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Prevention of Colonization and Infection by *Klebsiella pneumoniae* Carbapenemase–Producing Enterobacteriaceae in Long-term Acute-Care Hospitals

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Abstract

Background.—*Klebsiella pneumoniae* carbapenemase–producing Enterobacteriaceae (hereafter "KPC") are an increasing threat to healthcare institutions. Long-term acute-care hospitals (LTACHs) have especially high prevalence of KPC.

Methods.—Using a stepped-wedge design, we tested whether a bundled intervention (screening patients for KPC rectal colonization upon admission and every other week; contact isolation and geographic separation of KPC-positive patients in ward cohorts or single rooms; bathing all patients daily with chlorhexidine gluconate; and healthcare-worker education and adherence monitoring) would reduce colonization and infection due to KPC in 4 LTACHs with high endemic KPC prevalence. The study was conducted between 1 February 2010 and 30 June 2013; 3894 patients were enrolled during the preintervention period (lasting from 16 to 29 months), and 2951 patients were enrolled during the intervention period (lasting from 12 to 19 months).

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Results.—KPC colonization prevalence was stable during preintervention (average, 45.8%; 95% confidence interval [CI], 42.1%–49.5%), declined early during intervention, then reached a plateau (34.3%; 95% CI, 32.4%–36.2%; $P < .001$ for exponential decline). During intervention, KPC admission prevalence remained high (average, 20.6%, 95% CI, 19.1%–22.3%). The incidence rate of KPC colonization fell during intervention, from 4 to 2 acquisitions per 100 patient-weeks ($P = .004$ for linear decline). Compared to preintervention, average rates of clinical outcomes declined during intervention: KPC in any clinical culture (3.7 to 2.5/1000 patient-days; $P = .001$), KPC bacteremia (0.9 to 0.4/1000 patient-days; $P = .008$), all-cause bacteremia (11.2 to 7.6/1000 patient-days; $P = .006$) and blood culture contamination (4.9 to 2.3/1000 patient-days; $P = .03$).

Conclusions.—A bundled intervention was associated with clinically important and statistically significant reductions in KPC colonization, KPC infection, all-cause bacteremia, and blood culture contamination in a high-risk LTACH population.

Keywords

carbapenem-resistant Enterobacteriaceae; *Klebsiella pneumoniae* carbapenemase; long-term acute-care hospital; infection prevention; healthcare-associated infection

Healthcare-associated infections due to antibiotic-resistant bacteria often fail to respond to conventional therapy, resulting in greater risk of death and higher costs [1, 2]. Carbapenem-resistant Enterobacteriaceae (CRE) may be the most serious contemporary antibiotic resistance threat because of the number of different resistance mechanisms [3], concomitant resistance to all or nearly all alternative antibiotics [4], high attributable mortality associated with invasive infection [5, 6], and the ability of these pathogens to spread rapidly across geographic regions [7-9]. In 2013, the Centers for Disease Control and Prevention declared CRE an immediate public health threat requiring urgent and aggressive action [10].

Klebsiella pneumoniae carbapenemase-producing Enterobacteriaceae (hereafter “KPC”) are the most common CRE worldwide [3]. Colonization with KPC usually precedes infection; patients acquire colonization in healthcare settings, presumably via cross-transmission after breaches in infection prevention measures such as healthcare-worker hand hygiene [11]. Transfer of KPC-positive patients between healthcare facilities further enables dispersion of KPC throughout a geographic region [8, 12]. Thus, coordinated regional interventions have been promoted as necessary to achieve durable control [9, 13].

Long-term acute care hospitals (LTACHs) and other post-acute-care facilities, whose populations are at high risk for colonization and infection with multidrug-resistant bacteria, bear a disproportionate burden of KPC and have been shown to be a major contributor to its dissemination in multiple locales [8, 12, 14, 15]. In 2008, a cluster of KPC cases at one LTACH in metropolitan Chicago formed the epicenter of a regional outbreak that affected 42 patients and 26 healthcare facilities [8]. By 2011, the average prevalence of KPC colonization among patients in area LTACHs was 30%, more than 9-fold higher than colonization prevalence among patients in short-stay hospital intensive care units (ICUs) [14]. In response, a collaborative, LTACH-based, multifaceted regional KPC control program was developed and launched.

METHODS

Study Design and Population

The study was planned as a quality improvement project to prevent KPC colonization and infection in LTACHs in metropolitan Chicago, Illinois. Four of 7 LTACHs in the region were invited and agreed to participate in the project. LTACHs were selected for invitation based on proximity to short-stay hospitals in the city of Chicago, where regional control efforts were focused, and because they were members of a single corporation that included most LTACHs in the region. All general medical wards and high-acuity units were included in the study. A psychiatric illness and substance abuse treatment unit at one LTACH was excluded. Each LTACH employed a dedicated nurse infection preventionist. Facilities were certified by The Joint Commission; no infection-control citations were documented during the study.

A stepped-wedge design was used to introduce a bundled infection prevention intervention to LTACHs. This design was chosen because it was the most rigorous option available that allowed adoption of the intervention at all study sites [16].

Intervention Bundle and Data Collection

In the preintervention period, semiannual rectal swab culture surveys were conducted to measure prevalence of KPC colonization among patients [14]; results were reported to LTACHs. During the intervention period, patients were screened for KPC rectal colonization at the time of LTACH admission and every other week, with preemptive contact isolation of newly admitted patients pending culture results. Swabs were screened for KPC using ertapenem disks in a central laboratory [17]; bla_{KPC} was confirmed by a polymerase chain reaction assay [18, 19]. Patients with a KPC-positive screen or clinical cultures during the intervention period were presumed to remain colonized indefinitely and were not rescreened.

In addition to every other week rectal culture surveillance, components of the KPC intervention bundle included contact isolation [20] and geographic separation of KPC-positive patients in a ward cohort or single room; universal contact isolation of all patients in high-acuity units, where geographic separation of KPC-positive and KPC-negative patients was not possible; bathing all patients daily with 2% chlorhexidine gluconate (CHG)–impregnated cloths (Sage Products, Inc, Cary, Illinois); and healthcare-worker education and adherence monitoring, with a focus on hand hygiene. Bundle components were selected based on public health recommendations and expert guidance for control of CRE [11, 13], published reports of successful KPC control programs [9, 21-23], and our preintervention assessment of frequent colonization of LTACH patients' skin with KPC but rare contamination of the inanimate LTACH environment [24].

Demographic; admission, discharge, and transfer; and clinical culture data were obtained from corporate data warehouses. Medical device utilization was determined from review of infection-control department databases.

Study Outcomes

The primary outcome was prevalence of KPC rectal colonization. Secondary outcomes included incidence of KPC rectal colonization, KPC-positive clinical cultures, KPC bloodstream infection, bloodstream infection due to any pathogen, and blood culture contamination. Incident colonization was classified as definite (KPC-positive rectal surveillance swab on or after hospital day 4 in a patient at risk of KPC colonization, ie, no history of KPC-positive surveillance or clinical culture, and at least 1 prior KPC-negative rectal surveillance culture during hospital days 1–3) or possible (KPC-positive rectal surveillance culture on or after hospital day 4, no history of KPC-positive surveillance or clinical culture, and no prior KPC-negative rectal surveillance culture during hospital days 1–3). The National Healthcare Safety Network (NHSN) Module definition for "CRE-*Klebsiella* species" was used as a proxy for KPC-positive clinical culture; that is, any *Klebsiella* species testing intermediate or resistant to imipenem, meropenem, or doripenem by standard susceptibility testing was considered to be KPC [25]. This approach was validated by demonstrating that 87% (107/123) of KPC from a sample of surveillance swabs from LTACH patients was *K. pneumoniae*, and that 96% (107/112) of carbapenem-resistant *Klebsiella* species carried bla_{KPC} [14]. NHSN Multidrug-Resistant Organism Module definitions for "hospital-onset, LabID event" and contaminated blood culture were used to estimate rates of clinical infection and blood culture contamination [25]. Clinical cultures were obtained at clinicians' discretion. Sensitivity analyses included models that added the NHSN definition for "CRE-*Escherichia coli*" to the proxy definition of KPC [25].

Prevalence of KPC rectal colonization was chosen as the primary outcome because at the time of LTACH randomization, the only preintervention data available were results of semiannual KPC point prevalence rectal culture surveys (14 preintervention surveys at the 4 intervention LTACHs). Soon after initiation of the intervention, we determined that robust preintervention clinical culture data were available, which allowed us to take full advantage of the stepped-wedge design in the analysis. Because neither admission nor every other week surveillance was performed at participating LTACHs before the intervention, KPC incidence during the preintervention period was unknown.

Because we had few preintervention prevalence data and no preintervention incidence data, we examined these outcomes using an a priori 1-group, longitudinal change design. This design is quasi-experimental, and is a less valid indicator of causality than the a priori stepped-wedge experimental design used with the clinical culture data. To judge the causal inference of the intervention effect, we looked for convergence of results across all quasi-experimental and experimental analyses [26].

Implementation and Adherence Monitoring

Before the intervention was introduced at each LTACH, a series of mandatory educational sessions was held for all staff, including evening, night, and weekend workers. During the intervention period, educational sessions were repeated monthly for new employees. Additional training on CHG bathing was conducted for certified nursing assistants; initial and yearly bathing competency was demonstrated by direct observation or by completion of a standard written or oral quiz. Study personnel attended monthly LTACH staff meetings

and visited each LTACH 2–5 times weekly throughout the intervention to educate staff informally and assess adherence (total contact time, 10–20 person-hours per LTACH per week). Conference calls were held weekly with hospital leadership and infection preventionists at each LTACH to identify and resolve problems and to provide bidirectional feedback about the intervention, including rates of adherence with intervention bundle components.

Study Timeline

The study was conducted between 1 February 2010 (date of first available clinical culture result) and 30 June 2013 (last day of bundled intervention). The first point prevalence survey took place on 18 January 2011 [14]. LTACHs were randomized to adopt the intervention at approximately 2-month intervals beginning on 28 November 2011; after 7 months, the intervention was in effect at all LTACHs (Figure 1). Because of variability in availability of historical clinical culture data and the different dates of adoption of the intervention, the preintervention period at each LTACH ranged from 16 to 29 months and the intervention period from 12 to 19 months.

Statistical Analysis

The anticipated effect of the intervention on KPC prevalence was calculated as follows. Prior to any LTACH adopting the intervention, average prevalence at the 4 participating facilities was 41% (standard error of the mean, 12%) [14]. The intervention was anticipated to reduce cross-transmission (KPC incidence) at the LTACHs; cross-transmission was estimated to be responsible for 75% of prevalence (estimated preintervention KPC incidence, 30%) [21]. The intervention was expected to reduce KPC incidence in each LTACH by 50% (from 30% to 15%) 12 months after all LTACHs implemented the intervention. Thus, the anticipated effect size of the bundled intervention was $d = 1.25$. Using this estimated effect size, an α of .05 and a sample of 4 LTACHs, a power of 0.91 was obtained, which indicated that we were likely to be able to detect a difference in prevalence due to the intervention if one occurred.

We tested for change (linear and exponential trends) in KPC colonization prevalence and incidence in separate regression models, with the null hypotheses of no change in prevalence or incidence over time during the intervention period.

Clinical culture data were analyzed using a 2-level hierarchical model and a varying time effect; the unit of analysis was the time period (month) within LTACH. The model treated differences in clinical culture incidence among LTACHs as a random effect. It also allowed us to examine the staggered initiation of the intervention and correct for site differences, and to account for the repeated measures associated with these data by allowing the use of autocorrelated error terms. The staggered initiation also corrected for seasonality effects because the staggering occurred over 7 months, with each site beginning the intervention in a different season of the year.

Compared to the preintervention period, there are 2 possible improvements that can occur for this sort of design: a simple drop in rate, and a drop in the rate over time. The combined mean effects and slope interaction term was used as the primary test of intervention effectiveness because the slopes and means were correlated and differed significantly across

LTACHs. As a consequence of this interaction effect, simple mean and slope effects were uninterpretable.

Models were constructed that controlled for possible confounding effects of proportion of days patients received mechanical ventilation or urinary bladder catheterization. These factors were removed from the final model when they were found to be insignificant.

Analyses were conducted using SPSS software version 19 (IBM SPSS, Chicago, Illinois) and R version 2.13.1 (http://CRAN.R-project.org).

Ethical Review

Participating LTACHs deemed the study to be a quality improvement project and not research. The project was reviewed and determined to be a minimal-risk study by the institutional review board at Rush University Medical Center, which granted approval of the study along with a waiver of consent and Health Insurance Portability and Accountability Act waiver.

RESULTS

Study Participants and Adherence Monitoring

Patient characteristics were similar during preintervention and intervention periods, although the proportion of days that patients received mechanical ventilation or urinary bladder catheterization was smaller during the intervention period (Table 1).

Adherence to most components of the intervention bundle was high (Table 2). Healthcare-worker hand hygiene before room entry was low, observed in only 24% of opportunities. A total of 145 986 packages of CHG-impregnated cloths was delivered to the LTACHs during the intervention period for an estimated 116 789 baths, or approximately 1 bath per patient per day, based on baseline observations in which 1 package of 6 CHG-impregnated cloths was used for 75% of baths and 2 packages were used for 25% of baths.

Outcomes

The prevalence of KPC rectal colonization was stable during the preintervention period (average, 45.8%; 95% confidence interval [CI], 42.1%–49.5% for preintervention point prevalence surveys; slope = 0.054, ie, almost zero; $P = .47$ for linear change; Figure 2), declined early in the intervention period, and then reached a plateau (34.3%; 95% CI, 32.4%–36.2%; $P < .001$ for exponential decline). Admission prevalence during the intervention period was stable (average, 20.6%; 95% CI, 19.1%–22.3%; Figure 2).

When only definite KPC acquisitions were considered, the incidence rate of KPC rectal colonization fell during the intervention period, from approximately 4 to 2 KPC acquisitions per 100 patient-weeks ($P = .004$ for linear decline; Figure 3); results were similar when possible incident cases were included.

The intervention resulted in a 32% reduction in the rate of isolation of KPC from any clinical culture and a 56% reduction in KPC bacteremia (Table 3). Rates of bloodstream

infection due to any pathogen declined by 32%; blood culture contamination declined by 53%. The magnitudes of the reductions are displayed in Figure 4A-D. There was a clear drop in rates of infection and blood culture contamination as the staggered intervention effects began, and there was some evidence that the rates continued to drop after the initiation of the intervention (based on the downward slopes of the linear trends). Neither adding the NHSN definition for "CRE *Escherichia coli*" to the proxy definition of KPC nor adjustment for the proportion of days that patients received mechanical ventilation or urinary bladder catheterization changed results of clinical culture analyses.

DISCUSSION

Implementation of a bundled intervention was associated with clinically important and statistically significant reductions in KPC colonization and infection at 4 LTACHs in metropolitan Chicago: colonization incidence was reduced by 50%, colonization prevalence and all KPC infections declined by >30%, and the rate of KPC bloodstream infection fell by almost 60%. Reductions occurred despite high KPC prevalence—nearly 50% of patients were colonized with KPC at the start of the intervention—and ongoing admission of a large number of patients who already were colonized with KPC. These results demonstrate that control is possible despite high colonization pressure and repeated introduction of KPC-positive patients, and should provide support for other healthcare facilities that are working to lower the burden of KPC in their patient populations.

To our knowledge, this is the first multicenter study to show sustained decreases in cross-transmission of a multidrug-resistant pathogen and in healthcare-associated infections in an LTACH population. Patients in LTACHs are chronically critically ill [27] and at high risk of infection from multidrug-resistant organisms because of prolonged hospital stays, repeated antibiotic exposures, and elevated rates of medical device use [28, 29]. Yet, because little research has been conducted on the characterization and mitigation of risk factors for infection in this population, best practices for infection prevention in LTACHs have not been established [30]. The present study demonstrates the ability of LTACHs to participate successfully in research and adds to our understanding of how best to care for this vulnerable group of patients, which is expected to continue to grow over the next decade [31].

In addition to the targeted decreases in KPC colonization and infection, collateral benefits of the intervention were observed on relative rates of all-cause bacteremia and on blood culture contamination, which declined 32% and 53%, respectively. Because the intervention comprised a bundle of infection prevention measures, it is not possible to know with certainty which bundle component(s) were necessary and sufficient for the KPC-specific or broader improvements. Daily bathing with CHG has been shown to reduce catheter-associated bloodstream infection in both ICU and LTACH populations and to reduce blood culture contamination in ICUs [32-34]. We speculate that bathing all LTACH patients with CHG during the intervention period was largely responsible for the sharp declines observed in KPC and all-cause bloodstream infection and in blood culture contamination, reflecting rapid onset of protection of each bathed patient. In contrast, declines in KPC incidence and

prevalence were more gradual, presumably reflecting the greater effort needed to control cross-colonization in a setting of high KPC admission prevalence and colonization pressure.

Although concerns have been raised about decreased susceptibility of KPC to CHG [35], we found that CHG bathing was effective in reducing KPC skin colonization in LTACH patients [36]. Thus, CHG bathing may also have helped reduce cross-transmission of KPC by lessening the risk of healthcare-worker hand contamination during direct care of KPC-positive patients. Still, active surveillance for KPC, contact isolation, and geographic separation of KPC-positive patients may have contributed to declines in KPC incidence, prevalence, and infection. Preintervention hand hygiene rates were not known, but improvements in healthcare-worker hand hygiene adherence and education about prevention of healthcare-associated infections may also have had positive effects on all outcomes.

While the intervention conferred clear benefit on patients who were cared for in participating LTACHs, it is likely to also have had a favorable effect on prevalence of KPC in other healthcare facilities in the region. In Chicago, as in much of the United States, LTACHs serve as a reservoir for KPC [14]. Nationally in 2012, 3.9% of short-stay hospitals that submitted data to NHSN reported at least 1 healthcare-associated infection due to CRE, compared with 17.8% of LTACHs [37]. Patients in LTACHs typically have contact with multiple different healthcare facilities over time as their clinical needs change [8]. Transfer from an LTACH is a risk factor for KPC colonization at the time of short-stay hospital admission [12, 38]. Reducing the number of LTACH patients who are colonized and infected with KPC should result in fewer KPC-positive patients transferred from an LTACH to another healthcare facility, thus slowing regional dissemination. Formal testing of this hypothesis using simulation modeling and highly discriminating molecular epidemiologic methods such as whole-genome sequencing is needed.

Our study has limitations. The study was conducted in hospitals with high KPC prevalence, and results may not be generalizable to settings with lower prevalence of KPC. Few preintervention colonization data were available for analysis, but convergent responses to the intervention of all colonization and infection outcomes strengthen our confidence in the validity of the observed declines. Sequential rollout of the intervention and contact between personnel at different LTACHs may have resulted in some intervention effect on LTACHs before they officially implemented the intervention; this effect would have reduced the difference between preintervention and intervention outcomes. Infections were identified using NHSN standardized laboratory surveillance definitions without clinical assessment, which may have resulted in misclassification of colonization as infection, or of infection acquired prior to LTACH admission as LTACH onset. Data on severity of patient illness and antibiotic use were not available; these variables remain potential unmeasured confounders. Our bundle did not include antimicrobial stewardship and so the effect of inclusion of stewardship in the bundle is unknown. Whether daily CHG bathing will select for CHG resistance in KPC or other skin microbes is unknown and should be monitored. Finally, the bundled intervention preluded assessment of the impact of individual bundle components.

In conclusion, a bundled intervention was associated with reduced colonization and infection due to KPC, declines in bloodstream infection due to all pathogens, and decreased blood

culture contamination in a high-risk LTACH population. Evaluation of long-term and regional effects of the intervention is warranted.

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		Staggered Introduction of Intervention				
		February 1, 2010 – November 27, 2011	November 28, 2011 – February 4, 2012	February 5, 2012 – April 8, 2012	April 9, 2012 – June 17, 2012	June 18, 2012 – June 30, 2013
LTACH	A	0	X	X	X	X
	B	0	0	X	X	X
	D	0	0	0	X	X
	C	0	0	0	0	X

Figure 1.

Stepped-wedge design implementation at the 4 long-term acute-care hospitals (LTACHs) participating in the study. The symbol “0” in an unshaded cell indicates preintervention period. The symbol “X” in a shaded cell indicates intervention period. The start date for the preintervention period varied for each LTACH depending on availability of historical clinical culture data: February 1, 2010 (LTACH C), July 1, 2010 (LTACH B), August 1, 2010 (LTACH A), and November 1, 2010 (LTACH D).

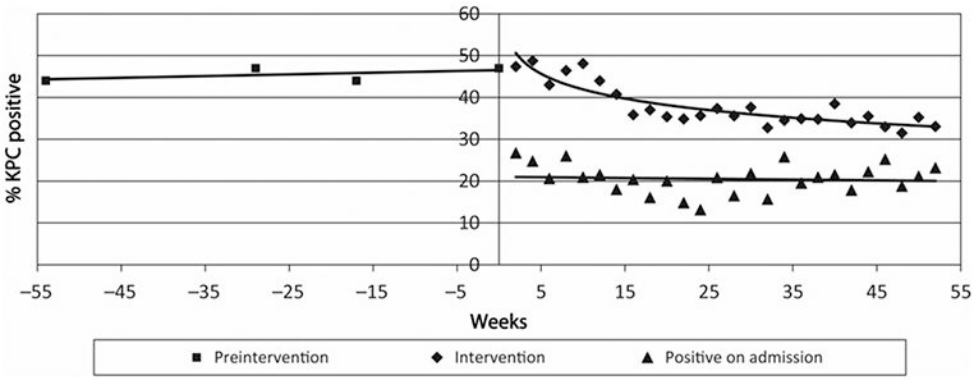

Figure 2.

Prevalence rate of *Klebsiella pneumoniae* carbapenemase–producing Enterobacteriaceae (KPC) rectal colonization during the preintervention and intervention periods. Each data point in the preintervention period represents the average prevalence across the 4 long-term acute-care hospitals (LTACHs) for 1 semiannual point prevalence survey. Only 2 LTACHs (LTACHs D and C) are included in the week −17 point prevalence survey, as LTACHs A and B were already participating in the intervention at that time. During the intervention period, each data point represents the average prevalence across the 4 LTACHs for 1 every other week point prevalence survey. Data for the first 52 weeks of the intervention are shown. $P <$ .001 for exponential decline in prevalence during the intervention period.

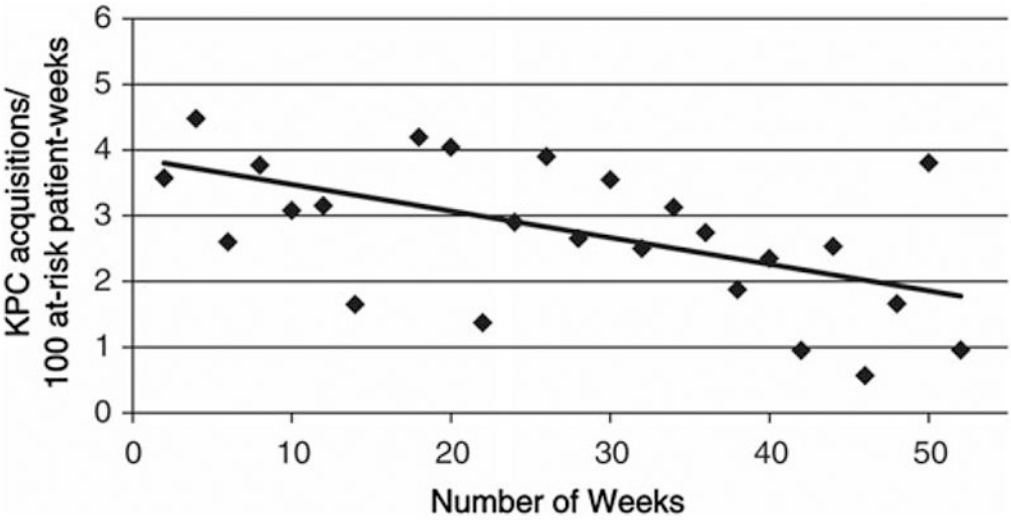

Figure 3.

Incidence rate of *Klebsiella pneumoniae* carbapenemase–producing Enterobacteriaceae (KPC) rectal colonization during the intervention period. Each data point represents the number of patients who acquired KPC per 100 patient-weeks, averaged over the preceding 2 weeks. Definite incident cases and data for the first 52 weeks during which each of the 4 long-term acute-care hospitals participating in the study are shown. $P = .004$ for linear decline.

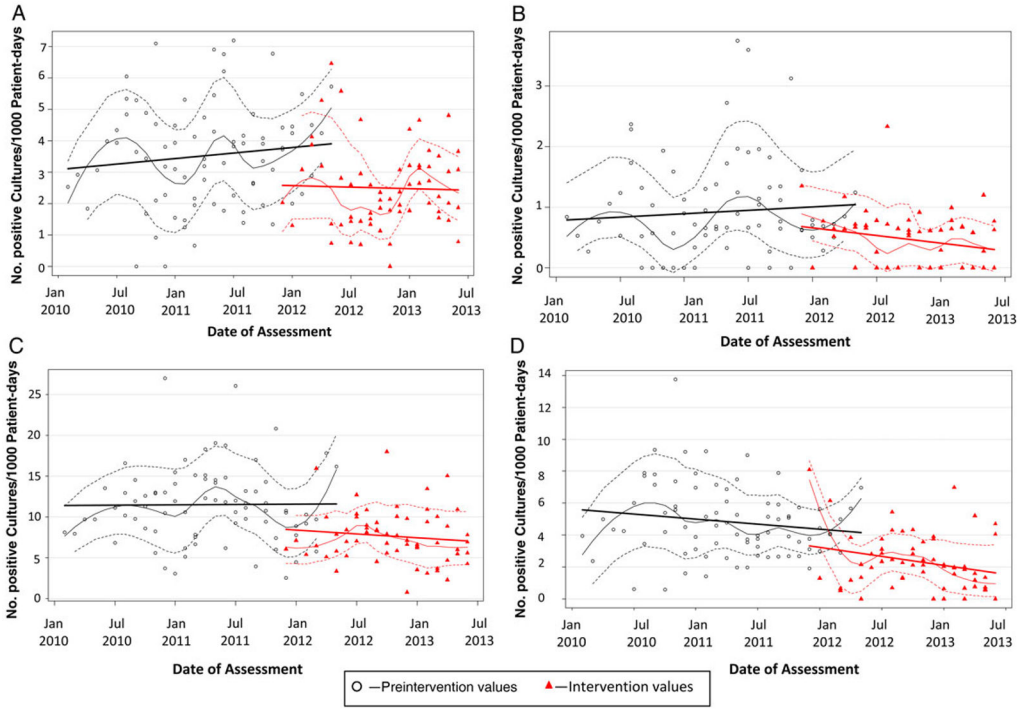

Figure 4.

Effect of the intervention bundle on clinical culture outcomes. Shown are the moving averages of the rates of clinical infections (curved solid lines) and 95% confidence limits (curved hatched lines) for preintervention (open black circles) and intervention (closed red triangles) periods. Each data marker represents average number of clinical cultures at 1 long-term acute-care hospital (LTACH) in 1 month. Trend lines for each period are shown in black (preintervention) or red (intervention) solid bold type. Note the different ranges for y-axis in each panel. *A*, *Klebsiella pneumoniae* carbapenemase (KPC) in any clinical culture. *B*, KPC bloodstream infection. *C*, Bloodstream infection due to any pathogen. *D*, Contaminated blood culture.

Table 1.

Characteristics of the Long-term Acute-Care Hospital Population, According to Study Period

Variable	Preintervention Period[a]	Intervention Period[a]
Present on admission		
Patients, No.	3894	2951
Admissions, No.	5282	3738
Admissions per month, mean (SD)	231 (21)	234 (22)
Age, y, mean (SD)	63 (16)	64 (16)
Female sex, %	45.6	45.8
Measured during hospital stay		
Patient-days, No.	178 516	114 070
High-acuity unit patient-days, %	8.3	10.1
Invasive medical device utilization, %[b]		
Mechanical ventilation	50.5	43.1
Central venous catheter	50.3	51.9
Urinary bladder catheter	63.0	50.9
Hospital stay, d, median (IQR)	28 (16–43)	26 (17–39)
In-hospital mortality, %	21.5	17.6

Abbreviations: IQR, interquartile range; LTACH, long-term acute-care hospital; SD, standard deviation.

[a]The preintervention period spanned 16–29 months and the intervention period spanned 12–19 months. Study period lengths differed at each LTACH because of variability in availability of historical clinical culture data and because of the different dates on which each LTACH was randomly assigned to adopt the bundled intervention.

[b]Invasive medical device utilization was calculated as [(number of days a medical device was utilized by each patient/total number of patient-days) ×100.

Table 2.

Adherence With Components of Intervention Bundle During the Intervention Period

Adherence Measure	No. Adherent/No. Opportunities	% Adherence	95% CI
Collection of admission surveillance swabs[a]	2872/3152	91.1	90.1–92.1
Collection of every other week surveillance swabs	5072/5316	95.4	94.8–96.0
KPC-positive patient-days on a cohort floor or in a private room[b]	17 921/19 295	92.9	92.5–93.2
HCW hand hygiene adherence at room entrance	365/1499	24.4	22.2–26.6
HCW hand hygiene adherence at room exit	1304/1843	70.8	68.6–72.8
Donning gloves and gown before room entry[c]	387/489	79.1	75.3–82.5

Abbreviations: CI, confidence interval; HCW, healthcare worker; KPC, *Klebsiella pneumoniae* carbapenemase–producing Enterobacteriaceae; LTACH, long-term acute-care hospital.

[a]Adherence was defined as collection of a rectal surveillance swab for KPC culture within 3 calendar days of admission. Median time from admission to availability of swab culture results was 3 days (interquartile range, 2–4 days).

[b]Adherence was measured 3–6 days per week at each LTACH. Three LTACHs cared for KPC-positive patients on patient cohort wards. The fourth LTACH cared for KPC-positive patients in private rooms. The percentage of KPC-negative patient-days on a KPC cohort floor or in a room with a KPC-positive patient was 13% (5109/40 777).

[c]High-acuity unit rooms only, where universal contact isolation was in effect.

Table 3.

Effect of Intervention Bundle on Clinical Cultures and Blood Culture Contamination

	Preintervention[a]			Intervention[a]				
Outcome	**No. of Events**	**Events/1000 Patient-days**	**95% CI**	**No. of Events**	**Events/1000 Patient-days**	**95% CI**	**Change in Event Rate**	***P* Value**
KPC in any clinical culture	656	3.7	3.4–4.0	285	2.5	2.2–2.8	−1.2	.001
KPC bloodstream infection	165	0.9	.8–1.1	48	0.4	.3-.5	−0.5	.008
Bloodstream infection due to any pathogen	2004	11.2	10.7–11.7	870	7.6	7.1–8.1	−3.6	.006
Contaminated blood culture	865	4.9	4.5–5.2	261	2.3	2.0–2.6	−2.6	.03

Abbreviations: CI, confidence interval; KPC, *Klebsiella pneumoniae* carbapenemase–producing Enterobacteriaceae.

[a]There were 178 516 patient-days in the preintervention period and 114 070 patient-days in the intervention period.