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Sustained reduction of healthcare-associated infections after the introduction of a bundle for prevention of ventilator-associated pneumonia in medical-surgical intensive care units

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ABSTRACT

Background: Infection control interventions can be erroneously interpreted if outcomes are assessed in short periods. Also, statistical methods usually applied to compare outcomes before and after interventions are not appropriate for analyzing time series.

Aims: To analyze the impact of a bundle directed at reducing the incidence of ventilator-associated pneumonia (VAP) and other device-associated infections in two medical-surgical intensive care units (ICU) in Brazil.

Methods: Our study had a quasi-experimental design. Interrupted time series analyses (ITS) was performed assessing monthly rates of overall healthcare-associated infections (HCAI), VAP, laboratory-confirmed central line associated bloodstream infections (CLABSI) and catheter-associated urinary tract infections (CAUTI), from January 2007 through June 2019. Moreover, multivariate ITS was adjusted for seasonality in Poisson regression models. An intervention based on a bundle for VAP prevention was introduced in August 2010.

Findings: The intervention was followed by sustained reduction in overall HCAI, VAP and CLABSI in both ICU. Continuous post-intervention trends towards reduction were detected for overall HCAI and VAP.

Conclusion: Interventions aimed at preventing one specific site of infection may have sustained impact on other HCAI, which can be documented using time series analyses.

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Introduction

In the past decade, the focus of infection control practice has switched from surveillance to interventions.[1,2] The combined application of measures (collectively referred to as ̈bundles)̈ aimed at prevention and control of healthcare-associated infections (HCAI) has been extensively studied.[3–5]

In this setting, there are concerns over the energy and time spent in applying simultaneously several bundles directed at different sites of infection.[6] Furthermore, the successful results in some reports may have been biased by short-time post-intervention follow-up. Short-run results may imply statistical variations around the historical average.[7] Finally, since monthly rates of HCAI are not independent among themselves, usual statistical tests (such as Chi-square, Student's T and ANOVA) are not appropriate for detecting changes in incidence before and after interventions.[8,9]

Therefore, we studied the impact of a bundle aimed at preventing ventilator-associated pneumonia (VAP) on the incidence of overall and device-associated infections in adult medical-surgical intensive care units (ICU) in a Brazilian hospital.

Methods

Study setting

The study was conducted in a 500-bed teaching hospital of Faculdade de Medicina de Botucatu (Botucatu Medical School). It is a tertiary-care reference hospital for a São Paulo inner-state area, Brazil, comprising approximately one million inhabitants. The hospital has five ICU, two of which are medical-surgical units for adult patients, with 17 and 10 beds. The study intervention was performed in those medical-surgical ICU.

Study design

This was a quasi-experimental (before and after) study.

Intervention

In August 2010, a bundle for preventing VAP was introduced in the two study units. The bundle included the following measures: (1) 30°–45° bed head elevation; (2) chlorhexidine mouthwash twice daily; (3) cuff pressure measurement twice daily; (4) keeping breathing circuits bellow the patients bed height; (5) whenever feasible, interrupt sedation for one hour daily. Several meetings with medical doctors and nursing staff were held in the two months preceding the intervention. Adherence to bundle items was checked twice weekly, on randomly chosen days. The intervention goal was to reduce VAP incidence bellow the median rates reported by São Paulo State HCAI surveillance system.[10]

HCAI surveillance

Continuous surveillance of HCAI in the ICU followed guidelines from the Brazilian National HCAI Surveillance Program.[11] Minor variations on HCAI governmental definitions during the study were carefully analyzed by the authors, revising records of individual cases notified in active surveillance. Our conclusion was that they did have a relevant impact on results of the time series. It is also worth noting that, though largely based on Centers for Disease Control and Prevention's (CDC) National Healthcare Safety Network (NHSN) definitions, Brazilian HCAI prevention program did not adhere to the "ventilator-associated events" surveillance, as recently recommended by the CDC.[12]

Descriptive statistics

Pre- and post-intervention rates of HCAI (per 1000 patient-days, or patient days with devices) and device use (patient days with devices/overall patient days) were analyzed using the Chi-square test in the free software OpenEpi 3.03 (Emory University, Atlanta, GA, USA).

Time series

Time series of overall and device-associated HCAI were analysed in two adult medical-surgical ICU from January 2007 through June 2019. Interrupted time series (ITS) was conducted using the "itsa" package in STATA 14 (Statacorp, College Station, TX, USA).[13] We used multivariate Poisson regression models to adjust ITS for potential seasonality.

Ethical issues

This study project was approved by the Committee for Ethics in Research from Faculdade de Medicina de Botucatu (Botucatu Medical School).

Results

Complete adherence to the bundle was 53%. Adherence to specific items was above 80% in most surveillance instances, except for daily interruption of sedation. The ICU staff was reluctant to implement this measure, so adherence remained around 50%.

The overall HCAI rate during the study period was 37.71 per 1000 patient-days. The proportions of infectious sites were: VAP, 43.5%; bloodstream infection (BSI), 20.3%; catheter-associated urinary tract infection (CAUTI), 18.8%; other sites, 17.4%.

Pre- and post-intervention HCAI rates in the included ICU and use of invasive devices are presented in Table 1. It should be pointed out that the original goal of the VAP bundle was achieved in both ICU. Tables 2 and 3 present results from multivariate Poisson models of ITS for HCAI and use of invasive devices, respectively. Briefly, ITS models documented the impact of the intervention on overall HCAI (in ICU #1), VAP and BSI (in both ICU). The ITS graphics are presented in Fig. 1.

Discussion

In recent years, HCAI have been recognized by the World Health Organization [WHO] as a major threat for public health,

Table 1 – Rates of healthcare-associated infections in two intensive care units from a Brazilian teaching hospital, before and after the introduction of a *bundle* aimed at preventing ventilator-associated infections.

HCAI and device use	Pre-intervention(January 2007–July 2010)	Post-intervention(August 2010–June 2019)	*P-value*
ICU #1 (17 beds)			
HCAI			
Overall HCAI	50.09	31.96	<0.001
VAP	34.95	13.27	<0.001
CLABSI	12.59	5.94	<0.001
CAUTI	12.59	6.97	<0.001
Device use			
Mechanical ventilation	70.52%	65.07%	<0.001
Central line	87.70%	85.11%	<0.001
Urinary catheter	91.61%	92.83%	<0.001
ICU #2 (10 beds)			
Overall HCAI	52.02	36.29	<0.001
VAP	36.58	12.04	<0.001
CLABSI	12.13	7.10	<0.001
CAUTI	16.61	8.89	<0.001
Device use			
Mechanical ventilation	71.76%	67.16%	<0.001
Central line	80.69%	84.18%	<0.001
Urinary catheter	88.36%	88.04%	0.38

Note. HCAI expressed by 1000 patient-days, overall and with devices (mechanical ventilation for VAP; central line for CLABSI; urinary catheter for CAUTI). Device use expressed in proportion (patient-days with devices/total patient days).

HCAI, healthcare associated infections; ICU, Intensive Care Unit; VAP, ventilator associated pneumonia; CLABSI, central-line associated bloodstream infection; CAUTI, catheter-associated urinary tract infection.

Bold values signifies $p < 0.05$.

especially in developing countries.[14,15] In our study, we faced the challenge of reducing VAP in a resource-limited and understaffed setting.[16] Not surprisingly, our team encountered nihilistic attitudes from ICU staff. This challenge was managed with continuous education during visits of infection control nurses to the ICU to perform surveillance and measure adherence to the bundle.

The positive impact of bundles in preventing VAP (or, more recently, "ventilator-associated events") has been reported by several authors,[17–20] with few exceptions.[21] The serendipity

Table 2 – Multivariate Poisson regression models for Interrupted Time Series Analysis of the impact of the intervention (VAP bundle) on HCAI incidence in the two study ICU.

	ICU #1		ICU #2	
Models/variables	IRR (95%CI)	P	IRR (95%CI)	*p-value*
Overall HCAI				
Time (month)	0.99 (0.99–1.00)	0.37	0.99 (0.99–1.00)	0.39
Intervention	**0.75 (0.63–0.89)**	**0.001**	0.94 (0.77–1.17)	0.62
Intervention_time[a]	1.00 (0.99–1.01)	0.84	0.99 (0.99–1.01)	0.63
Season				
Winter (reference)	...	...	...	...
Spring	1.00 (0.88–1.13)	0.97	0.93 (0.80–1.07)	0.32
Summer	1.06 (0.94–1.20)	0.32	0.94 (0.81–1.09)	0.41
Autumn	1.09 (0.97–1.23)	0.12	1.09 (0.95–1.25)	0.20
VAP				
Time (month)	**0.99 (0.98–0.99)**	**0.02**	**1.01 (1.00–1.01)**	**0.001**
Intervention	**0.61 (0.46–0.79)**	**<0.001**	**0.43 (0.37–0.49)**	**<0.001**
Intervention_time[a]	1.00 (0.99–1.01)	0.29	**0.98 (0.98–0.99)**	**<0.001**
Season				
Winter (reference)	...	...	...	
Spring	1.03 (0.83–1.27)	0.76	**0.89 (0.91–0.99)**	**0.04**
Summer	1.09 (0.89–1.34)	0.39	1.08 (0.72–1.19)	0.16
Autumn	1.16 (0.95–1.42)	0.14	**0.90 (0.81–0.99)**	**0.04**
CLABSI				
Time (month)	0.99 (0.98–1.01)	0.83	**1.01 (1.01–1.02)**	**<0.001**

– Table 2 (Continued)

	ICU #1		ICU #2	
Models/variables	IRR (95%CI)	P	IRR (95%CI)	p-value
Intervention	**0.44 (0.29–0.65)**	**<0.001**	**0.56 (0.45–0.69)**	**<0.001**
Intervention_time[a]	1.00 (0.98–1.01)	0.71	**0.98 (0.97–0.99)**	**<0.001**
Season				
Winter (reference)	...	...	...	...
Spring	0.82 (0.61–1.10)	0.19	1.03 (0.87–1.22)	0.70
Summer	0.93 (0.71–1.23)	0.62	**1.20 (1.03–1.41)**	**0.02**
Autumn	1.02 (0.78–1.34)	0.87	**1.52 (1.31–1.76)**	**<0.001**
CAUTI				
Time (month)	0.99 (0.98–1.00)	0.15	0.99 (0.98–1.00)	0.17
Intervention	0.98 (0.62–1.28)	0.55	0.77 (0.50–1.17)	0.22
Intervention_time[a]	1.00 (0.99–1.01)	0.65	1.01 (0.99–1.02)	0.39
Season				
Winter (reference)	...	...	...	...
Spring	1.06 (0.82–1.38)	0.64	0.79 (0.58–1.07)	0.13
Summer	1.05 (0.82–1.36)	0.68	**0.70 (0.51–0.95)**	**0.02**
Autumn	0.92 (0.71–1.20)	0.56	1.17 (0.89–1.53)	0.25

Note. Statistically significant results are presented in boldface. ICU, Intensive Care Unit; IRR, Incidence Rate Ratio; CI, Confidence interval; HCAI, healthcare-associated infections; VAP, ventilator-associated pneumonia; CLABSI, central line-associated bloodstream infections; CAUTI, catheter-associated urinary tract infection.

Bold values signifies $p < 0.05$.

[a] Interaction of intervention and time variable, which describes the inclination in time trends.

Table 3 – Multivariate poisson regression models for interrupted time series analysis of the impact of the intervention (VAP bundle) on use of invasive devices in the two study ICU.

	ICU #1		ICU #2	
Models/variables	IRR (95%CI)	P	IRR (95%CI)	p-value
Mechanical ventilation				
Time (month)	0.99 (0.99–1.00)	0.18	**0.99 (0.99–0.99)**	**<0.001**
Intervention	**0.92 (0.88–0.96)**	**<0.001**	**1.07 (1.01–1.14)**	**0.01**
Intervention_time[a]	1.00 (0.99–1.00)	0.07	**1.00 (1.00–1.01)**	**<0.001**
Season				
Winter (reference)	...	...	...	...
Spring	0.99 (0.96–1.03)	0.87	0.97 (0.94–1.01)	0.16
Summer	1.00 (0.98–1.03)	0.74	1.00 (0.97–1.04)	0.86
Autumn	1.02 (0.99–1.04)	0.27	1.00 (0.97–1.04)	0.83
Central line				
Time (month)	**0.99 (0.98–0.99)**	**0.04**	**0.99 (0.99–0.99)**	**<0.001**
Intervention	**0.95 (0.02–0.98)**	**0.01**	**1.08 (1.03–1.14)**	**0.002**
Intervention_time[a]	**1.01 (1.00–1.03)**	**0.001**	**1.01 (1.00–1.08)**	**<0.001**
Season				
Winter (reference)	...	...	...	...
Spring	**1.01 (0.99–1.03)**	**0.32**	**0.96 (0.92–0.99)**	**0.01**
Summer	1.02 (0.99–1.05)	0.06	**0.96 (0.93–0.99)**	**0.02**
Autumn	1.03 (1.01–1.06)	0.004	0.99 (0.95–1.01)	0.23
Urinary Catheter				
Time (month)	1.00 (0.99–1.00)	0.09	**0.99 (0.99–0.99)**	**0.04**
Intervention	0.97 (0.94–1.01)	0.13	1.01 (0.96–1.06)	0.61
Intervention_time[a]	**0.99 (0.99–1.00)**	**0.26**	**1.00 (1.00–1.01)**	**0.02**
Season				
Winter (reference)	...	...	...	...
Spring	0.99 (0.97–1.02)	0.92	0.98 (0.95–1.02)	0.33
Summer	1.01 (0.99–1.04)	0.22	1.01 (0.97–1.04)	0.73
Autumn	1.02 (0.99–1.04)	0.18	0.98 (0.95–1.01)	0.30

Note. Statistically significant results are presented in boldface. ICU, Intensive Care Unit; IRR, Incidence Rate Ratio; CI, Confidence interval.

[a] Interaction of Intervention and time variable, which describes the inclination in time trends.

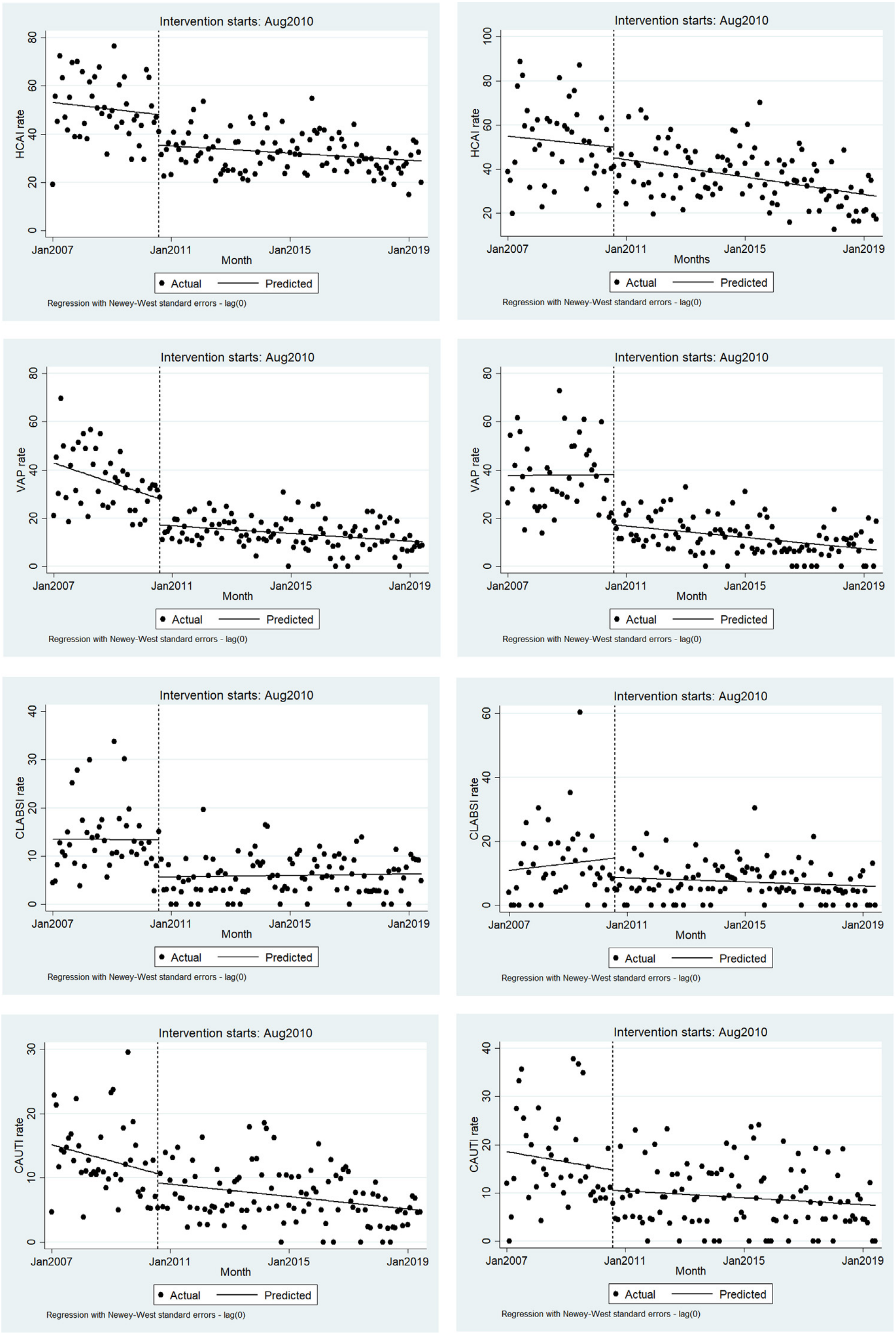

Fig. 1 – Interrupted time series graphics for time trends of healthcare-associated infections in two medical-surgical intensive care units before and after the implementation of a bundle aimed at preventing ventilator-associated pneumonia.

in our results was that improved surveillance for adherence to the bundle seemed to impact on the incidence of other HCAI. It is worth noting that there were no changes in policies for prevention of other device-associated infections during the study period.

Recent emphasis has been placed in socio adaptive approaches to improve adherence to infection control practices.[22] Positive deviance, link nurses, behavioural economics and social network interventions have been tested, often with positive results.[22–24] Our argument is that even simple measures which reinforce the presence and interaction of infection control team with other HCWs can improve safety culture, with widespread beneficial approach. Naturally, that interaction can be improved by more robust theory-laden approaches.[22] One should notice that adherence to the whole bundle was only moderate, but we still achieved reduction in VAP and other HCAI rates. So, the bundle itself does not fully explain our results. We hypothesize a phenomenon similar to the so-called "surveillance effect", in which adherence to a national surveillance system leads to decrease in HCAI incidence.[25] In both cases, there is mobilization of infection control and other healthcare workers towards improving outcome indicators.

Our results also reinforce the importance of using ITS methods, instead of comparing "before and after" rates. The latter approach is suboptimal, since tests like Chi-square, Student's t-test and others were developed for comparing independent variables, and adjacent time periods do not meet the criteria of statistic independence.[8] Furthermore, impacts on time trends may be lost or even misunderstood.[9] Finally, ITS requires long-term follow up, which is appropriate to identify sustainable impact of interventions.

As a secondary finding, there was evidence of seasonality for central-line associated bloodstream infection (CLABSI) in ICU #2, a finding in line with our previous studies.[26,27] Finally, trends of use of invasive devices before and after the intervention may vary towards increasing or diminishing.

Our study has some limitations. First, over such a long period, it is evident that the infection control team performed continuous normative and educational measures, which possibly reinforced the prevention of HCAI. However, there was no other strong point intervention, so we believe that our premise that VAP bundle had a wide impact in infection control remains valid. Indeed, the continuous visits necessary for observing adherence to items of the bundle probably increased the proximity between infection control nurses and the ICU team. Second, we targeted the "old-fashioned" VAP, using diagnostic criteria often described as subjective.[12] However, using this stable definition allowed us to study a long-term time series. Also, the impact of our intervention was noticed in the much more objectively defined CLABSI. Third, adherence to hand hygiene was continuously measured only after year 2016. This information was missing for most of the study period, and therefore could not be included in our model. Data on individual severity-of-illness was not included in the analysis. It should stressed that both hospital administrative data and information collected in previous studies from our group[27] found no variation of severity-of-illness of patients in the evaluated ICU. Finally, the methodological design of this study shares the usual limitations of ecologic epidemiological approaches (mainly not adjusting for individual-based factors). Still, ecologic studies are the most appropriate methods for addressing collective exposures and/or interventions.[28] Other strengths of our study include using ITS and the long-term follow up of the intervention. In developing countries, where structure for infection control is often suboptimal,[15,29] intensification of interventions and the appropriate analysis of their results may be especially useful for improving patient safety.

In conclusion, we found that a partially successful implementation of a bundle aimed at reducing VAP resulted in long-term, positive impact on overall HCAI, VAP and CLABSI. Novel and continuous approaches may result in further improvement.

Conflicts of interest

The author declares no conflicts of interest.

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REFERENCES

1. Marcel JP, Alfa M, Baquero F, et al. Healthcare-associated infections: think globally, act locally. Clin Microbiol Infect. 2008;14:895–907.
2. Padoveze MC, Fortaleza CMCB. Healthcare-associated infections: challenges to public health in Brazil. Rev Saude Publica. 2014;48:995–1001.
3. Carter EB, Temming LA, Fowler S, et al. Evidence-based bundles and cesarean delivery surgical site infections: a systematic review and meta-analysis. Obstet Gynecol. 2017;130:735–46.
4. Sampathkumar P. Reducing catheter-associated urinary tract infections in the ICU. Curr Opin Crit Care. 2017;23:372–7.
5. Lachman P, Yuen S. Using care bundles to prevent infection in neonatal and paediatric ICUs. Curr Opin Infect Dis. 2009;22:224–8.
6. Bogue TL, Bogue RL. Unbundling the bundles: using apparent and systemic cause analysis to prevent health care-associated infection in pediatric intensive care units. Crit Care Nurs Clin North Am. 2017;29:217–31.
7. Blot K, Bergs J, Vogelaers D, Blot S, Vandijck D. Prevention of central line-associated bloodstream infections through quality improvement interventions: a systematic review and meta-analysis. Clin Infect Dis. 2014;59:96–105.
8. Bernal JL, Cummins S, Gasparrini A. Interrupted time series regression for the evaluation of public health interventions: a tutorial. Int J Epidemiol. 2017;46:348–55.
9. Lopez Bernal J, Soumerai S, Gasparrini A. A methodological framework for model selection in interrupted time series studies. J Clin Epidemiol. 2018;103:82–91.
10. Padoveze MC, Assis DB, Freire MP, et al. Surveillance Programme for Healthcare Associated Infections in the State of São Paulo, Brazil. Implementation and the first three years' results. J Hosp Infect. 2010;76:311–5.
11. Agência Nacional de Vigilância Sanitária. Critérios Diagnósticos de Infecções Relacionadas à Assistência à Saúde/Agência Nacional de Vigilância Sanitária. Brasília: Anvisa; 2017.
12. Klompas M. Barriers to the adoption of ventilator-associated events surveillance and prevention. Clin Microbiol Infect. 2019;25:1180–5.
13. Penfold RB, Zhang F. Use of interrupted time series analysis in evaluating health care quality improvements. Acad Pediatr. 2013;13:S38–44.
14. Allegranzi B, Donaldson LJ, Kilpatrick C, et al. Infection prevention: laying an essential foundation for quality universal health coverage. Lancet Glob Health. 2019;7:e698–700.
15. Allegranzi B, Bagheri Nejad S, Combescure C, et al. Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis. Lancet. 2011;377:228–41.

16. Bardossy AC, Zervos J, Zervos M. Preventing hospital-acquired infections in low-income and middle-income countries: impact, gaps, and opportunities. Infect Dis Clin North Am. 2016;30:805–18.
17. de Neef M, Bakker L, Dijkstra S, Raymakers-Janssen P, Vileito A, Ista E. Effectiveness of a ventilator care bundle to prevent ventilator-associated pneumonia at the PICU: a systematic review and meta-analysis. Pediatr Crit Care Med. 2019;20:474–80.
18. Klompas M. Prevention of intensive care unit-acquired pneumonia. Semin Respir Crit Care Med. 2019;40:548–57.
19. Kallet RH. Ventilator bundles in transition: from prevention of ventilator-associated pneumonia to prevention of ventilator-associated events. Respir Care. 2019;64:994–1006.
20. Ochoa-Hein E, Choi SJ, Gómez-Santillán JA, et al. Near-zero ventilator-associated pneumonia rates after implementation of a multimodal preventive strategy in a Mexican hospital [published online ahead of print, 2019 Oct 30]. Am J Infect Control. 2019, http://dx.doi.org/10.1016/j.ajic.2019.09.018. S0196-6553(19)30854-30855.
21. Osman S, Al Talhi YM, AlDabbagh M, Baksh M, Osman M, Azzam M. The incidence of ventilator-associated pneumonia (VAP) in a tertiary-care center: comparison between pre- and post-VAP prevention bundle [published online ahead of print, 2019 Oct 25]. J Infect Public Health. 2019, http://dx.doi.org/10.1016/j.jiph.2019.09.015. S1876-0341(19)30315-30316.
22. Sreeramoju P. Reducing infections “Together”: a review of socioadaptive approaches. Open Forum Infect Dis. 2019;6, ofy348.
23. Gesser-Edelsburg A, Cohen R, Halavi AM, et al. Beyond the hospital infection control guidelines: a qualitative study using positive deviance to characterize gray areas and to achieve efficacy and clarity in the prevention of healthcare-associated infections. Antimicrob Resist Infect Control. 2018;7:124.
24. Gilbert GL, Kerridge I. The politics and ethics of hospital infection prevention and control: a qualitative case study of senior clinicians’ perceptions of professional and cultural factors that influence doctors’ attitudes and practices in a large Australian hospital. BMC Health Serv Res. 2019;19:212.
25. Gastmeier P, Schwab F, Sohr D, Behnke M, Geffers C. Reproducibility of the surveillance effect to decrease nosocomial infection rates. Infect Control Hosp Epidemiol. 2009;30:993–9.
26. Fortaleza CM, Caldeira SM, Moreira RG, et al. Tropical healthcare epidemiology: weather determinants of the etiology of bloodstream infections in a Brazilian hospital. Infect Control Hosp Epidemiol. 2014;35:85–8.
27. Rodrigues FS, Clemente de Luca FA, Ribeiro da Cunha A, Fortaleza CMCB. Season, weather and predictors of healthcare-associated Gram-negative bloodstream infections: a case-only study. J Hosp Infect. 2019;101:134–41.
28. Richard L, Gauvin L, Raine K. Ecological models revisited: their uses and evolution in health promotion over two decades. Annu Rev Public Health. 2011;32:307–26.
29. Padoveze MC, Fortaleza CM, Kiffer C, et al. Structure for prevention of health care-associated infections in Brazilian hospitals: a countrywide study. Am J Infect Control. 2016;44:74–9.