ORIGINAL ARTICLE

Ventilator Bundle Compliance and Risk of Ventilator-Associated Events

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OBJECTIVE. Ventilator bundles encompass practices that reduce the risk of ventilator complications, including ventilator-associated pneumonia. The impact of ventilator bundles on the risk of developing ventilator-associated events (VAEs) is unknown. We sought to determine whether decreased compliance to the ventilator bundle increases the risk for VAE development.

DESIGN. Nested case-control study.

SETTING. This study was conducted at 6 adult intensive care units at an academic tertiary-care center in Tennessee.

PATIENTS. In total, 273 patients with VAEs were randomly matched in a 1:4 ratio to controls by mechanical ventilation duration and ICU type.

METHODS. Controls were selected from the primary study population at risk for a VAE after being mechanically ventilated for the same number of days as a specified case. Using conditional logistic regression analysis, overall cumulative compliance, and compliance with individual components of the bundle in the 3 and 7 days prior to VAE development (or the control match day) were examined.

RESULTS. Overall bundle compliance at 3 days (odds ratio [OR], 1.15; $P = .34$) and 7 days prior to VAE diagnosis (OR, 0.96; $P = .83$) were not associated with VAE development. This finding did not change when limiting the outcome to infection-related ventilator-associated complications (IVACs) and after adjusting for age and gender. In the examination of compliance with specific bundle components increased compliance with chlorhexidine oral care was associated with increased risk of VAE development in all analyses.

CONCLUSIONS. Ventilator bundle compliance was not associated with a reduced risk for VAEs. Higher compliance with chlorhexidine oral care was associated with a greater risk for VAE development.

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In the United States, ~ 800,000 patients are placed on mechanical ventilators each year.[1] These patients are at substantial risk for complications related to ventilatory support, including ventilator-associated pneumonia (VAP), acute respiratory distress syndrome (ARDS), barotrauma, and pulmonary edema. These complications often lead to prolonged hospital stays and increase mortality and morbidity.[1–4] Ventilator-associated pneumonia is associated with an increased duration of mechanical ventilation, increased length of stay in the intensive care unit (ICU), and increased mortality.[5–7] These outcomes have driven many investigators to study interventions that can reduce the risk of VAP. Additionally, institutional VAP rates have historically been an important quality and safety metric, although limitations exist when using this outcome as a measure to compare facilities.[8–10]

Many practices, including elevation of the head of bed (HOB), routine oral care (including the use of chlorhexidine swabs and teeth brushing), hypopharyngeal suctioning, and daily spontaneous awakening and breathing trials, have been noted to reduce the risk of VAP.[11] These practices are commonly deployed together as part of a ventilator bundle, and in many studies ventilator bundles have been associated with a reduction in VAP rates.[12–27]

In 2007, our institution developed a real-time ventilator bundle compliance dashboard that tracks the status of all bundle practices and serves to remind bedside caregivers when a specific practice is due. A major advantage of this approach is that it captures compliance over the entire duration of ventilation in real time as opposed to other methods such as spot audits. Our data suggest that deployment and real-time monitoring of a ventilator bundle led to a sustained reduction in VAP rates.[28]

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Prior to 2013, surveillance for ventilator-associated complications was limited to VAP. The surveillance definition for VAP was neither sensitive nor specific and relied on considerable subjectivity.[9,29,30] Therefore, in January 2013, the Centers for Disease Control and Prevention (CDC) retired the VAP surveillance definition for adult patients and released new definitions for ventilator-associated events (VAEs). Ventilator-associated events comprise several subcomponents including ventilator-associated complications (VAC), infection-related ventilator-associated complications (IVAC), and probable ventilator-associated pneumonia (PVAP), each defined by objective criteria that are increasingly stringent from VAC to IVAC to PVAP. While ventilator bundles have been shown in some studies to be associated with a reduction in VAP rates, data on their impact on VAEs are lacking. The primary objective of this study was to determine whether noncompliance to the ventilator bundle is a risk factor for the development of VAEs.

METHODS

Institutional Ventilator Bundle and Compliance Dashboard

The development of our institutional ventilator bundle and compliance dashboard has been previously described.[28] The ventilator bundle includes elevation of the head of the patient's bed between 30° and 45°, daily assessment of readiness for a spontaneous breathing trial (SBT), SBT completion (if ready), both target setting and assessment of the Richmond Agitation Sedation Scale (RASS) score, oral care (including hypopharyngeal suctioning, oral chlorhexidine swabbing, and teeth brushing), stress ulcer prophylaxis, and deep vein thrombosis (DVT) prophylaxis. Although it is a part of the bundle, stress ulcer prophylaxis and DVT prophylaxis were excluded from this analysis because these measures were not intended to reduce VAP.

Every 5 minutes, the compliance dashboard flags bundle components as green (fully compliant), yellow (soon to fall out of compliance), and red (out of compliance) as described previously.[28] We calculated the percentage of total ventilator time in which each individual component of the bundle was marked green or yellow (ie, percent compliant). We also calculated an overall bundle score to indicate the percentage of ventilator time in which all components of the bundle were in compliance. Such bundle scores were separately calculated to indicate bundle compliance for 3 and 7 days prior to VAE onset (or match date for controls). We also examined the specific impact of oral care practices by calculating 3- and 7-day oral care scores, which indicated the percentage of time all oral care components were in compliance.

Study Population

The primary study base for this nested case-control study was all adult ICU patients who were mechanically ventilated at any point during calendar years 2013 and 2014. The ICUs at our urban tertiary-care academic medical center include medical, surgical, cardiovascular, neurological, burn, and trauma units. Patients were excluded if they were not on a ventilator for at least 3 days because a patient must have at least 2 days of stable positive end-expiratory pressure (PEEP) and fractional inspired percentage of oxygen (FiO_2) followed by 2 days of worsening of these measures to qualify as a VAE. Cases and controls were excluded from analysis if they were intubated for >1 calendar day prior to transfer to our hospital or were in our palliative care unit (where the ventilator bundle dashboard is not active).

The Vanderbilt Institutional Review Board approved this study.

Selection of Cases

Initial VAE case-finding was carried out in real time by the Vanderbilt Infection Prevention Electronic Resource (VIPER), an infection surveillance program that monitors electronic ventilator records for changes in FiO_2 and PEEP that may be consistent with a VAE. Cases were confirmed and adjudicated by infection preventionists (IPs) according to CDC definitions. The IPs were blinded to patient-specific ventilator bundle compliance. Follow-up for patients terminated when they developed their first VAE during the study period (ie, only the first VAE for any patient was included in the study).

Selection of Controls

Controls were randomly selected from those at risk of developing a VAE with at least as many days since intubation as the onset of the VAE for the case. Controls were also matched by type of ICU given underlying differences in these populations. Cases and controls were matched at a 1:4 ratio. Each case had a defined number of days between intubation and the day of the VAE onset. Each control was thus assigned a "match date" that allowed the period of ventilation prior to their match date to equal the same ventilator period of interest to its matched case. All ventilator bundle data reported are referenced to the date of VAE onset for cases and the match date for controls.

Statistical Considerations

We anticipated 250 cases with controls matched in a 1:4 ratio. Based on a small internal sample, we estimated a within-group standard deviation of 0.25. If the true difference in the experimental and control means (not accounting for matching) were 0.05, we would have 81% power to reject the null hypothesis with a type 1 error of 0.05. P values $< .05$ were considered statistically significant.

To account for matching, conditional logistic regression models were used, and odds ratios were reported for univariate analyses. For univariate age comparisons, paired t tests were conducted using the mean of matched controls. A multivariate conditional logistical regression analysis was also conducted; it included age and gender a priori as well as candidate variables with a $P < 0.15$ in univariate analysis. All analyses were performed in Stata IC 13 software (StataCorp, College Station, TX).

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Sensitivity Analyses

Because most previous work on the ventilator bundle investigated the impact on VAP, there may not be a significant role in preventing other clinical entities such as pulmonary edema, ARDS, and atelectasis, which may lead to VAEs.[31] Including all VAEs could bias this study towards the null, and as such, we planned an analysis to only include IVACs and PVAPs because they may be more likely to describe pneumonia.

RESULTS

There were 301 cases of VAEs at our institution between January 1, 2013, and December 31, 2014. Of these cases, 17 were excluded from analysis because those patients were intubated for >1 calendar day prior to transfer to our institution. In addition, 7 VAE cases were excluded because they occurred in patients who had already had a VAE during the study period. We excluded 1 patient because the VAE occurred in the palliative care unit where the ventilator dashboard was not active. Furthermore, 3 cases were excluded due to the ventilator dashboard failing to capture the ventilator bundle data. A total of 273 cases remained for analysis, along with 984 controls. Of these cases, 137 were VAC only and 136 were IVAC or PVAP. The trauma ICU had the highest number of VAEs (n = 85), with another 46 cases in the cardiovascular ICU, 45 in the medical ICU, 44 in the neurosurgical ICU, 36 in the surgical ICU, and 17 in the burn ICU.

The mean ages were 54.4 years for cases and 55.0 years for controls ($P = .66$); 68% of cases were male, and 62% of controls were male ($P = .09$). The mean time to VAE was 7 days. The mean overall bundle scores were 0.73 for cases and 0.70 for controls in the 3 days prior to VAE onset or match day, and the mean oral care scores were 0.80 for cases and 0.79 for controls. Individual components of the bundle ranged in mean compliance from 0.83 to 0.99 (see Supplemental Material).

The odds ratios (ORs) and 95% confidence intervals for ventilator bundle compliance for 3 days prior to VAE onset (or match date for controls) are shown in Figure 1. There was no association between overall bundle scores and risk of VAE in the 3 days prior to VAE onset (OR, 1.15; $P = .34$). Also, we detected no association between the risk of VAE and the oral care score for 3 days prior to VAE onset (OR, 1.13; $P = .38$). Of all the individual components of the ventilator bundle, compliance with oral chlorhexidine was the only component associated with VAE risk. Compliance with oral chlorhexidine care was associated with a higher risk of VAE using cumulative compliance 3 days prior to the VAE (OR, 1.45; $P = .007$).

The amount of time needed from a lapse in care to lead to the onset of a VAE is unknown. We thus performed a similar analysis but extended the period of interest to include up to 7 days prior to the event or match date (Figure 2). Of the 273 cases, 107 were intubated for at least 7 days prior to VAE and were able to be included in this analysis along with their matched cases. Overall bundle score (OR, 0.96; $P = .83$), oral care score (OR, 1.10; $P = .55$), and individual component

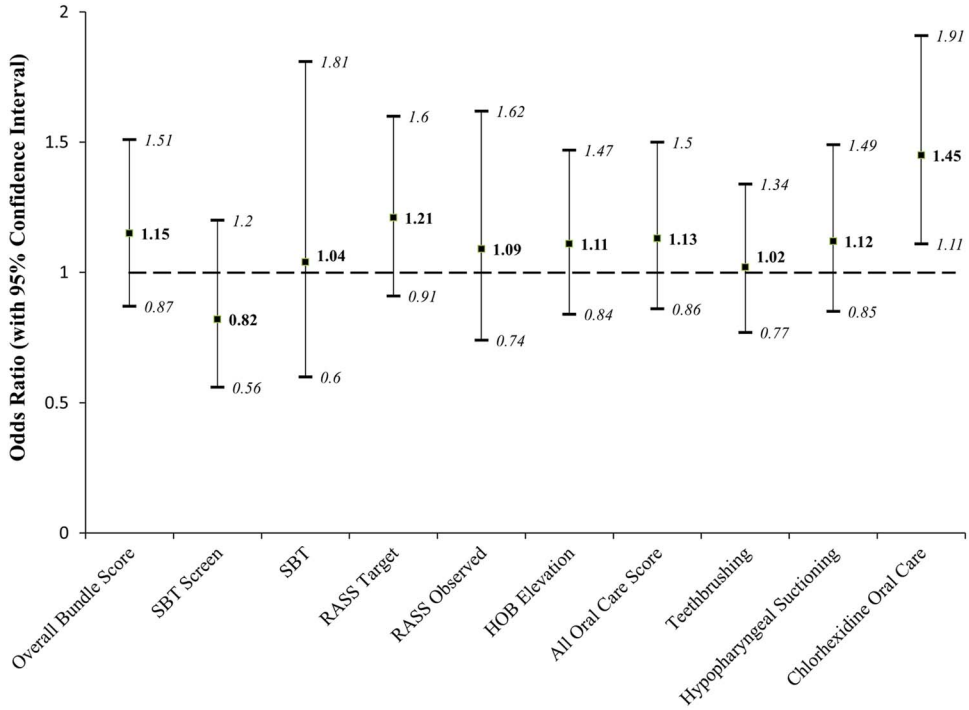

FIGURE 1. Odds ratios (bold) with 95% confidence interval (italics) for ventilator-associated event (VAE) risk by ventilator bundle component compliance 3 days prior to the VAE. NOTE. SBT, spontaneous breathing trial; RASS, Richmond Agitation Sedation Score; HOB, head of bed.

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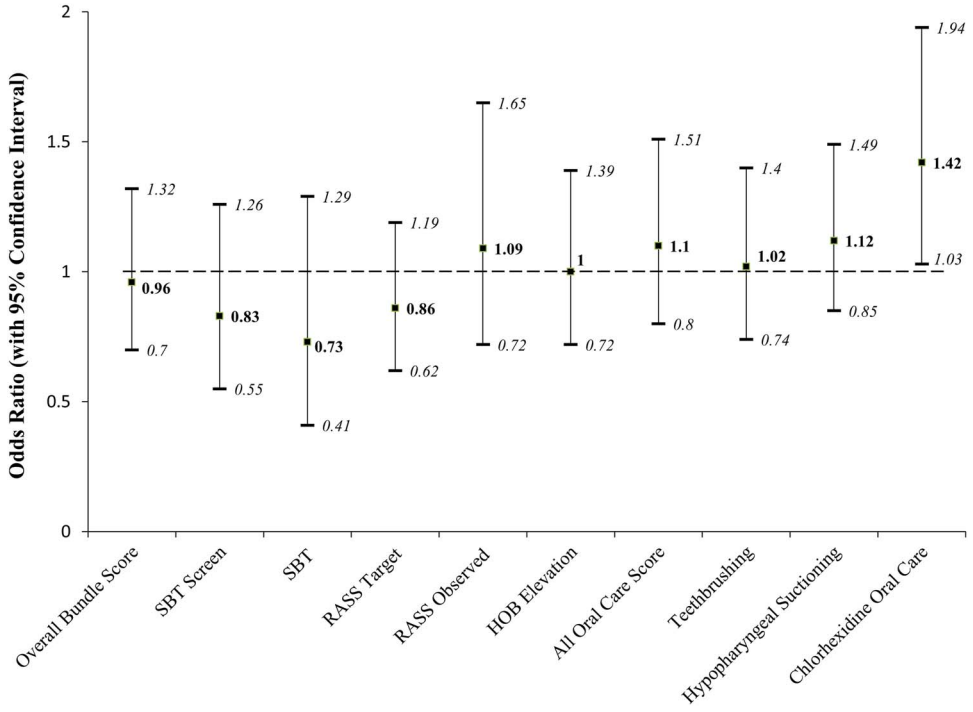

FIGURE 2. Odds ratios (bold) with 95% confidence interval (italics) for ventilator-associated event (VAE) risk by ventilator bundle component compliance 7 days prior to the VAE. NOTE. SBT, spontaneous breathing trial; RASS, Richmond Agitation Sedation Score; HOB, head of bed.

associations with VAE did not change. Compliance with oral chlorhexidine care remained a risk factor for VAE (OR, 1.42; $P = .03$) when extending the compliance to 7 days.

As IVACs and PVAPs could be more likely to be of infectious etiology than all types of VAEs, we performed an analysis limited to these 2 VAE types. The results for this analysis, however, were similar to those of the all-VAE analysis (Figure 3). Compliance with chlorhexidine mouth swabs was again associated with increased risk of VAE (OR, 1.73; $P = .0006$).

Finally, a multivariable analysis including age, gender, and compliance with chlorhexidine mouth swabs for 3 days prior to the event or match date was conducted, and the association with compliance with chlorhexidine mouth swabs persisted (OR, 1.45; $P = .008$) (Table 1).

DISCUSSION

We did not find an association between increased bundle compliance and reduced risk of VAE. Compliance with chlorhexidine oral swabs, however, was associated with an increased risk of developing a VAE, a finding that held when examining the subset of VAE including IVAC and PVAP. Recent studies have suggested that the use of oral chlorhexidine may be associated with increased mortality.[32,33] Some authors have suggested this may be due to aspiration of chlorhexidine, which can lead to lung injury. Other studies, however, suggest that chlorhexidine oral care may protect against PVAP.[34] As PVAP is dependent on the variable practices of the decision to obtain a respiratory culture, we did not perform a subgroup analysis on PVAP alone.

Prior studies examining the impact of ventilator bundles have largely shown reductions in rates of VAP as it was previously defined.[12–27] A previous study at our institution implementing the same ventilator dashboard utilized in this study showed that VAP rates decreased significantly with the rollout of the ventilator bundle.[28] VAPs and VAEs are different outcomes; however, previous research has shown that the entities often have little overlap.[35] The ventilator bundles currently employed by many hospitals are largely untested against the prevention of VAEs. There was no VAE surveillance at the time of many ventilator bundle rollouts, including the one in this study. Thus, we were unable to determine whether implementation of the ventilator bundle would lead to a similar change in rates of VAEs. In this study, however, we were able to determine that the VAEs that still occur in this institution are not associated with significant lapses in bundle adherence.

This study has several limitations. We were unable to control for severity of illness, which has confounding potential, though the direction of the potential bias is unknown. To limit confounding, patients were matched according to ventilator time and ICU type. We are therefore unable to determine whether components of the ventilator

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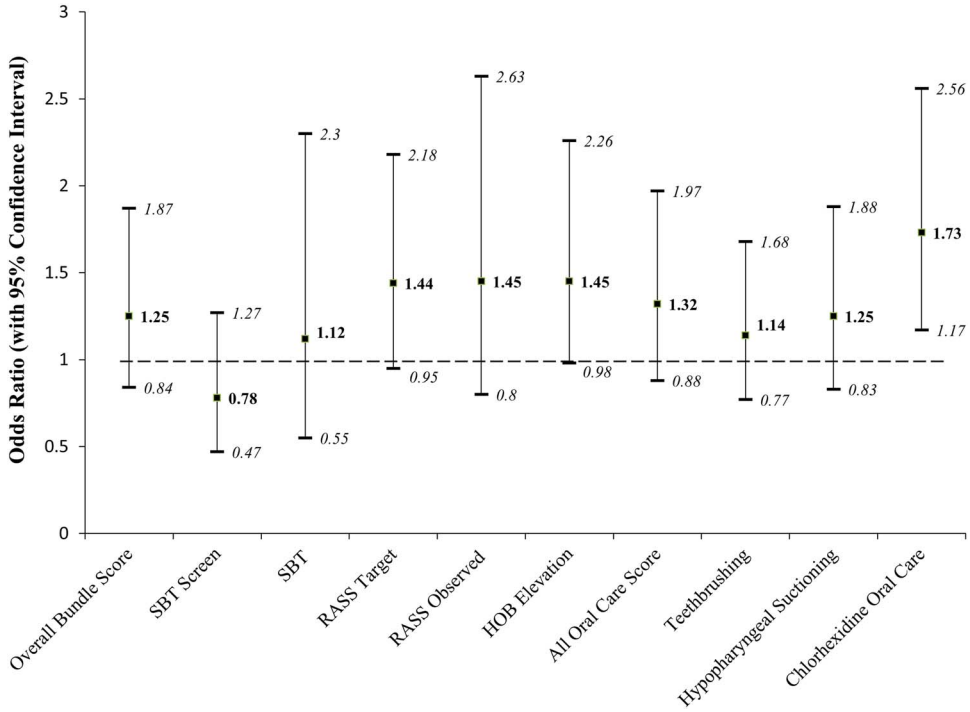

FIGURE 3. Odds ratios (bold) with 95% confidence interval (italics) for infection-related ventilator-associated complication (IVAC) and probable ventilator-associated pneumonia (PVAP) risk by ventilator bundle component compliance three days prior to the IVAC or PVAP. NOTE. SBT, spontaneous breathing trial; RASS, Richmond Agitation Sedation Score; HOB, head of bed.

TABLE 1. Multivariable Analysis Adjusting for Age and Gender With Ventilator Bundle Compliance 3 Days Prior to the Ventilator-Associated Event

Characteristic	Odds Ratio	*P* Value	95% Confidence Interval
Chlorhexidine mouth swab compliance	1.45	0.008	1.10–1.90
Age, y	1.00	0.63	0.99–1.01
Male	1.27	0.10	0.96–1.69

bundle may be more effective in certain ICU populations or in the prevention of early versus late VAEs. Compliance to the ventilator bundle was high in this study in both cases and controls. This finding suggests that improvements from previous interventions, such as implementation of the ventilator bundle dashboard, have been sustained. High rates of compliance, however, do limit our ability to detect a difference in the exposure of interest in this study. Our results suggest that VAEs that occur at this institution are not driven by noncompliance to the ventilator bundle. For institutions in which ventilator bundle compliance is already high, there may be greater benefit in focusing efforts on other VAE risk factors such as fluid balance and choice of ventilatory modes.[35,36]

It is unclear what level of compliance (ie, the "dose") might be adequate to lead to protection from either the previously defined VAP or the current framework of VAE. Previous studies compared rates of VAP before and after implementation of ventilator bundles, but optimal intervals for interventions have not been well studied. Although our bundle scores are able to quantify the degree of compliance for an individual patient, they are unable to differentiate between infrequent yet prolonged periods of noncompliance versus more frequent but shorter periods of noncompliance.

To further reduce VAEs, it may be time to add new components to ventilator bundles, to develop new approaches to VAE prevention, and to further study the impact of chlorhexidine oral care. Because VAEs require FiO_2 and PEEP changes to be sustained for 2 days, early VAE warning systems that signal a patient's respiratory decline coupled with interventions to reduce pulmonary edema, atelectasis, and secretions may also have potential to provide value in this setting.

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SUPPLEMENTARY MATERIAL

To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2018.30

REFERENCES

1. Wunsch H, Linde-Zwirble WT, Angus DC, Hartman ME, Milbrandt EB, Kahn JM. The epidemiology of mechanical ventilation use in the United States. *Crit Care Med* 2010;38: 1947–1953.
2. Esteban A, Anzueto A, Frutos F, et al. Characteristics and outcomes in adult patients receiving mechanical ventilation: a 28-day international study. *JAMA* 2002;287:345–355.
3. Kahn JM, Goss CH, Heagerty PJ, Kramer AA, O'Brien CR, Rubenfeld GD. Hospital volume and the outcomes of mechanical ventilation. *N Engl J Med* 2006;355:41–50.
4. Rubenfeld GD, Caldwell E, Peabody E, et al. Incidence and outcomes of acute lung injury. *N Engl J Med* 2005;353:1685–1693.
5. Mizgerd JP. Acute lower respiratory tract infection. *N Engl J Med* 2008;358:716–727.
6. Heyland DK, Cook DJ, Griffith L, Keenan SP, Brun-Buisson C. The attributable morbidity and mortality of ventilator-associated pneumonia in the critically ill patient. The Canadian Critical Trials Group. *Am J Respir Crit Care Med* 1999;159:1249–1256.
7. Bekaert M, Timsit JF, Vansteelandt S, et al. Attributable mortality of ventilator-associated pneumonia: a reappraisal using causal analysis. *Am J Respir Crit Care Med* 2011;184:1133–1139.
8. Klompas M. The paradox of ventilator-associated pneumonia prevention measures. *Crit Care* 2009;13:315.
9. Klompas M. Eight initiatives that misleadingly lower ventilator-associated pneumonia rates. *Am J Infect Control* 2012;40:408–410.
10. Klompas M, Platt R. Ventilator-associated pneumonia—the wrong quality measure for benchmarking. *Ann Intern Med* 2007;147:803–805.
11. Muscedere J, Rewa O, McKechnie K, Jiang X, Laporta D, Heyland DK. Subglottic secretion drainage for the prevention of ventilator-associated pneumonia: a systematic review and meta-analysis. *Crit Care Med* 2011;39:1985–1991.
12. Zilberberg MD, Shorr AF, Kollef MH. Implementing quality improvements in the intensive care unit: ventilator bundle as an example. *Crit Care Med* 2009;37:305–309.
13. Berenholtz SM, Pham JC, Thompson DA, et al. Collaborative cohort study of an intervention to reduce ventilator-associated pneumonia in the intensive care unit. *Infect Control Hosp Epidemiol* 2011;32:305–314.
14. Lawrence P, Fulbrook P. The ventilator care bundle and its impact on ventilator-associated pneumonia: a review of the evidence. *Nurs Crit Care* 2011;16:222–234.
15. Ferreira CR, de Souza DF, Cunha TM, et al. The effectiveness of a bundle in the prevention of ventilator-associated pneumonia. *Braz J Infect Dis* 2016;20:267–271.
16. Sachetti A, Rech V, Dias AS, Fontana C, Barbosa Gda L, Schlichting D. Adherence to the items in a bundle for the prevention of ventilator-associated pneumonia. *Rev Bras Ter Intensiva* 2014;26:355–359.
17. Sen S, Johnston C, Greenhalgh D, Palmieri T. Ventilator-associated pneumonia prevention bundle significantly reduces the risk of ventilator-associated pneumonia in critically ill burn patients. *J Burn Care Res* 2016;37:166–171.
18. Al-Thaqafy MS, El-Saed A, Arabi YM, Balkhy HH. Association of compliance of ventilator bundle with incidence of ventilator-associated pneumonia and ventilator utilization among critical patients over 4 years. *Ann Thorac Med* 2014;9: 221–226.
19. Sulis CA, Walkey AJ, Abadi Y, Campbell Reardon C, Joyce-Brady M. Outcomes of a ventilator-associated pneumonia bundle on rates of ventilator-associated pneumonia and other health care-associated infections in a long-term acute care hospital setting. *Am J Infect Control* 2014;42:536–538.
20. Eom JS, Lee MS, Chun HK, et al. The impact of a ventilator bundle on preventing ventilator-associated pneumonia: a multicenter study. *Am J Infect Control* 2014;42:34–37.
21. Lim KP, Kuo SW, Ko WJ, et al. Efficacy of ventilator-associated pneumonia care bundle for prevention of ventilator-associated pneumonia in the surgical intensive care units of a medical center. *J Microbiol Immunol Infect* 2015; 48:316–321.
22. Bukhari SZ, Hussain WM, Banjar AA, Fatani MI, Karima TM, Ashshi AM. Application of ventilator care bundle and its impact on ventilator associated pneumonia incidence rate in the adult intensive care unit. *Saudi Med J* 2012;33:278–283.
23. Pogorzelska M, Stone PW, Furuya EY, et al. Impact of the ventilator bundle on ventilator-associated pneumonia in intensive care unit. *Int J Qual Health Care* 2011;23:538–544.
24. Morris AC, Hay AW, Swann DG, et al. Reducing ventilator-associated pneumonia in intensive care: impact of implementing a care bundle. *Crit Care Med* 2011;39:2218–2224.
25. Bird D, Zambuto A, O'Donnell C, et al. Adherence to ventilator-associated pneumonia bundle and incidence of ventilator-associated pneumonia in the surgical intensive care unit. *Arch Surg* 2010;145:465–470.
26. Al-Tawfiq JA, Abed MS. Decreasing ventilator-associated pneumonia in adult intensive care units using the Institute for Healthcare Improvement bundle. *Am J Infect Control* 2010;38:552–556.
27. Blamoun J, Alfakir M, Rella ME, et al. Efficacy of an expanded ventilator bundle for the reduction of ventilator-associated pneumonia in the medical intensive care unit. *Am J Infect Control* 2009;37:172–175.
28. Talbot TR, Carr D, Parmley CL, et al. Sustained reduction of ventilator-associated pneumonia rates using real-time course correction with a ventilator bundle compliance dashboard. *Infect Control Hosp Epidemiol* 2015;36:1261–1267.
29. Raoof S, Baumann MH, Critical Care Societies Collaborative cotlotAAoC-CNtACoCPtATS, the Society of Critical Care M. Ventilator-associated events: the new definition. *Am J Crit Care* 2014;23:7–9.
30. Klompas M. Ventilator-associated events surveillance: a patient safety opportunity. *Curr Opin Crit Care* 2013;19: 424–431.
31. Klompas M, Khan Y, Kleinman K, et al. Multicenter evaluation of a novel surveillance paradigm for complications of mechanical ventilation. *PLoS One* 2011;6:e18062.
32. Price R, MacLennan G, Glen J, Su DC. Selective digestive or oropharyngeal decontamination and topical oropharyngeal chlorhexidine for prevention of death in general intensive care: systematic review and network meta-analysis. *BMJ* 2014;348:g2197.

33. Klompas M, Li L, Kleinman K, Szumita PM, Massaro AF. Associations between ventilator bundle components and outcomes. *JAMA Intern Med* 2016;176:1277–1283.
34. Enwere EN, Elofson KA, Forbes RC, Gerlach AT. Impact of chlorhexidine mouthwash prophylaxis on probable ventilator-associated pneumonia in a surgical intensive care unit. *Int J Crit Illn Inj Sci* 2016;6:3–8.
35. Klompas M. Ventilator-associated conditions versus ventilator-associated pneumonia: different by design. *Curr Infect Dis Rep* 2014;16:430.
36. Lewis SC, Li L, Murphy MV, Klompas M, Epicenters CDCP. Risk factors for ventilator-associated events: a case-control multivariable analysis. *Crit Care Med* 2014;42: 1839–1848.

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