (1 January 2006 through 31 December 2006), and period 3 was the follow-up period (1 January 2007 through 31 December 2007). Categorical variables were compared using the χ^2 or Fisher's exact test, as appropriate. A 2-tailed Student's *t* test was performed to compare continuous variables. APACHE, Acute Physiology and Chronic Health Evaluation.

^a Includes skin and soft-tissue infections, intra-abdominal infections, and CNS infections.

^b Because combined occupancy was counted, daily occupancy was >8 patient-days for each of the 8-bed intervention units.

^c The statistically significant decrease in contact isolation days in the intervention units over time ($P = .02$) occurred because of reductions in the prevalence of multidrug-resistant *A. baumannii* infection and colonization.

^d $P < .05$, compared with the intervention units during the same period.

period 3 ($P < .001$) (table 2). Daily admission rates of patients colonized or infected with PDR *A. baumannii* were 0.25 patients per day in period 1, 0.20 patients per day in period 2, and 0.21 patients per day in period 3 ($P = .45$). The rate of PDR *A. baumannii* acquisition decreased from 15.9 isolates per 1000 patient-days at-risk in period 2 to 11.9 isolates per 1000 patient-days at-risk in period 3 ($P = .36$). There was no difference between any of the units with respect to the antimicrobial prescribing pattern throughout the study.

Rate of PDR *A. baumannii* infection and colonization.

During period 1, there were 53 cases of PDR *A. baumannii* colonization and infection (3.6 cases per 1000 patient-days) in all ICUs. During period 2, the rate of PDR *A. baumannii* colonization and infection decreased by 66% (17 cases; 1.2 cases per 1000 patient-days; $P < .001$). This rate was further reduced by 76% (13 cases; 0.85 cases per 1000 patient-days; $P < .001$)

in period 3 (figure 1). Rates of PDR *A. baumannii* colonization and infection in individual ICUs are given in table 3. Segmented regression analysis of the PDR *A. baumannii* colonization and infection rates are given in table 4.

Cost of surveillance culture versus the monthly cost of hospitalization and antibiotics for treatment of PDR *A. baumannii* infection.

The total cost for ASCs was \$19,862 for the entire study. The intervention resulted in a significant reduction in the total cost of antibiotics used to treat PDR *A. baumannii* infection and in the cost of hospitalization (table 2). Compared with the costs in period 1, the monthly hospital antibiotic costs to treat PDR *A. baumannii* infection and the hospitalization costs for each patient in the intervention units in periods 2 and 3 were reduced by 36%–42% (mean cost of antibiotics, \$3762 vs. \$1722 vs. \$1278; $P < .001$) and 25%–36% (mean cost of hospitalization, \$366 vs. \$253 vs. \$204; $P < .001$)

Table 2. Patients colonized or infected with pandrug-resistant (PDR) *Acinetobacter baumannii*, infection-control compliance monitoring, and outcomes in intervention intensive care units.

Variable	Period 1	Period 2	Period 3
Daily admission rate for patients with PDR <i>A. baumannii</i> infection of colonization, no. of cases per day	0.25	0.20	0.21
Ratio of PDR <i>A. baumannii</i> infection to colonization to acquisition	1:2.7:NA	1:4.2:6.1	1:5.2:6.0
No. of patient-days at risk for PDR <i>A. baumannii</i> infection or colonization	7404	6615	6741
Daily colonization pressure ^a , mean value \pm SD	0.36 \pm 0.18	0.24 \pm 0.12 ^b	0.12 \pm 0.05 ^b
Environmental cleaning			
No. of observations	...	166	165
Mean no. of observation per week \pm SD	...	3 \pm 0.6	3 \pm 0.4
Environmental cleaning rate ^c , mean \pm SD	...	0.85 \pm 0.08	0.83 \pm 0.09
Hand hygiene adherence			
No. of observations	154	166	165
Hand hygiene adherence rate before and after contact ^d , mean \pm SD	0.31 \pm 0.07	0.75 \pm 0.08 ^b	0.54 \pm 0.10 ^b
Hand hygiene adherence rate before and after contact and glove and gown use, mean \pm SD	0.24 \pm 0.02	0.63 \pm 0.02 ^b	0.51 \pm 0.09 ^b
Outcomes			
Rate of PDR <i>A. baumannii</i> acquisitions, isolate per 1000 patient-days at-risk	...	15.9	11.9
Rate of PDR <i>A. baumannii</i> infection and colonization (/1000 patient-days)	3.6	1.2 ^b	0.85 ^b
Monthly antibiotic cost for PDR <i>A. baumannii</i> treatment (USD) ^e	3762 \pm 605	1722 \pm 96 ^b	1278 \pm 87 ^b
Hospitalization cost for each patient (USD) ^e	366 \pm 100	252 \pm 96 ^b	204 \pm 88 ^b

NOTE. *P* values are given for comparisons of period 1 to periods 2 or 3. Period 1 was the baseline period (1 January 2005 through 31 December 2005), period 2 was the intervention period (1 January 2006 through 31 December 2006), and period 3 was the follow-up period (1 January 2007 through 31 December 2007). NA, not applicable.

^a Daily colonization pressure is defined as the prevalence of patients colonized with PDR *A. baumannii* each day.

^b *P* < .05, compared with period 1.

^c Environmental cleaning rate is defined as the number of sites cleaned/total no. of sites observed.

^d Hand hygiene adherence rate is defined as the no. of observations confirming adherence to hand hygiene requirements/no. of observations.

^e Estimated conversion rate, 35 baht to 1 US dollar.

.001), respectively. There were no antibiotic-related cost-cutting measures introduced during the study period.

DISCUSSION

This study showed that a multifaceted infection-control intervention can dramatically decrease the long-term incidence of PDR *A. baumannii* infection and colonization, the hospital cost of antibiotics for treatment of PDR *A. baumannii* infection, and the cost of hospitalization. The change in slope without a change in intercept in period 2 versus period 1 and in period 3 versus period 2 indicates a gradual rather than a sudden decrease in PDR *A. baumannii* infection and colonization. This intervention was well-accepted by housekeepers and intensive care HCWs and was sustained for 2 years.

Infections caused by multidrug-resistant (MDR) *A. baumannii*, particularly during outbreaks, usually represent the “iceberg phenomenon” [11], in which ratios of infection to colonization range from 1:3.5 to 1:12 [15, 22, 23]. In our study, we identified an infection-to-colonization ratio of 1:2.7 in the preintervention period. This ratio was reduced to 1:4.2 during period 2 and 1:5.2 during period 3, despite ongoing admission of patients with PDR *A. baumannii* infection and colonization to the ICUs and only moderate rates of adherence to proper hand hygiene. This study supports the effectiveness of ASCs to help control MDR *A. baumannii* infection and colonization in ICUs, as has been described elsewhere [11, 24].

Survival of *Acinetobacter* species on environmental surfaces may be an important determinant of transmission [25]. Pre-

vious studies have reported isolation of *Acinetobacter* species from environmental sites in ICUs with high rates of endemic colonization or during outbreaks [26–28]. The role of environmental cleaning in controlling MDR *A. baumannii* has also been emphasized in previous outbreaks of MDR *A. baumannii* infection [15, 25, 29–31]. As a result, environmental cleaning has been emphasized as one of the important parts of an effective infection-control strategy. The rationale for using sodium hypochlorite for environmental cleaning in our study was based on the fact that (1) several studies have used 1:100 sodium hypochlorite to control MDR *A. baumannii* outbreaks successfully [29–33], (2) existing data suggested that cleaning floors with either detergent or disinfectant did not affect nosocomial infection rates [34], and (3) a study reported that a quaternary ammonium compound was inadequate for disinfecting bathrooms and toilets [29]. In contrast, studies have suggested that hypochlorite-based environmental cleaning can be associated with a reduced incidence of hospital-acquired *Clostridium difficile* infection [35–37]. Although *A. baumannii* does not form spores, the persistent survival of this pathogen when desiccated is partly analogous to that of *C. difficile* [38]. However, because of the impact of sodium hypochlorite solution on HCW's skin and hospital surfaces [39], its use was discontinued after 6 months, during period 2, after the rate of PDR *A. baumannii* infection decreased significantly (figure 1).

Other important infection-control measures in our study included cohorting, ASCs, enhanced contact isolation, and improvement in hand hygiene adherence. Notably, adherence to hand hygiene improved early in period 2, perhaps as a result of the Hawthorne effect, but decreased slightly during period

Table 3. Rate of pandrug-resistant *Acinetobacter baumannii* infection and colonization among intervention intensive care units.

Unit	No. of cases per 1000 patient-days		
	Period 1	Period 2	Period 3
Medical intensive care	1.4	0.5 ^a	0.4 ^a
Surgical intensive care	1.2	0.45 ^a	0.25 ^a
Coronary care	1.0	0.25 ^a	0.2 ^a

NOTE. Period 1 was the baseline period (1 January 2005 through 31 December 2005). Period 2 was the intervention period (1 January 2006 through 31 December 2006). Period 3 was the follow-up period (1 January 2007 through 31 December 2007).

^a $P < .05$, compared with period 1.

3, even with continuous education and feedback regarding hand hygiene and PDR *A. baumannii* infection rates to HCWs. Despite only moderate hand hygiene adherence rates and continuing admission of patients with PDR *A. baumannii* colonization and infection, the infection and colonization rate decreased significantly during period 2 and remained low during period 3. This study reemphasizes the role of multifaceted infection-control interventions (e.g., ASCs, environmental cleaning, contact isolation, and hand hygiene) to control the spread of PDR *A. baumannii*. The difficulty of achieving high levels of hand hygiene adherence in ICUs, which have high workloads, is consistent with the findings of previous studies [40, 41].

There are some limitations to this study. This was not a randomized trial; therefore, other unmeasured factors might have coincided with the intervention, resulting in lower infec-

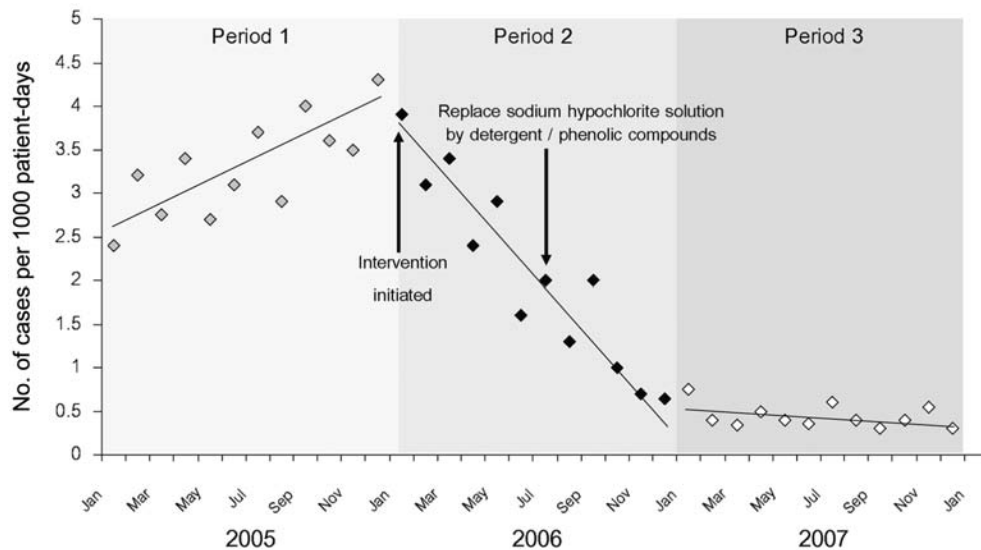


Figure 1. Rates of pandrug-resistant *Acinetobacter baumannii* infection and colonization in 3 intensive care units. Period 1 was the baseline period (1 January 2005 through 31 December 2005), period 2 was the intervention period (1 January 2006 through 31 December 2006), and period 3 was the follow-up period (1 January 2007 through 31 December 2007).

Table 4. Change in rates of pandrug-resistant *Acinetobacter baumannii* infection and colonization in intervention intensive care units from interrupted time series analysis, with segmented regression analysis during the entire duration of the study.

Period comparison, hospital unit	Change in γ -intercept ^a		Change in slope ^b	
	Mean value (95% CI)	P	Mean value (95% CI)	P
Period 2 vs. period 1				
All units	-2.94 (-14.4 to 4.6)	.46	-3.36 (-5.45 to -1.14)	<.001
Medical intensive care	-3.81 (-12.1 to 7.3)	.51	-2.14 (-3.36 to -0.11)	<.001
Surgical intensive care	-2.29 (-11.9 to 3.7)	.63	-1.71 (-2.12 to -0.21)	<.001
Coronary care unit	-3.1 (-10.5 to 4.6)	.43	-1.62 (-2.04 to -0.24)	<.001
Period 3 vs. period 2				
All units	-2.1 (-12.4 to 3.6)	.36	-1.45 (-6.5 to -0.10)	<.001
Medical intensive care	-2.4 (-10.1 to 6.9)	.41	-1.15 (-5.6 to 1.4)	.20
Surgical intensive care	-1.0 (-8 to 5.3)	.54	-0.98 (-1.4 to 2.1)	.25
Coronary care	-1.5 (-6 to 4.6)	.38	-0.64 (-1.81 to 3.6)	.38

NOTE. Period 1 was a baseline period (1 January 2005 through 31 December 2005). Period 2 was the intervention period (1 January 2006 through 31 December 2006). Period 3 was the follow-up period (1 January 2007 through 31 December 2007).

^a The calculation of the sudden change γ -intercept (immediate change) is based on the difference between the intercept of the last point in the preintervention regression line and the first point in the postintervention line.

^b The change in slope was calculated as the magnitude of change from the preintervention slope to the postintervention slope.

tion and colonization rates. However, this bias is conservative, because we collected the data for 12 months in each period to control for possible seasonal variations, and the patients' characteristics in each period were comparable. Because all ICUs in the hospital experienced an increase in PDR *A. baumannii* infection and colonization rates, a comparable control ICU could not be examined. The lack of environmental cultures and of cultures of swab samples from HCWs' hands make it difficult to prove the significance of environmental contamination or hand contamination in cross-transmission of PDR *A. baumannii* in settings of endemicity. Because this intervention was performed at a single medical center, these results may not be applicable to other hospitals. However, the achievement of similar effects in other settings suggests that the intervention may be generalizable to other facilities [14, 25, 29–33]. Because several interventions were made simultaneously, it is difficult to know which of the specific interventions was the most effective in controlling PDR *A. baumannii* infection and colonization. Because the IDC responsible for the implementation of this intervention also reviewed and recorded the use of antibiotics for treatment of PDR *A. baumannii* infection and colonization, bias may have been introduced, but the bias is conservative, because the IDC was experienced and consistently used explicit criteria and a checklist to monitor antibiotic use. Lastly, this intervention was labor intensive, time-consuming for the ICS, and required resources for ASC.

Despite these limitations, our study has broadened the support for the efficacy of multifaceted infection-control interventions to control PDR *A. baumannii* infection in a resource-limited setting. Because treatment of PDR *A. baumannii*

infection can be associated with high morbidity, mortality, and costs, these basic infection-control strategies remain key to the control of PDR *A. baumannii* infection in developing countries.

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References

1. Hsueh PR, Teng LJ, Chen CY, et al. Pandrug-resistant *Acinetobacter baumannii* causing nosocomial infections in a university hospital, Taiwan. *Emerg Infect Dis* 2002; 8:827–32.
2. Kuo LC, Yu CJ, Lee LN, et al. Clinical features of pandrug-resistant *Acinetobacter baumannii* bacteremia at a university hospital in Taiwan. *J Formos Med Assoc* 2003; 102:601–6.
3. Falagas ME, Bliziotis IA. Pandrug-resistant Gram-negative bacteria: the dawn of the post-antibiotic era? *Int J Antimicrob Agents* 2007; 29: 630–6.
4. Falagas ME, Rafailidis PI. Attributable mortality of *Acinetobacter baumannii*: no longer a controversial issue. *Crit Care* 2007; 11:134.
5. Dejsirilert S, Apisarnthanarak A, Kitphati R, et al. The status of antimicrobial resistance in Thailand among gram-negative pathogens in bloodstream infections: NARST data, 2000–2003 [abstract FP-A-3]. In: Program and abstracts of the 9th Western Pacific Congress on Chemotherapy and Infectious Diseases (Bangkok). Bangkok: Medinfo GD, 2004:185.
6. Lortholary O, Fagon JY, Hoi AB, et al. Nosocomial acquisition of

- multiresistant *Acinetobacter baumannii*: risk factors and prognosis. *Clin Infect Dis* **1995**; 20:790–6.
7. Koeleman JG, Parlevliet GA, Dijkshoorn L, Savelkoul PH, Vandembroucke-Grauls CM. Nosocomial outbreak of multi-resistant *Acinetobacter baumannii* on a surgical ward: epidemiology and risk factors for acquisition. *J Hosp Infect* **1997**; 37:113–23.
 8. Wang SH, Sheng WH, Chang YY, et al. Healthcare-associated outbreak due to pan-drug resistant *Acinetobacter baumannii* in a surgical intensive care unit. *J Hosp Infect* **2003**; 53:97–102.
 9. El Shafie SS, Alishaq M, Leni Garcia M. Investigation of an outbreak of multidrug-resistant *Acinetobacter baumannii* in trauma intensive care unit. *J Hosp Infect* **2004**; 56:101–5.
 10. Villers D, Espaze E, Coste-Burel M, et al. Nosocomial *Acinetobacter baumannii* infections: microbiological and clinical epidemiology. *Ann Intern Med* **1998**; 129:182–9.
 11. Abbo A, Navon-Venezia S, Hammer-Muntz O, et al. Multidrug-resistant *Acinetobacter baumannii*. *Emerg Infect Dis* **2005**; 11:22–9.
 12. Maragakis LL, Cosgrove SE, Song X, et al. An outbreak of multidrug-resistant *Acinetobacter baumannii* associated with pulsatile lavage wound treatment. *JAMA* **2004**; 292:3006–11.
 13. Husni RN, Goldstein LS, Arroliga AC, et al. Risk factors for an outbreak of multi-drug-resistant *Acinetobacter* nosocomial pneumonia among intubated patients. *Chest* **1999**; 115:1378–82.
 14. Mulin B, Talon D, Viel JF, et al. Risk factors for nosocomial colonization with multiresistant *Acinetobacter baumannii*. *Eur J Clin Microbiol Infect Dis* **1995**; 14:569–76.
 15. Chan PC, Huang LM, Lin HC, et al. Control of an outbreak of pandrug-resistant *Acinetobacter baumannii* colonization and infection in a neonatal intensive care unit. *Infect Control Hosp Epidemiol* **2007**; 28:423–9.
 16. Apisarnthanarak A, Danchaiwijitr S, Khawcharoenporn T, et al. Effectiveness of education and an antibiotic-control program in a tertiary care hospital in Thailand. *Clin Infect Dis* **2006**; 42:768–75.
 17. Apisarnthanarak A, Srichomkwun P, Sutepvarnon A, Bailey TC, Fraser VJ. The long-term outcomes of an antibiotic control program with and without education. *Clin Infect Dis* **2007**; 45:1245–7.
 18. Clinical and Laboratory Standards Institute (CLSI). Performance standards for antimicrobial susceptibility testing: seventeenth informational supplement. Wayne, PA: CLSI, 2007:M100-S17.
 19. Horan TC, Gaynes RP. Surveillance of nosocomial infections. In: Mayhall CG, ed. *Hospital epidemiology and infection control*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 2004:1659–1702.
 20. Maxwell M, Heaney D, Howie JG, Noble S. General practice fund holding: observations on prescribing patterns and costs during the defined daily dose method. *BMJ* **1993**; 307:1190–4.
 21. Kunin CM, Tupasi T, Craig WA. Use of antibiotics; a brief exposition of the problem and some tentative solutions. *Ann Intern Med* **1973**; 79:555–60.
 22. Schloesser RL, Laufkoetter EA, Lehnert T, Mietens C. An outbreak of *Acinetobacter calcoaceticus* infection in a neonatal care unit. *Infection* **1990**; 18:230–3.
 23. McDonald LC, Walker M, Carson L, et al. Outbreak of *Acinetobacter* spp. bloodstream infections in a nursery associated with contaminated aerosols and air conditioners. *Pediatr Infect Dis J* **1998**; 17:716–22.
 24. Webster CA, Crowe M, Humphreys H, Towner KJ. Surveillance of an adult intensive care unit for long-term persistence of a multi-resistant strain of *Acinetobacter baumannii*. *Eur J Clin Microbiol Infect Dis* **1998**; 17:171–6.
 25. Wilks M, Wilson A, Warwick S, et al. Control of an outbreak of multidrug-resistant *Acinetobacter baumannii-calcoaceticus* colonization and infection in an intensive care unit (ICU) without closing the ICU or placing patients in isolation. *Infect Control Hosp Epidemiol* **2006**; 27:654–8.
 26. Villegas MV, Hartstein AI. *Acinetobacter* outbreaks, 1977–2000. *Infect Control Hosp Epidemiol* **2003**; 24:284–95.
 27. Houang ET, Chu YW, Leung CM, et al. Epidemiology and infection control implications of *Acinetobacter* spp. in Hong Kong. *J Clin Microbiol* **2001**; 39:228–34.
 28. Catalano M, Quelle LS, JERIC PE, Di Martino A, Maimone SM. Survival of *Acinetobacter baumannii* on bed rails during an outbreak and during sporadic cases. *J Hosp Infect* **1999**; 42:27–35.
 29. Denton M, Wilcox MH, Parnell P, et al. Role of environmental cleaning in controlling an outbreak of *Acinetobacter baumannii* on a neurosurgical intensive care unit. *Intensive Crit Care Nurs* **2005**; 21:94–8.
 30. Denton M, Wilcox MH, Parnell P, et al. Role of environmental cleaning in controlling an outbreak of *Acinetobacter baumannii* on a neurosurgical intensive care unit. *J Hosp Infect* **2004**; 56:106–10.
 31. Pimental JD, Low J, Styles K, Harris OC, Hughes A, Athan E. Control of an outbreak of multi-drug resistant *Acinetobacter baumannii* in an intensive care unit and a surgical unit. *J Hosp Infect* **2005**; 59:249–53.
 32. Aygün G, Demirkiran O, Utku T, et al. Environmental contamination during a carbapenem-resistant *Acinetobacter baumannii* outbreak in an intensive care unit. *J Hosp Infect* **2002**; 52:259–62.
 33. Das I, Lambert P, Hill D, Noy M, Bion J, Elliott T. Carbapenem-resistant *Acinetobacter* and role of curtains in an outbreak in intensive care units. *J Hosp Infect* **2002**; 50:110–4.
 34. Danforth D, Nicolle LE, Hume K, Alfieri N, Sims H. Nosocomial infections on nursing units with floors cleaned with a disinfectant compared with detergent. *J Hosp Infect* **1987**; 10:229–35.
 35. Mayfield JL, Leet T, Miller J, Mundy LM. Environmental control to reduce transmission of *Clostridium difficile*. *Clin Infect Dis* **2000**; 31:995–1000.
 36. Apisarnthanarak A, Zack JE, Mayfield JL, et al. Effectiveness of environmental and infection control programs to reduce transmission of *Clostridium difficile*. *Clin Infect Dis* **2004**; 39:601–2.
 37. Wilcox MH, Fawley WN, Wigglesworth N, Parnell P, Verity P, Freeman J. Comparison of the effect of detergent versus hypochlorite cleaning on environmental contamination and incidence of *Clostridium difficile* infection. *J Hosp Infect* **2003**; 54:109–14.
 38. 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**; 36:1938–41.
 39. Rutala WA, Weber DJ. Disinfection and sterilization in health care facilities: what clinicians need to know. *Clin Infect Dis* **2004**; 39:702–9.
 40. Boyce JM, Pittet D. Guideline for hand hygiene in health-care settings. Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA Hand Hygiene Task Force. Society for Healthcare Epidemiology of America/Association for Professionals in Infection Control/Infectious Diseases Society of America. *MMWR Recomm Rep* **2002**; 51(RR-16):1–45; CE1–4.
 41. Pittet D, Simon A, Hugonnet S, Pessoa-Silva CL, Sauvan V, Perneger TV. Hand hygiene among physicians: performance, beliefs, and perceptions. *Ann Intern Med* **2004**; 141:1–8.