Using Ventilator-Associated Events Surveillance to Improve Outcomes for Ventilated Patients

Alaska State Hospital Association
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Michael Klompas MD, MPH, FIDSA, FSHEA
Harvard Medical School, Harvard Pilgrim Health Care Institute, and
Brigham and Women’s Hospital, Boston, USA
Disclosures

Grant funding from CDC for studies on VAE, VAP, and sepsis
Developing a New, National Approach to Surveillance for Ventilator-Associated Events

Shelley S. Magill, MD, PhD¹; Michael Klompas, MD, MPH²,³,⁴; Robert Balk, MD⁵,⁶; Suzanne M. Burns, RN, ACNP, MSN, RRT⁶,⁷; Clifford S. Deutschman, MS, MD⁶,⁸; Daniel Diekema, MD⁹,¹⁰; Scott Fridkin, MD¹¹; Linda Greene, RN, MPS¹¹,¹²; Alice Guh, MD, MPH¹; David Gutterman, MD⁶,¹³; Beth Hammer, RN, MSN, ANP-BC⁶,¹⁴; David Henderson, MD¹⁵; Dean Hess, PhD, RRT¹⁶,¹⁷,¹⁸; Nicholas S. Hill, MD⁶,¹⁹; Teresa Horan, MPH¹; Marin Kollef, MD⁶,²⁰; Mitchell Levy, MD⁶,²¹; Edward Septimus, MD²²,²³; Carole VanAntwerpen, RN, BSN²⁴,²⁵; Don Wright, MD, MPH²⁶; Pamela Lipsett, MD, MHPE⁶,²⁷
The challenge of VAP diagnosis

Many complications of critical care present with subjective clinical signs that mimic VAP:

- Radiographic opacities
- Fever
- Abnormal white blood cell count
- Impaired oxygenation
- Increased pulmonary secretions
“Diffuse patchy airspace disease right greater than left with obliteration of both hemi-diaphragms. Opacities possibly slightly increased since yesterday accounting for changes in patient position and inspiration. This could represent atelectasis, pneumonia, or effusion.”
Sources of fever and infiltrates

- ARDS
- Diffuse alveolar damage
- Thromboembolic disease
- Hemorrhage
- Infarction
- Fibrosis
- Carcinoma
- Lymphoma
- Contusion

PLUS

Tracheobronchitis
CLABSI
UTI
Drug fever

Pulmonary edema
Atelectasis
Contusion
Fibrosis

Meduri, Chest 1994; 106:221-235
Petersen, Scand J Infect Dis 1999; 31:299-303
Accuracy of clinical diagnosis of VAP
Relative to 253 autopsies

Sensitivity / Positive Predictive Value

- **Loose definition:** Infiltrate and 2 of temp / wbc / purulence
- **Strict definition:** Infiltrate and 3 of temp / wbc / purulence

Tejerina et al., J Critical Care 2010;25:62
Accuracy of quantitative BAL cultures

Relative to histology

Sensitivity / Positive Predictive Value

100%
80%
60%
40%
20%
0%

Sensitivity
Positive Predictive Value

Kirtland, Chest 1997;112:445
Fabregas, Thorax 1999;54:867
Chastre, Am Rev Respir Dis 1984;130:924
Torres, Am J Resp Crit Care Med 1994;149:324
Implications for prevention
The Classic Ventilator Bundle

Elevate the head of the bed
Daily sedative interruption
Daily assessment of readiness to wean
Stress ulcer prophylaxis
DVT prophylaxis
Oral care with chlorhexidine
Circularity Between Mechanisms of Prevention and the VAP Definition

VAP Definition
- Fever
- Leukocytosis
- Purulent Secretions
- Positive cultures

Oral care with CHG
- Silver Coated ETT
- Subglottic secretion drainage
- Semi-recumbent position etc.

positive cultures and / or
secretions
Oral Care with Chlorhexidine

Meta-analysis of RCTs: lower VAP rates

Risk Ratio 0.72 (0.55-0.94)

Lancet Infectious Dis 2011;11:845
**Oral Care with Chlorhexidine**

Meta-Analysis of RCTs: **higher** mortality rates

<table>
<thead>
<tr>
<th>Study</th>
<th>No of events/total</th>
<th>Mortality Odds ratio, M-H random (95% CI)</th>
<th>Weight (%)</th>
<th>Mortality Odds ratio, M-H random (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fourier 2000</td>
<td>3/30 7/30</td>
<td>2 0.37 (0.08 to 1.58)</td>
<td>8</td>
<td>0.89 (0.48 to 1.64)</td>
</tr>
<tr>
<td>MacNaughton 2004</td>
<td>29/101 29/93</td>
<td>9 1.40 (0.76 to 2.58)</td>
<td>12</td>
<td>1.47 (0.87 to 2.46)</td>
</tr>
<tr>
<td>Fourrier 2005</td>
<td>31/114 24/114</td>
<td>10 1.00 (0.57 to 1.77)</td>
<td>10</td>
<td>1.00 (0.57 to 1.77)</td>
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<tr>
<td>Koeman 2006</td>
<td>49/127 39/130</td>
<td>4 1.09 (0.46 to 2.58)</td>
<td>9</td>
<td>1.06 (0.59 to 1.91)</td>
</tr>
<tr>
<td>Tantipong 2008</td>
<td>36/102 37/105</td>
<td>18 1.60 (1.06 to 2.43)</td>
<td>18</td>
<td>1.60 (1.06 to 2.43)</td>
</tr>
<tr>
<td>Scannapieco 2009</td>
<td>19/116 9/59</td>
<td>21 1.35 (0.91 to 2.00)</td>
<td>21</td>
<td>1.35 (0.91 to 2.00)</td>
</tr>
<tr>
<td>Bellissimo-Rodrigues 2009</td>
<td>35/98 33/96</td>
<td>&lt;1 0.31 (0.03 to 3.17)</td>
<td>&lt;1</td>
<td>0.31 (0.03 to 3.17)</td>
</tr>
<tr>
<td>Munro 2009</td>
<td>69/275 47/272</td>
<td>7 1.42 (0.72 to 2.80)</td>
<td>7</td>
<td>1.42 (0.72 to 2.80)</td>
</tr>
<tr>
<td>Panchabhai 2009</td>
<td>78/224 70/247</td>
<td>100 1.25 (1.05 to 1.50)</td>
<td>100</td>
<td>1.25 (1.05 to 1.50)</td>
</tr>
<tr>
<td>Cabov 2010</td>
<td>1/30 3/30</td>
<td>0.1 0.01 (0.00 to 0.82)</td>
<td>0.1</td>
<td>0.01 (0.00 to 0.82)</td>
</tr>
<tr>
<td>Berry 2011</td>
<td>17/71 28/154</td>
<td>0.1 0.01 (0.00 to 0.82)</td>
<td>0.1</td>
<td>0.01 (0.00 to 0.82)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>367/1288 326/1330</td>
<td>0.01 0.1 1 10 100</td>
<td>0.01</td>
<td>0.1 1 10 100</td>
</tr>
</tbody>
</table>

Test for heterogeneity: $\chi^2=8.41$, $\text{df}=10$, $P=0.59$, $I^2=0\%$

Test for overall effect: $z=2.47$, $P=0.01$
VAP

ARDS

Pneumothorax

Sepsis

Pulmonary Emboli

Pulmonary Edema

Atelectasis
Implications for surveillance
CDC’s old surveillance definition for VAP

Patient must fulfill each of the three categories below:

<table>
<thead>
<tr>
<th>Chest Radiograph</th>
<th>Any one of the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1. New, progressive, or persistent infiltrate</td>
</tr>
<tr>
<td></td>
<td>2. Consolidation</td>
</tr>
<tr>
<td></td>
<td>3. Cavitation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Systemic Signs</th>
<th>Any one of the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1. Temperature $&gt;38^\circ$C</td>
</tr>
<tr>
<td></td>
<td>2. WBC $&lt;4,000$ or $&gt;12,000$ WBC/mm$^3$</td>
</tr>
<tr>
<td></td>
<td>3. For adults 70 years old, altered mental status with no other recognized cause</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pulmonary Signs</th>
<th>Any two of the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1. New onset of purulent sputum, or change in character of sputum, or increased respiratory secretions, or increased suctioning requirements</td>
</tr>
<tr>
<td></td>
<td>2. New onset or worsening cough, or dyspnea, or tachypnea</td>
</tr>
<tr>
<td></td>
<td>3. Rales or bronchial breath sounds</td>
</tr>
<tr>
<td></td>
<td>4. Worsening gas exchange, increased oxygen requirements, or increased ventilation demand</td>
</tr>
</tbody>
</table>
Complicated
Labor Intensive
Subjective
Non-Specific
Interobserver agreement in VAP surveillance

50 ventilated patients with respiratory deterioration

Kappa = 0.40

Klompas, AJIC 2010:38:237
U.S. National VAP Rates
United States, 2004-2012

VAPs per 1000 vent-days

Source: CDC NNIS and NHSN
U.S. National VAP Rates
CMS Audits, 2005-2013

VAPs per 100 Ventilated Patients

JAMA 2016;316:2427-2429
We need to publicly report VAP rates to catalyze improved quality of care and save lives!

But the definition of VAP is ambiguous, hard to implement, and open to be gamed!

Where does this leave hospitals?
Developing a New, National Approach to Surveillance for Ventilator-Associated Events*

Shelley S. Magill, MD, PhD; Michael Klompas, MD, MPH; Robert Balk, MD; Suzanne M. Burns, RN, ACNP, MSN, RRT; Clifford S. Deutschman, MS, MD; Daniel Diekema, MD; Scott Fridkin, MD; Linda Greene, RN, MPS; Alice Guh, MD, MPH; David Guterman, MD; Beth Hammer, RN, MSN, ANP-BC; David Henderson, MD; Dean Hess, PhD, RRT; Nicholas S. Hill, MD; Teresa Horan, MPH; Marin Kollef, MD; Mitchell Levy, MD; Edward Septimus, MD; Carole VanAntwerpen, RN, BSN; Don Wright, MD, MPH; Pamela Lipsett, MD, MHPE.
An alternative approach to surveillance

Broaden the focus from pneumonia alone to the syndrome of ventilator complications in general

- More accurate description of what can be reliably determined using surveillance definitions
- Emphasizes the importance of preventing all complications of mechanical ventilation, not just pneumonia

Streamline the definition using quantitative criteria

- Reduce ambiguity
- Improve reproducibility
- Enable electronic collection of all variables
### Ventilator-associated conditions (VAC)

A sustained rise in daily minimum PEEP ≥3cm or FiO2 ≥20 points after a period of stable or improving daily minimum PEEP or FiO2 was monitored over several days in January.

<table>
<thead>
<tr>
<th>Date</th>
<th>PEEP (min)</th>
<th>FiO2 (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jan 1</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>Jan 2</td>
<td>5</td>
<td>50</td>
</tr>
<tr>
<td>Jan 3</td>
<td>5</td>
<td>40</td>
</tr>
<tr>
<td>Jan 4</td>
<td>5</td>
<td>40</td>
</tr>
<tr>
<td>Jan 5</td>
<td>8</td>
<td>60</td>
</tr>
<tr>
<td>Jan 6</td>
<td>8</td>
<td>50</td>
</tr>
<tr>
<td>Jan 7</td>
<td>8</td>
<td>40</td>
</tr>
<tr>
<td>Jan 8</td>
<td>5</td>
<td>40</td>
</tr>
<tr>
<td>Jan 9</td>
<td>5</td>
<td>40</td>
</tr>
</tbody>
</table>
VAC
Ventilator-Associated Condition

IVAC
Infection-related Ventilator-Associated Complication

Possible Pneumonia
Infection-related ventilator-associated complications (IVAC)

**VAC with concurrent abnormal temp or WBC count AND ≥4 days of new antibiotics**

<table>
<thead>
<tr>
<th>Date</th>
<th>PEEP (min)</th>
<th>FiO2 (min)</th>
<th>T min</th>
<th>T max</th>
<th>WBC min</th>
<th>WBC max</th>
<th>Antibiotic</th>
<th>Antibiotic</th>
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<tbody>
<tr>
<td>Jan 1</td>
<td>10</td>
<td>100</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jan 2</td>
<td>5</td>
<td>50</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jan 3</td>
<td>5</td>
<td>40</td>
<td>99.1</td>
<td>99.9</td>
<td>8.4</td>
<td>10.1</td>
<td>Linezolid</td>
<td></td>
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<tr>
<td>Jan 4</td>
<td>5</td>
<td>40</td>
<td>99.9</td>
<td>101.9</td>
<td>9.9</td>
<td>11.2</td>
<td>Linezolid</td>
<td>Cefepime</td>
</tr>
<tr>
<td>Jan 5</td>
<td>8</td>
<td>60</td>
<td>98.6</td>
<td>102.2</td>
<td>12.1</td>
<td>15.3</td>
<td>Linezolid</td>
<td>Cefepime</td>
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<tr>
<td>Jan 6</td>
<td>8</td>
<td>50</td>
<td>98.8</td>
<td>100.3</td>
<td>14.1</td>
<td>17.4</td>
<td>Cefepime</td>
<td></td>
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<tr>
<td>Jan 7</td>
<td>8</td>
<td>40</td>
<td>96.8</td>
<td>99.1</td>
<td>15.0</td>
<td>16.1</td>
<td>Cefepime</td>
<td></td>
</tr>
<tr>
<td>Jan 8</td>
<td>5</td>
<td>40</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cefepime</td>
<td></td>
</tr>
<tr>
<td>Jan 9</td>
<td>5</td>
<td>40</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cefepime</td>
<td></td>
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</table>
### Ventilator-associated pneumonia

*IVAC with concurrent purulent sputum (Gram stain neutrophils) and / or positive pulmonary cultures*

<table>
<thead>
<tr>
<th>Date</th>
<th>PEEP (min)</th>
<th>FiO2 (min)</th>
<th>Gram Stain Polys</th>
<th>Gram Stain Epis</th>
<th>Culture</th>
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</thead>
<tbody>
<tr>
<td>Jan 1</td>
<td>10</td>
<td>100</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jan 2</td>
<td>5</td>
<td>50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jan 3</td>
<td>5</td>
<td>40</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jan 4</td>
<td>5</td>
<td>40</td>
<td><strong>3+</strong></td>
<td><strong>0</strong></td>
<td>Klebsiella pneumoniae</td>
</tr>
<tr>
<td>Jan 5</td>
<td>8</td>
<td>60</td>
<td></td>
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<td>Jan 6</td>
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<tr>
<td>Jan 9</td>
<td>5</td>
<td>40</td>
<td></td>
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</tr>
</tbody>
</table>

**POSSIBLE PNEUMONIA**
Electronic Implementation of a Novel Surveillance Paradigm for Ventilator-associated Events
Feasibility and Validation

Peter M. C. Klein Klouwenberg¹,²,³*, Maaike S. M. van Mourik¹, David S. Y. Ong¹,²,³, Janneke Horn⁴, Marcus J. Schultz⁴, Olaf L. Cremer², and Marc J. M. Bonten¹,³; on behalf of the MARS Consortium

Automated Surveillance for Ventilator-Associated Events

Jennifer P. Stevens, MD; George Silva; Jean Gillis, RN, MPH; Victor Novack, MD, PhD; Daniel Talmor, MD, MPH; Michael Klompas, MD, MPH; and Michael D. Howell, MD, MPH
Attributable Mortality of VAE versus VAP

USA - 3 centers
*PLoS ONE* 2011;6:e18062

USA - 8 centers
*Crit Care Med* 2012;40:3154

Canada - 11 centers
*Chest* 2013;144:1453

Netherlands - 2 centers
*Am J Resp Crit Care Med* 2014;189:947

USA - 2 centers
*Crit Care Med* 2014;ePub

USA - 1 center
*Infect Control Hosp Epidemiol* 2014;5:502

Odds Ratio or Hazard Ratio
Canadian Critical Care Trials Group ABATE Study
11 ICUs, 1330 patients, VAE vs VAP Surveillance

VAE
9.9 events per 1000 vent days

VAP
10.6 events per 1000 vent days

Muscedere et al. Chest 2013;144:1453
VAE ≠ VAP
Qualitative analysis of 153 VAEs
Royal Brisbane & Women’s Hospital, Queensland, Australia

- Pneumonia: 38%
- Edema: 26%
- Atelectasis: 15%
- ARDS: 6%
- Abx + Furosemide: 6%
- Other: 8%

VAE = VAP + Fluids + ARDS + Atelectasis
Fewer VAEs

How do we get there?
Strategies for preventing VAEs

- Decrease duration of mechanical ventilation
- Target the primary conditions associated with VAEs
Strategies for preventing VAEs

- Decrease duration of mechanical ventilation
- Target the primary conditions associated with VAEs
- Minimize sedation
- Paired SATs and SBTs
- Early mobility
- Low tidal volume ventilation
- Conservative fluid management
- Minimize blood transfusions
### Possible (evidence from observational studies alone or inconsistent RCT data)

- Minimize sedation
- Paired SATs and SBTs
- Early Mobility
- Low tidal volume ventilation
- Conservative fluid management
- Conservative transfusion thresholds

### Probable (evidence from RCTs and/or meta-analyses)

- Duration of Ventilation
- Pneumonia
- Atelectasis
- ARDS
- Fluid Overload

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*Am J Resp Crit Care Med 2015;192:1420-1430*
Minimize Sedation
Early Intensive Care Sedation Predicts Long-Term Mortality in Ventilated Critically Ill Patients

- Prospective analysis of 251 patients started on ventilators in 25 ICUs
- Assessed association between initial depth of sedation (RASS -3 to -5 vs -2 to +1) and time to extubation + mortality
- Analysis adjusted for age, sex, diagnosis, APACHE II, elective admit, surgery, hospital type, vasopressors, dialysis

Fraction of Population Remaining on Ventilator

Days

Lightly Sedated
Deeply Sedated

Am J Resp Crit Care Med 2012;186:724
Early Intensive Care Sedation Predicts Long-Term Mortality in Ventilated Critically Ill Patients

Fraction of Population Remaining Alive

Days

Lightly Sedated

Deeply Sedated

Am J Resp Crit Care Med 2012;186:724
Associations between different sedatives and ventilator-associated events, length-of-stay, and mortality

- Observational study of 9,603 patients vented for ≥3 days

- Measured associations between daily benzodiazepine, propofol, and dexmedetomidine exposures and VAEs, time to extubation, time to hospital discharge, and mortality

- Proportional subdistribution hazard ratios with competing risks

- Analyses adjusted for demographics, ICU type, recent procedures, severity of illness, hypotension, impaired oxygenation, renal function, use of SATs and SBTs, and calendar year

Chest 2015 Online First; doi: 10.1378/chest.15-1389
Ventilator-associated events

Hazard Ratios

Benzodiazepines

Propofol

Dexmedetomidine

Fewer VAEs

More VAEs

Chest 2015 Online First; doi: 10.1378/chest.15-1389
Hazards for extubation

- Benzodiazepines
- Propofol
- Dexmedetomidine

Hazard Ratios

- More time on vent
- Less time on vent

Chest 2015 Online First; doi: 10.1378/chest.15-1389
140 patients randomized to routine sedation versus no sedation

- 70 prescribed routine sedation (propofol then midazolam)
- 70 prescribed no sedation (morphine boluses PRN)

Patients with no sedation

- Mean 4.2 (95% CI 0.3-8.1) fewer days on the vent
- Shorter ICU stay (HR 1.86, 95% CI 1.1-3.2)
- Shorter hospital stay (HR 3.6, 95% CI 1.5-9.1)
- More agitated delirium (20% versus 7%) but no difference in self-extubations
- 1:1 nursing
Paired SATs and SBTs
Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial

-2 days
-3.8 days
-4.3 days
The Preventability of Ventilator-associated Events
The CDC Prevention Epicenters Wake Up and Breathe Collaborative

- Prospective care improvement collaborative
- 12 ICUs (mix of med, surg, mixed & academic, community)
- 19 months
- Goal: prevent VAEs through earlier liberation from mechanical ventilation
- Mechanism: enhance the uptake and performance of paired daily SATs and SBTs (“Every Patient, Every Day”)
SBTs: 40% increase

SATs: 100% increase

Performance Rates

Jan-12, Mar-12, May-12, Jul-12, Sep-12, Nov-12, Jan-13, Mar-13, May-13

Am J Resp Crit Care Med 2015;191:292-301
**Ventilator-Associated Events**

CDC Prevention Epicenters Wake Up and Breathe Collaborative

- VAEs: 37% decrease
- IVAC: 65% decrease

*Am J Resp Crit Care Med 2015;191:292-301*
Ventilator Days and ICU Days

CDC Prevention Epicenters Wake Up and Breathe Collaborative

ICU: 3 day decrease

Ventilator: 2.4 day decrease

Mean ICU Days / Vent Days

0 5 10 15

Nov-11  Jan-12  Mar-12  May-12  Jul-12  Sep-12  Nov-12  Jan-13  Mar-13  May-13

Am J Resp Crit Care Med 2015;191:292-301
Early mobility
Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial

104 vented patients randomized to early exercise & mobilization during daily sedative interruptions vs usual care

![Bar chart showing the difference in delirium days, duration of ventilation, and ICU stay between usual care and early mobility.]

- Delirium Days: -2 days
- Duration of Ventilation: -2.4 days
- ICU Stay: -2.0 days

Lancet 2009;373:874-882
Low tidal volume ventilation
Association Between Use of Lung-Protective Ventilation With Lower Tidal Volumes and Clinical Outcomes Among Patients Without Acute Respiratory Distress Syndrome

A Meta-analysis

Ary Serpa Neto, MD, MSc
Sérgio Oliveira Cardoso, MD
José Antônio Manetta, MD
Victor Calvão Moura Pereira, MD
Daniel Crepaldi Espósito, MD
Manoela de Oliveira Prado Pasqualucci, MD
Maria Cecília Toledo Damasceno, MD, PhD
Marcus J. Schultz, MD, PhD

Context   Lung-protective mechanical ventilation with the use of lower tidal volumes has been found to improve outcomes of patients with acute respiratory distress syndrome (ARDS). It has been suggested that use of lower tidal volumes also benefits patients who do not have ARDS.

Objective   To determine whether use of lower tidal volumes is associated with improved outcomes of patients receiving ventilation who do not have ARDS.

Data Sources   MEDLINE, CINAHL, Web of Science, and Cochrane Central Register of Controlled Trials up to August 2012.

Study Selection   Eligible studies evaluated use of lower vs higher tidal volumes in patients without ARDS at onset of mechanical ventilation and reported lung injury development, overall mortality, pulmonary infection, atelectasis, and biochemical alterations.
Lung Injury

<table>
<thead>
<tr>
<th></th>
<th>High Vₜ, No.</th>
<th>Low Vₜ, No.</th>
<th>Weight, %</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung injury</td>
<td>32</td>
<td>100</td>
<td>18.1</td>
<td>0.47 (0.22-1.00)</td>
</tr>
<tr>
<td>Gajic et al,2004</td>
<td>6</td>
<td>26</td>
<td>4.6</td>
<td>0.43 (0.10-1.97)</td>
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<tr>
<td>Michelet et al,2006</td>
<td>60</td>
<td>212</td>
<td>40.7</td>
<td>0.29 (0.16-0.53)</td>
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<tr>
<td>Yilmaz et al,2007</td>
<td>20</td>
<td>533</td>
<td>17.7</td>
<td>0.23 (0.09-0.62)</td>
</tr>
<tr>
<td>Licker et al,2009</td>
<td>10</td>
<td>74</td>
<td>8.6</td>
<td>0.17 (0.04-0.82)</td>
</tr>
<tr>
<td>Determann et al,2010</td>
<td>4</td>
<td>50</td>
<td>3.4</td>
<td>0.23 (0.03-1.28)</td>
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<tr>
<td>Yang et al,2011</td>
<td>10</td>
<td>74</td>
<td>5.6</td>
<td>0.67 (0.20-2.17)</td>
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<tr>
<td>Fernandez-Bustamante et al,2011</td>
<td>5</td>
<td>75</td>
<td>1.3</td>
<td>0.32 (0.01-8.26)</td>
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<tr>
<td>Weingarten et al,2012</td>
<td>1</td>
<td>20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>138</td>
<td>1090</td>
<td>100.0</td>
<td>0.33 (0.23-0.47)</td>
</tr>
<tr>
<td>Total events</td>
<td>47</td>
<td>47</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi^2 = 3.74; P = .01, I^2 = 0$

Test for overall effect: $z = 6.06; P < .001$

Pneumonia

<table>
<thead>
<tr>
<th></th>
<th>High Vₜ, No.</th>
<th>Low Vₜ, No.</th>
<th>Weight, %</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
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<td></td>
</tr>
<tr>
<td>Pulmonary infection</td>
<td>10</td>
<td>56</td>
<td>16.6</td>
<td>0.20 (0.04-0.99)</td>
</tr>
<tr>
<td>Lee et al,1999</td>
<td>10</td>
<td>26</td>
<td>14.6</td>
<td>0.48 (0.14-1.60)</td>
</tr>
<tr>
<td>Michelet et al,2006</td>
<td>30</td>
<td>533</td>
<td>55.8</td>
<td>0.72 (0.41-1.26)</td>
</tr>
<tr>
<td>Licker et al,2009</td>
<td>7</td>
<td>50</td>
<td>13.0</td>
<td>0.13 (0.01-1.06)</td>
</tr>
<tr>
<td>Yang et al,2011</td>
<td>10</td>
<td>74</td>
<td>5.6</td>
<td>0.67 (0.20-2.17)</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>57</td>
<td>665</td>
<td>100.0</td>
<td>0.52 (0.33-0.82)</td>
</tr>
<tr>
<td>Total events</td>
<td>32</td>
<td>681</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi^2 = 4.39; P = .22, I^2 = 32$

Test for overall effect: $z = 2.79; P = .005$

Atelectasis

<table>
<thead>
<tr>
<th></th>
<th>High Vₜ, No.</th>
<th>Low Vₜ, No.</th>
<th>Weight, %</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atelectasis</td>
<td>2</td>
<td>20</td>
<td>3.1</td>
<td>1.59 (0.24-10.70)</td>
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<tr>
<td>Lin et al,2008</td>
<td>5</td>
<td>8</td>
<td>1.1</td>
<td>4.20 (0.33-53.12)</td>
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<tr>
<td>Cai et al,2007</td>
<td>47</td>
<td>533</td>
<td>83.1</td>
<td>0.55 (0.34-0.89)</td>
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<tr>
<td>Licker et al,2009</td>
<td>3</td>
<td>50</td>
<td>5.4</td>
<td>0.32 (0.03-3.18)</td>
</tr>
<tr>
<td>Yang et al,2011</td>
<td>5</td>
<td>20</td>
<td>7.3</td>
<td>0.75 (0.17-3.33)</td>
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<tr>
<td>Subtotal (95% CI)</td>
<td>62</td>
<td>631</td>
<td>100.0</td>
<td>0.62 (0.41-0.95)</td>
</tr>
<tr>
<td>Total events</td>
<td>43</td>
<td>656</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: $\chi^2 = 3.76; P = .44, I^2 = 0$

Test for overall effect: $z = 2.18; P = .03$

Relative Risk
- Lung Injury: 0.33 (0.23-0.47)
- Pneumonia: 0.52 (0.33-0.82)
- Atelectasis: 0.62 (0.41-0.95)

JAMA 2012;308:1651-1659
High Tidal Volumes are Independently Associated with Developing VAEs

Nested case-control study set in 2 hospitals 2013-2014
• 167 VAEs matched to 668 controls

Multivariable conditional logistic regression
• Mean daily tidal volume associated with increased VAE risk
• OR 1.21 for each ml above 6ml/kg predicted body weight
Conservative Fluid Management
Deplettive Fluid Management

- Randomized controlled trial of ventilator weaning

- 304 patients randomized to daily BNP levels versus usual care

- Patients randomized to daily BNP levels
  - More diuretics
  - More negative fluid balance
  - Less time to extubation
  - 50% fewer VAEs

VAEs

Usual Care

Daily BNP

P=.02

Mekontso Dessap et al. *Chest* 2014;146:58-65
Conservative Transfusion Thresholds
Red Blood Cell Transfusions

Associated with increased risk for:

- Volume overload
- ARDS
- Pneumonia
Risk of Serious Infections

<table>
<thead>
<tr>
<th>Source</th>
<th>Restrictive Transfusion Threshold</th>
<th>Liberal Transfusion Threshold</th>
<th>Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Events</td>
<td>Total No. of Patients</td>
<td>No. of Events</td>
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<tr>
<td>All serious infections, combined</td>
<td>5</td>
<td>212</td>
<td>3</td>
</tr>
<tr>
<td>Bracey et al,20 1999</td>
<td>42</td>
<td>418</td>
<td>50</td>
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<tr>
<td>Hébert et al,26 1999</td>
<td>65</td>
<td>320</td>
<td>79</td>
</tr>
<tr>
<td>LaCroix et al,27 2007</td>
<td>6</td>
<td>60</td>
<td>11</td>
</tr>
<tr>
<td>Foss et al,31 2009</td>
<td>29</td>
<td>249</td>
<td>25</td>
</tr>
<tr>
<td>Hajjar et al,32 2010</td>
<td>18</td>
<td>299</td>
<td>31</td>
</tr>
<tr>
<td>So-Osman et al,33 2010</td>
<td>56</td>
<td>1009</td>
<td>74</td>
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<tr>
<td>Carson et al,34 2011</td>
<td>84</td>
<td>444</td>
<td>94</td>
</tr>
<tr>
<td>Villanueva et al,35 2013</td>
<td>5</td>
<td>212</td>
<td>3</td>
</tr>
</tbody>
</table>

Risk Ratio
0.84 (0.73-0.96)
A MULTICENTER, RANDOMIZED, CONTROLLED CLINICAL TRIAL OF TRANSFUSION REQUIREMENTS IN CRITICAL CARE

Paul C. Hébert, M.D., George Wells, Ph.D., Morris A. Blajchman, M.D., John Marshall, M.D., Claudio Martin, M.D., Giuseppe Pagliarello, M.D., Martin Tweeddale, M.D., Ph.D., Irwin Schweitzer, M.Sc., Elizabeth Yetisir, M.Sc., and the Transfusion Requirements in Critical Care Investigators

Transfusion Strategies for Acute Upper Gastrointestinal Bleeding

Cândid Villanueva, M.D., Alan Colomo, M.D., Alba Bosch, M.D., Mar Concepción, M.D., Virginia Hernandez-Gea, M.D., Carles Aracil, M.D., Isabel Graupera, M.D., María Poca, M.D., Edurne Alonso, M.D., Maria E. Santander, M.D., Carles Carmona, M.D., and Mikel Santaló, M.D.

Restrictive Versus Liberal Transfusion Strategies for Older Mechanically Ventilated Critically Ill Patients: A Randomized Pilot Trial

Timothy S. Walsh, MD1; Julia A. Boyd, PhD2; Douglas Watson, MSc3; David Hope, Pg Dip1; Steff Lewis, PhD4; Ashma Krishan, MSc24; John F. Forbes, PhD4; Pamela Ramsay, PhD1; Rupert Barnes, MD; Charles Wallis, FRCA1; Christopher Cairns, FRCA1; Stephen Gade, FRCA1; Mark R. G. Green, MD, FRCP

Transfusion Requirements After Cardiac Surgery
The TRACS Randomized Controlled Trial

Ludhmila A. Hajjar, MD, PhD
Laurence Vicaut, MD, PhD

Context Perioperative red blood cell transfusion is commonly used to address anemia in patients undergoing cardiac surgery, but its effects on patient outcomes are unknown. This randomized controlled trial.
Criticisms of VAE

1. Most VAEs are not pneumonias

2. VAE surveillance misses many pneumonias

1. VAEs are not preventable
Most VAEs are not Pneumonias

VAE ≠ VAP

VAE = VAP + Fluids+ ARDS + Atelectasis
## VAE Misses Many Pneumonias

<table>
<thead>
<tr>
<th>Date</th>
<th>PEEP (min)</th>
<th>FiO2 (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jan 1</td>
<td>10</td>
<td>100</td>
</tr>
<tr>
<td>Jan 2</td>
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<td>Jan 3</td>
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<td>Jan 7</td>
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<td>Jan 8</td>
<td>5</td>
<td>40</td>
</tr>
<tr>
<td>Jan 9</td>
<td>5</td>
<td>40</td>
</tr>
</tbody>
</table>
VAP with Minimal and Stable Ventilator Settings

1-3 Day Rx (N=257)  >3 Day Rx (N=257)

Days of Antibiotics (Median)  Days to Extubation  Days to Hospital Discharge  Hospital Death

Clin Infect Dis 2017;64:870-876
Most VAEs are not Preventable

A Prospective Evaluation of Ventilator-Associated Conditions and Infection-Related Ventilator-Associated Conditions

Anthony F. Boyer, MD; Noah Schoenberg, MD; Hilary Babcock, MD, MPH; Kathleen M. McMullen, MPH; Scott T. Micek, PharmD; and Marin H. Kollef, MD. FCCP

Prospective survey: 1,209 patients vented ≥2 days, Barnes-Jewish Hospital

Identified 67 VAEs. Most common causes were:
• Pneumonia (31%)
• ARDS (16%)
• Pulmonary edema (15%)
• Atelectasis (9%)

Adjudicated 37% of VAEs as potentially preventable

Chest 2015;147:68-81
Canadian Critical Care Trials Group ABATE Study
Enhanced care for vented patients, 11 ICUs, 1330 patients

29% Decrease in VAEs

Muscedere et al. Chest 2013;144:1453-1460
Two State Collaborative to Prevent VAEs

56 ICUs in Maryland and Pennsylvania, Oct 2012 to Mar 2015

VAE

IVAC

PVAP

Incidence Rate per 1,000 Ventilator Days

Crit Care Med 2017;45:1208-1215
Depletive Fluid Management

50% Decrease in VAEs

Mekontso Dessap et al. Chest 2014;146:58-65
## VAE Prevention Strategies
Well Aligned with Other Best Practice Initiatives

<table>
<thead>
<tr>
<th>VAE Prevention Strategies</th>
<th>ABCDE</th>
<th>Choosing Wisely</th>
<th>PAD Guidelines</th>
<th>Surviving Sepsis</th>
<th>Strategies to Prevent VAP</th>
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</thead>
<tbody>
<tr>
<td>Minimize sedation</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
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<td>☑</td>
</tr>
<tr>
<td>Paired SATs and SBTs</td>
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<td>☑</td>
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<tr>
<td>Early Mobility</td>
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<td>Low tidal volume ventilation</td>
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<td>Conservative fluid management</td>
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<tr>
<td>Conservative transfusion thresholds</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
<td>☑</td>
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</tr>
</tbody>
</table>
Ventilator-associated events
A patient safety opportunity

Broaden Awareness
• VAE surveillance provides hospitals with a fuller picture of serious complications in mechanically ventilated patients

Catalyze Prevention
• A significant portion of VAEs are likely preventable

Reflect and Inform Progress
• VAE surveillance provides an efficient and objective yardstick to track one’s progress relative to oneself and to peers

NEJM 2013;368:1472
Thank You!

Michael Klompas (mklompas@bwh.harvard.edu)