



ELSEVIER

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.e-jmii.com



ORIGINAL ARTICLE

Efficacy of ventilator-associated pneumonia care bundle for prevention of ventilator-associated pneumonia in the surgical intensive care units of a medical center



Kim-Peng Lim^{a,b}, Shuenn-Wen Kuo^c, Wen-Je Ko^d,
Wang-Huei Sheng^{a,b,*}, Ying-Ying Chang^b, Mei-Chaun Hong^b,
Chun-Chuan Sun^b, Yee-Chun Chen^{a,b}, Shan-Chwen Chang^b

^a Center for Infection Control, National Taiwan University Hospital, Taipei, Taiwan

^b Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan

^c Department of Surgery, National Taiwan University Hospital, Taipei, Taiwan

^d Department of Traumatology, National Taiwan University Hospital, Taipei, Taiwan

Received 30 April 2013; received in revised form 20 August 2013; accepted 31 August 2013

Available online 31 October 2013

KEYWORDS

Surgical intensive care unit;
Ventilator-associated pneumonia care bundle

Background: Ventilator-associated pneumonia (VAP) is one of the most serious treatment-related infections resulting in high mortalities and costs. Our hospital has implemented bundle care in the intensive care units (ICUs) with special focus on VAP prevention. This is a retrospective study to evaluate its efficacy.

Methods: We implemented a six-item VAP care bundle modified from that of the Institute for Healthcare Improvement at five surgical ICUs (SICUs) in the National Taiwan University Hospital. A multidisciplinary teamwork was involved in this bundle care. This study analyses the SICU utilization, ventilator utilization, and VAP incidence between January 2006 and March 2013 to assess the impact of VAP bundle in a clinical setting.

Results: A total of 28,454 SICU patients were analyzed in this study and patients under the age of 18 were excluded ($n = 1329$); eventually, 27,125 patients were enrolled, with 12,913 patients from the pre-VAP bundle phase and 14,212 from the post-VAP bundle phase. Patients from the post-VAP phase tended to be older ($p = 0.024$) and with shorter SICU stay

* Corresponding author. Department of Internal Medicine, National Taiwan University Hospital, Number 7, Chung-Shan South Road, Taipei 100, Taiwan.

E-mail address: whsheng@ntu.edu.tw (W.-H. Sheng).

($p = 0.006$), and disease severity scores (Therapeutic Intervention Scoring System, Glasgow Coma Scale, and Acute Physiology and Chronic Health Evaluation II score) were lower in the post-VAP bundle phase ($p < 0.001$), except the Injury Severity Score ($p = 0.729$). In response to VAP bundle interventions, no difference in SICU utilization ($p = 0.982$) between the pre-VAP and post-VAP bundle phases was noted, whereas the ventilator utilization was significantly decreased, from 1148.5 ventilator days to 956.1 ventilator days ($p < 0.001$) monthly; the VAP density had remarkably decreased from 3.3 to 1.4 cases per 1000 ventilator days ($p < 0.001$).

Conclusion: Implementation of VAP bundle care decreases the incidence of VAP at SICU. Multidisciplinary teamwork, education, and a comprehensive checklist to improve health-care workers' compliance are the keys to success.

Copyright © 2013, Taiwan Society of Microbiology. Published by Elsevier Taiwan LLC. All rights reserved.

Introduction

Ventilator-associated pneumonia (VAP), one of the most serious health-care-associated infections, not only lengthens the intensive care unit (ICU) and hospital stay but also results in higher morbidity, mortality, and medical cost.^{1–3} The Centers for Disease Control and Prevention of the National Healthcare Safety Network Hospitals had reported a mean VAP density of 3.6 cases/1000 ventilator days in medical–surgical ICUs in the United States, whereas in developing countries, it varied from 10 to 41.7 cases/1000 ventilator days.^{4,5} Safdar et al reported that nearly 10–20% patients receiving mechanical ventilation over 48 hours developed VAP.⁶ Thus, much more effort is needed to prevent VAP in critical care.

The Institute for Healthcare Improvement (IHI) had held a “100 Mile for Lives” campaign from 2004 to 2006 by introducing a “bundle” that collectively and reliably performs a small, straightforward set of evidence-based practices, which have been proven to improve patient outcomes.⁷ It generally includes three to five independent and evidence-based interventions.^{7,8} The VAP bundle, which is derived from the IHI bundle, is composed of the following five major interventions: (1) head-of-bed elevation between 30° and 45°; (2) a daily “sedation vacation” and a readiness-to-wean assessment; (3) peptic ulcer disease prophylaxis; (4) deep vein thrombosis prophylaxis; and (5) daily oral care with chlorhexidine (a new intervention added since 2010). Several studies have proved the efficacy of VAP care bundle worldwide.^{9–11} Al-Tawfiq et al reported that the mean VAP density decreased from 9.3 cases/1000 ventilator days to 2.2 cases/1000 ventilator days after 2 years of utilizing this bundle in surgical ICUs (SICUs).⁹

Continued improvement of the clinical care quality and patient safety to improve the clinical outcome is important. VAP is the second most common health-care-associated infection following catheter-related bloodstream infection in SICUs of National Taiwan University Hospital (NTUH). A VAP bundle was designed to reduce the VAP density at NTUH in 2009. The implementation of the VAP bundle was commenced in all five SICUs since November 1, 2009. Our aim was to decrease VAP density by 50% in all SICUs. We retrospectively reviewed the data to evaluate the efficacy of the VAP bundle.

Materials and methods

Study design

The primary aim of this study was to check the efficacy of the VAP bundle by comparing the before- and after-the-bundle VAP density with a goal to decrease 50% of the VAP density at SICUs. A multidisciplinary teamwork was set up including administrator (vice superintendent), quality improvement and infection control professionals, SICU doctors and nurses, respiratory therapists, pharmacists, and general affairs and information technology specialists.

This bundle campaign was guided by the Infection Control Center at NTUH. NTUH is a 2200-bed tertiary referral medical center in Northern Taiwan. It consisted of five SICUs (total 63 beds), seven medical ICUs (MICUs; totally 79 beds), and four pediatric ICUs (PICUs; totally 62 beds). The implementation of the VAP bundle was started in all SICUs from November 1, 2009. Therefore, we retrospectively reviewed the demographic data and analyzed the occurrence of VAP of all SICU patients. This study was approved by the Institute of Research Board at NTUH NTUH201003093RINC.

Definition

The VAP is defined as a respiratory tract infection developed after 48 hours of intubation with mechanical ventilation or within 48 hours after disconnecting the ventilator.^{12,13} The respiratory tract infection follows the definition in the Nosocomial Infection Surveillance guideline from the Taiwan Centers for Disease Control,¹⁴ and it is determined by the clinicians according to the clinical presentations after ruling out all other cause-induced systemic inflammatory response syndrome. The ventilators were limited to the invasive types by either tracheostomy or endotracheal tube only, and other noninvasive ventilation devices were excluded.

The “SICU utilization” is defined as the total SICU patient number from a certain period measured by “patient days,” and equals the summation of each patient multiplied by his/her SICU admission days; the “ventilator utilization” is a total ventilated patient count in a period and in unit of

Table 1 Contents of the daily rounding checklist for quality VAP bundle care

Interventions	Checkers
Direct elements that decrease infections	
Hand hygiene before and after intubation procedure and patient contact	Nurse
Aspiration prophylaxis	
Head-of-bed elevation: 30 to 45°	Nurse
Adequate endotracheal tube cuff pressure (>20–25 cmH ₂ O)	Respiratory therapist
Oral cavity secretion clearance before changing position or supination	Nurse
Oral care with chlorhexidine solution every 8 h	Nurse
Decrease contamination to respiratory tract devices	
High-level sterilization and storage of the ventilator tubing	Nurse
Moisten the devices with sterile water	Respiratory therapist
Indirect elements that decrease infections	
Daily “sedation vacation” and daily assessment of readiness for extubation	Doctor
Prophylactic medications	
Peptic ulcer disease	Doctor
Deep vein thrombosis	Doctor
Intubation indication	Doctor

VAP = ventilator-associated pneumonia.

“ventilator days,” and equals the summation of each patient multiplied by his/her ventilated days in SICU; the “ventilator utilization ratio” is a ratio of ventilator utilization to SICU admission, and is expressed in percentage; the “VAP count” is a total number of VAP patients in the pre-VAP bundle and post-VAP bundle phases of SICU admission, in unit of “cases”; the “VAP incidence” is a ratio of VAP patients/1000 ventilated patients during the pre-VAP bundle and post-VAP bundle phases; the VAP density is ratio of “VAP count” to “ventilator utilization,” and is expressed in unit of “cases/1000 ventilator days.”

VAP bundle

Besides the five primary interventions adopted from the IHI bundle, some additional evidence-based interventions were modified and added to the daily quality rounding checklist.^{8,15} We set up six-item interventions for VAP bundle in SICUs. A bedside VAP bundle quality rounding checklist modified from the IHI bundle⁸ was used to assist the doctors, nurses, and respiratory therapists in SICUs in complying with the daily protocol for each ventilated patient with standard care, the details of which are shown in Table 1.¹⁵

Data collection

We retrospectively analyzed the data from January 1, 2006 to March 31, 2013. The population included all SICU patients aged 18 or older during the period, without taking into account patients’ diagnoses or types of surgery. We selected the ventilated patients as our study target, and further analyzed the VAP density differences from the pre-VAP bundle phase and the post-VAP bundle phase. The dividing point was November 1, 2009, when the bundle was implemented in all SICUs.

Statistical analysis

All statistical data were analyzed on SPSS software, version 20.0 (SPSS Inc., Chicago, IL, USA). Differences in data of SICU inpatients and the outcomes were analyzed based on Mann–Whitney *U* test. The null hypothesis was that the VAP densities in the pre- and post-VAP bundle phases are the same. The descriptive statistics including median, mean, and standard deviation are presented for continuous variables, with $p < 0.05$ considered statistically significant.

Results

Demographic characteristics

The total SICU patients during the study period was 28,454, excluding 1329 patients who were under the age of 18, leaving 27,125 patients eligible for this study: 12,913 were from the pre-VAP bundle phase and 14,212 from the post-VAP bundle phase. Table 2 shows the demographic characteristics of SICU patients from both phases. There is no significant difference in sex ($p = 0.919$) and variable surgery types of patients (Table 2). In the post-VAP period, patients tended to be elderly ($p = 0.024$) and had shorter SICU stay ($p = 0.006$). Four disease severity scoring systems were used at the five SICUs. The results of Therapeutic Intervention Scoring System (TISS), Glasgow Coma Scale, and Acute Physiology and Chronic Health Evaluation II score showed that the disease severity scores were lower in the post-VAP bundle phase ($p < 0.001$); however, the Injury Severity Score showed it to be otherwise ($p = 0.729$).

Compliance of bundle care

The overall compliance rates of the post-VAP bundle phase of doctors, nurses, and respiratory therapist were 97.9%,

Table 2 Demographic characteristics of SICU patients from the pre- and post-VAP phases

Variables	Pre-VAP bundle phase	Post-VAP bundle phase	<i>p</i>
All SICU patients	12,913	14,212	
Type of surgery			
Cardiovascular surgery, <i>n</i> (%)	2644 (20.4%)	2886 (20.3%)	0.731
Neurosurgery, <i>n</i> (%)	2707 (21.0%)	3240 (22.8%)	<0.001
Thoracic surgery, <i>n</i> (%)	2013 (15.6%)	2537 (17.8%)	<0.001
General surgery, <i>n</i> (%)	4087 (31.7%)	3324 (23.4%)	<0.001
Traumatic surgery, <i>n</i> (%)	1462 (11.3%)	2225 (15.7%)	<0.001
Sex, male (%)	7730 (59.9%)	8499 (59.8%)	0.919
Age, median (25%, 75%) years	63.2 (50.6, 74.3)	62.8 (51.7, 74.5)	0.024
Age > 70 years, <i>n</i> (%)	4563 (35.3%)	5001 (35.2%)	0.799
SICU stay, median (25%, 75%) days	3 (2, 6)	3 (2, 6)	<0.001
Disease Severity Scoring Systems, median (25%, 75%) [<i>n</i>]			
TISS	39 (30, 45) [2604]	32 (23,38) [7665]	<0.001
GCS	11 (8, 14) [2615]	14 (10, 15) [3154]	<0.001
APACHE II	10 (7, 15) [7340]	10 (7, 14) [7591]	<0.001
ISS	18 (11, 27) [265]	19 (13, 25) [540]	0.729

APACHE II = Acute Physiology and Chronic Health Evaluation II score; GCS = Glasgow Coma Scale; ISS = Injury Severity Score; SICU = surgical intensive care unit; TISS = Therapeutic Intervention Scoring System; VAP = ventilator-associated pneumonia.

80.3%, and 73.7%, respectively. There was a cluster of higher VAP density from July 2011 to November 2011 (Fig. 1). We analyzed the factors that contributed to this result, and found that some health-care workers did not perform the VAP bundle well during this period. Hence, we had promoted the bundle care concept again through re-education, posters, and by standardizing medical interventions and equipment in December 2011. The compliance rates between before and after this re-education promotion were 92.4% versus 99.1% in the doctor group, 72.2% versus 89.3% in the nurse group, and 62.2% versus 84.0% in the respiratory therapist group.

Outcome

Both Table 3 and Fig. 1 showed there was a trend in significant decrease of ventilator utilization, VAP incidence, and VAP density (*p* < 0.001), but the SICU utilization remained similar between the pre-VAP and post-VAP phases. After the VAP bundle implementation, VAP incidence had decreased from 13.63 to 3.94/1000 ventilated patients (*p* < 0.001). The ventilator utilization ratio had decreased by 9.9% and VAP density had reduced by 1.9 cases/1000 ventilator days (up to a 57.6% reduction, which was higher than our study aim).

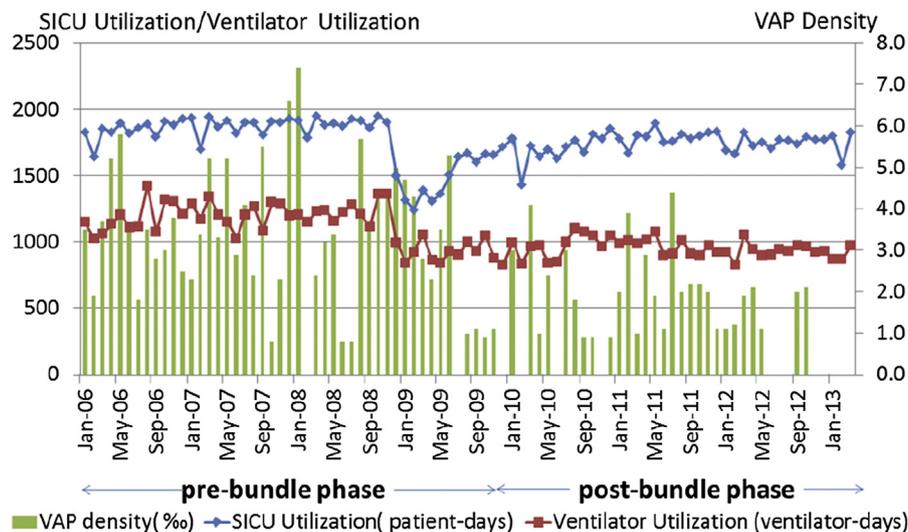


Figure 1. Distribution of monthly SICU utilization (diamonds), ventilator utilization (squares), and VAP density (vertical bars). SICU = surgical intensive care unit; VAP = ventilator-associated pneumonia.

Table 3 Ventilator utilization and incidences of VAP between the pre-VAP bundle and post-VAP bundle phases

Variables	Pre-VAP bundle phase	Post-VAP bundle phase	<i>p</i>
SICU utilization [mean] (patient days)	81,958 [1781.7]	71,753 [1750.1]	0.982
Ventilator utilization [mean] (ventilator days)	52,829 [1148.5]	39,201 [956.1]	<0.001
Ventilator utilization ratio (%)	64.5	54.6	<0.001
VAP counts [mean] (cases)	176 [3.8]	56 [1.4]	<0.001
VAP incidence (per 1000 patients)	13.6	3.9	<0.001
VAP density (cases/1000 ventilator days)	3.3	1.4	<0.001

SICU = surgical intensive care unit; VAP = ventilator-associated pneumonia.

Discussion

So far, we found only one article had reported on the VAP bundle efficacy in Taiwan, and this article is to date the largest and longest study to discuss the efficacy of VAP bundle in Taiwan.¹⁶ We used a risk-based approach to establish the focus of the health-care-associated infections and reduction programs. The infection control center recognized VAP as a significant health-care-associated infection in SICUs, and therefore, they adopted the bundle care to prevent VAP. Wip and Napolitano⁸ suggested that the respiratory care bundle was an effective method to reduce VAP density in ICUs, but should be modified and expanded to include effective and evidence-based practices with a focus on VAP prevention. Our VAP bundle design was modified from IHI and in consideration of other scientific evidences^{8,10,11} with several detailed interventions added, such as: (1) hand hygiene before and after procedures of intubation and patient contact, (2) adequate cuff pressure (>20–25 cmH₂O), (3) oral cavity secretion clearance before changing position or supination, (4) high-level sterilization and storage of the ventilator tubing, (5) device rinsed with sterile water, and (6) defined intubation indication. These additional interventions were added and modified from time to time. There were times when the clinicians found it confusing to follow, and thus we provided a VAP bundle quality rounding checklist to help them to perform the bundle jointly and consistently.

Based on the characteristics, VAP bundle interventions could be divided into two categories, namely, direct and indirect: the former had direct connection to infection decrease by decreasing pathogens' burden in the respiratory tract, such as "hand hygiene before and after procedures" and "oral care with chlorhexidine solution"¹⁷; the latter did not directly or specifically link to VAP prevention, such as "peptic ulcer disease and deep vein thrombosis prophylaxis," which were labeled as reasons for prevention of mechanical ventilation-induced mucosal disease and gastrointestinal bleeding^{8,18} in order to prevent other serious complications that could harm the patients.⁸ Doctors should always be aware of the risks and benefits of those prophylactic medications, such as bleeding tendency. Another two indirect interventions were the daily "sedation vacation and daily assessment of readiness to extubate" and "defined intubation indication." We used a daily checklist to remind the SICU doctors to perform early extubation, prolong or avoid inappropriate intubation, and incidentally less VAP developed, which echoed the findings of Schweickert et al.¹⁹

Our study result had confirmed the efficacy of VAP bundle care in decreasing the ventilator utilization and VAP density (reduction rate of 9.9% and 57.6%, respectively). This means not only life savings to the patients but also cost benefit to the society. The mean ventilator utilization in our hospital was 1058 ventilator days/month. Sheng et al.³ showed that the average extra cost for a hospital-acquired infection was US\$5058, which means that we could save US\$121,897.00 by cutting out 24.1 cases of VAP annually. The mean VAP density of our hospital before VAP bundle implementation was 3.3 cases/1000 ventilator days, which was similar to that reported in the United States.⁴ Through this VAP bundle care, we improved our SICU utilization (1.9 cases/1000 ventilator days) and patient care quality.

Our results show that SICU patients of the post-VAP bundle phase were older in age, had lesser SICU staying days, and lower disease severity scores. However, there might have some pitfalls from the statistic limitations. The scale of our study patients was large and the data diversity was wide, even though a milder variation may possibly cause a statistically significant (Supplementary Figure) but not a clinically relevant difference. For example, the median ages were 63.2 and 62.8 years and SICU stay were 3 and 3 days in the pre-VAP and post-VAP bundle phases, respectively. Similarly, the disease severity scoring systems were within the same class in clinical condition; for example, the TISS scores were classified into Class III severity in both phases. By contrast, shorter SICU stay might also indicate early weaning and extubation of endotracheal tube through the VAP bundle efforts.

When comparing the results, we found that the SICU patient count had increased but not the SICU utilization in the post-VAP bundle phase. The following two factors might dilute this effect: first, most young patients under the age of 18 were staying in SICU during the pre-VAP bundle phase, but they moved to our new PICU at the children's building after 2008, and they were excluded from this study; second, the SICU staying days had decreased and hence the SICU utilization was more available.

There was an obvious drop in both SICU and ventilator utilizations, but not in the VAP incidence in early 2009. The reason might be that our hospital had a fire disaster on December 18, 2008, which had damaged several operation rooms, cardiac and trauma SICUs, resulting in shortage of SICUs and subsequently in a decrease of SICUs and ventilator utilizations. However, the VAP incidence had increased during this chaotic period where other environmental factors might have contributed to the increase of

infection. After that event, our hospital had participated in the Joint Commission International evaluation to promote patient safety and care quality.

During the period of promotion of bundle care, we noticed that the VAP density had reduced just after VAP bundle implementation. However, there was a cluster of higher VAP density from July 2011 to November 2011. We analyzed the factors that contributed to this result, and found that some health-care workers did not perform the VAP bundle well during the period. Hence, we had promoted the bundle care concept again through re-education, posters, and by standardizing medical interventions and equipment in December 2011. Through this VAP bundle promotion and re-education, both bundle compliance rate and VAP density had improved well, and we believed that the VAP bundle compliance rate, to an extent, was an important assignable cause during this period. Our compliance rate remained unsatisfied by the IHI standard, which states that a successful implementation of bundle care means more than 95% compliance in each item to reach maximal prevention effects.⁷ Therefore, continuous education and promoting compliance of health-care workers to bundle care are important.

This study had certain limitations. First, although the VAP bundle was performed prospectively at all ICUs, we focused on retrospective chart review of SICU patients. The complexity of variable patients' characteristics, surgery types, different disease severity scoring systems at each SICU might all render the comparison to be difficult. Second, although several previous studies had reported positive results from VAP bundle care, and recommended this protocol for every ventilated patient,^{9,15,20} our study results were limited to the SICUs of a single center. To expand this VAP bundle protocol to MICU or PICU, we may require modification regarding specific characteristic of these units, especially those for patients with pneumonia and multicomborbidities before intubation. Third, our compliance to VAP bundle care needs to be better (overall health-care workers' compliance rate was below the 95% suggested by the IHI standard), and our study lacked the compliance rate to each element of VAP bundle, making it difficult to evaluate the bundle care comprehensively. Advocacy of good compliance of bundle care is necessary to improve VAP prevention.

In conclusion, our modified VAP bundle care is an effective measure for lowering the VAP incidence at SICU. Multidisciplinary teamwork, continuous education, and design a comprehensive checklist to improve health-care workers' compliance are the keys to success.

Acknowledgments

We thank all members of the infection control center and all SICUs staff in this VAP bundle care, who dedicated their efforts to collect data and complete all bundle care.

References

- Bercault N, Boulain T. Mortality rate attributable to ventilator-associated nosocomial pneumonia in an adult intensive care unit: a prospective case-control study. *Crit Care Med* 2001;29:2303–9.
- Leroy O, Sanders V, Girardie P, Devos P, Yazdanpanah Y, Georges H, et al. Mortality due to ventilator-associated pneumonia: impact of medical versus surgical ICU admittance status. *J Crit Care* 2001;16:90–7.
- Sheng WH, Wang JT, Lu DC, Chie WC, Chen YC, Chang SC. Comparative impact of hospital-acquired infections on medical costs, length of hospital stay and outcome between community hospitals and medical centres. *J Hosp Infect* 2005;59:205–14.
- Edwards JR, Peterson KD, Andrus ML, Tolson JS, Goulding JS, Dudeck MA, et al. National Healthcare Safety Network (NHSN) Report, data summary for 2006, issued June 2007. *Am J Infect Control* 2007;35:290–301.
- Arabi Y, Al-Shirawi N, Memish Z, Anzueto A. Ventilator-associated pneumonia in adults in developing countries: a systematic review. *Int J Infect Dis* 2008;12:505–12.
- Safdar N, Dezfulian C, Collard HR, Saint S. Clinical and economic consequences of ventilator-associated pneumonia: a systematic review. *Crit Care Med* 2005;33:2184–93.
- Institute for Healthcare Improvement. <http://www.ihf.org> [accessed 31.12.12].
- Wip C, Napolitano L. Bundles to prevent ventilator-associated pneumonia: how valuable are they? *Curr Opin Infect Dis* 2009;22:159–66.
- 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;38:552–6.
- Resar R, Pronovost P, Haraden C, Simmonds T, Rainey T, Nolan T. Using a bundle approach to improve ventilator care processes and reduce ventilator-associated pneumonia. *Jt Comm J Qual Patient Saf* 2005;31:243–8.
- Hawe CS, Ellis KS, Cairns CJ, Longmate A. Reduction of ventilator-associated pneumonia: active versus passive guideline implementation. *Intensive Care Med* 2009;35:1180–6.
- Taiwan Clinical Performance Indicator (TCPI). <http://tcpi.tjcha.org.tw/tcpi/> [accessed 01.06.11].
- Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. *Am J Infect Control* 2008;36:309–32.
- Centers for Disease Control, R.O.C Taiwan. Nosocomial infection surveillance guideline. <http://www.cdc.gov.tw/professional/info.aspx?treeid=beac9c103df952c4&nowtreeid=29e258298351d73e&tid=43F61FBCA4197> [Last accessed 01.12.12].
- DuBose JJ, Inaba K, Shiflett A, Trankiem C, Teixeira PG, Salim A, et al. Measurable outcomes of quality improvement in the trauma intensive care unit: the impact of a daily quality rounding checklist. *J Trauma* 2008;64:22–9.
- Liu WL, Lin HL, Lai CC, Hsueh PR. A multidisciplinary team care bundle for reducing ventilator-associated pneumonia at a hospital in southern Taiwan. *J Microbiol Immunol Infect* 2013;46:313–4.
- Chan EY, Ruest A, Meade MO, Cook DJ. Oral decontamination for prevention of pneumonia in mechanically ventilated adults: systematic review and meta-analysis. *BMJ* 2007;334:889.
- Cook DJ, Fuller HD, Guyatt GH, Marshall JC, Leasa D, Hall R, et al. Risk factors for gastrointestinal bleeding in critically ill patients. Canadian Critical Care Trials Group. *N Engl J Med* 1994;330:377–81.
- Schweickert WD, Gehlbach BK, Pohlman AS, Hall JB, Kress JP. Daily interruption of sedative infusions and complications of critical illness in mechanically ventilated patients. *Crit Care Med* 2004;32:1272–6.
- Bird D, Zambuto A, O'Donnell C, Silva J, Korn C, Burke R, et al. Adherence to ventilator-associated pneumonia bundle and incidence of ventilator-associated pneumonia in the surgical intensive care unit. *Arch Surg* 2010;145:465–70.