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# The Incidence of Ventilator-Associated Infections in Children Determined Using Bronchoalveolar Lavage

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## Introduction

Hospital-acquired infections are a major contributor to inpatient morbidity, mortality, and health care costs. Ventilator-associated pneumonia (VAP) is among the most common. It is associated with longer duration of mechanical ventilation (MV), longer intensive care unit stays, increase in cost per case of VAP of at least $40 000, and over 2-fold increased risk of mortality.[1,2] Hospital rates of VAP are subject to mandated reporting and measured against national benchmarks. However, because the definition of VAP is complex and includes subjective signs and symptoms, the reported incidence in children varies widely from 0.3 to 45.1 cases per 1000 ventilator days.[3] VAP may not include all clinically important infections associated with MV.[4] Another infection, ventilator-associated tracheobronchitis (VAT), has been described using varying definitions with unclear clinical significance. The incidence of VAT in pediatric intensive care unit (PICU) populations has been reported at 3.4% to 7.3% of ventilated patients, and as high as 21.2% in trauma patients.[5-9] VAT has been associated with longer duration of MV and length of stay but not increased mortality.[5-7]

Variable definitions have been used in studies of VAT, but generally include clinical signs of respiratory infection in the absence of pneumonia on chest radiograph combined with a positive respiratory culture.[8,9] Recent studies of VAT in pediatrics have all used a definition based on the Centers for Disease Control and Prevention/National Healthcare Safety Network (CDC/NHSN) definition of "lower respiratory tract infection other than pneumonia" and applied it to children on MV.[5-7,10] Definitions of VAT, and those of VAP, are complicated by their reliance on poor interpretability and subjectivity of data including clinical signs and chest radiographs. Microbiologic testing is complicated due to the lack of standard microbiologic methods.[3] Respiratory specimens can be obtained by bronchoscopic or non-bronchoscopic bronchoalveolar lavage (BAL), by protected specimen brush, or by endotracheal aspirate (ETA) via new or inline suction catheters. ETA may be preferred due to perceived safety, feasibility, and cost concerns.[4] However, validity of cultures obtained by ETA may be questioned due to bacterial colonization of endotracheal tubes. Quantitative bacterial cultures may improve specificity of ETA cultures for infection over colonization, and a threshold of $>10^5$ cfu/mL has been suggested.[9] Publications on VAT have invariably used ETA as the method to obtain specimens, but have varied in the use of quantitative culture.

In our institution, BAL is used for the routine evaluation of ventilator-associated infections including VAP and VAT. Surveillance cultures and ETA are not performed due to concerns of interpretability of results. Because of this, we are in a unique position to provide the first report of BAL results in a large cohort of PICU patients. We hypothesized that VAP represents only a small portion of positive BALs, suggesting that other potentially significant ventilator-associated infections are not well characterized.

## Methods

### *Setting and Patients*

This study was performed in a 34-bed mixed medical-surgical (including cardiac) PICU of a tertiary care children's hospital. All BAL cultures ordered at the discretion of the bedside provider from patients ventilated for any reason during the study period were evaluated.

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### Data Collection

Infection control practitioners maintained a prospective database of all BAL culture results for quality assurance and VAP monitoring and reporting. This de-identified database containing date of admission, date of culture, and culture results was retrospectively reviewed from January 1, 2011, to June 30, 2013. This was compared with institutionally collected data of reported VAPs, the number of ventilated patients, and MV days.

### Definitions of Comparison Groups

CDC/NHSN definition of VAP was used for monitoring and reporting purposes.[10] Any growth of pathogenic bacteria was defined as a positive BAL, and either no growth or growth of "normal flora" was defined as a negative BAL. Cultures done on the first or second day of admission were excluded in order to evaluate hospital-acquired infections versus those that were present on admission. The proportions of patients on MV with VAP or positive BAL were calculated. The rates of VAP and positive BAL were reported as number of events per 1000 ventilator days. Comparisons were made using Fisher's exact test.

### BAL and Microbiological Methodology

BAL, obtained either by bronchoscopy or non-bronchoscopically, was routinely used to evaluate for suspected infection. Generally, most cultures are obtained non-bronchoscopically for routine gram stain and bacterial culture. Bronchoscopy is preferred only when larger volumes of aspirate are needed to run additional diagnostic testing (such as cultures for fungus or atypical infection), or when bronchoscopy is otherwise therapeutically indicated.

Non-bronchoscopic specimens are obtained using sterile technique by the respiratory therapist using a telescoping protected catheter (Combicath, KOL Bio-Medical Instruments, Inc, Chantilly, VA). The catheter is wedged into the distal airway, and 0.5 mL/kg (up to 20 mL) of saline is instilled into the airway and then aspirated. The microbiology laboratory reports the results of a gram stain semiquantitatively. The results of the bacterial culture are reported quantitatively, if possible, or semiquantitatively in the case of an inadequate sample size to perform quantitation.

## Results

Over the 30-month study period, there were 2066 ventilated patients with 20 114 ventilator days. A total of 385 BALs were sent, of which 115 were done on the first or second day of admission. Of the 270 BALs done beyond the second day of admission, 143 grew pathogenic bacteria, which was 53% of BAL specimens. A positive BAL culture beyond the second day of admission occurred in 6.92% of ventilated patients, with a rate of 7.11/1000 ventilator days. Eight cases of VAP were reported over the same time period. VAP occurred in 0.39% of ventilated patients, with a rate of 0.40/1000 ventilator days. The proportion of patients and rates of VAP and positive BAL differed significantly ($P < 0.001$; Figure 1).

## Discussion

This is the first report of BAL culture results in a large population of children on MV in whom BAL was the standard method to evaluate for ventilator-associated infection. While a positive BAL is usually considered to represent a bacterial respiratory infection, our data indicate that many mechanically ventilated children acquire infections that do not meet the definition of VAP. The rate of positive BAL in our institution was comparable to the rate of VAT based on ETA cultures previously reported in similar PICU populations.[6-8] The frequency of a positive culture from a BAL specimen (53%) also compares to a recent report by Willson et al, which showed 37% to 53% of ETA surveillance cultures beyond the third day of MV with a new sterile catheter were positive.[3] These observations raise questions about the superiority of BAL over ETA, and of the specificity of either in diagnosing true infection. Differing microbiological methods may not improve the diagnosis of ventilator-associated infections.[3]

The retrospective analysis of our de-identified database limited our ability to contextualize culture results with clinical symptoms. Because of this, it is uncertain if the positive cultures represent bacterial colonization or clinically significant infection. However, our method of obtaining cultures eliminates concerns for contamination by the endotracheal tube or inline catheter, and we only send cultures to evaluate for suspected infection and not for surveillance. Therefore, we assume positive BAL patients likely had a ventilator-associated infection. The rate may be underestimated if there was variation in practice in obtaining cultures in the presence of clinical symptoms. Because the database contained day of PICU admission but not day of initiation of MV, some cultures evaluated may have been taken during the first 2 days of MV if this was initiated beyond the day of admission, leading to an overestimation.

There is a discrepancy between the numbers of VAP reported by hospitals, with many hospitals reporting a zero rate, and the numbers of patients treated clinically

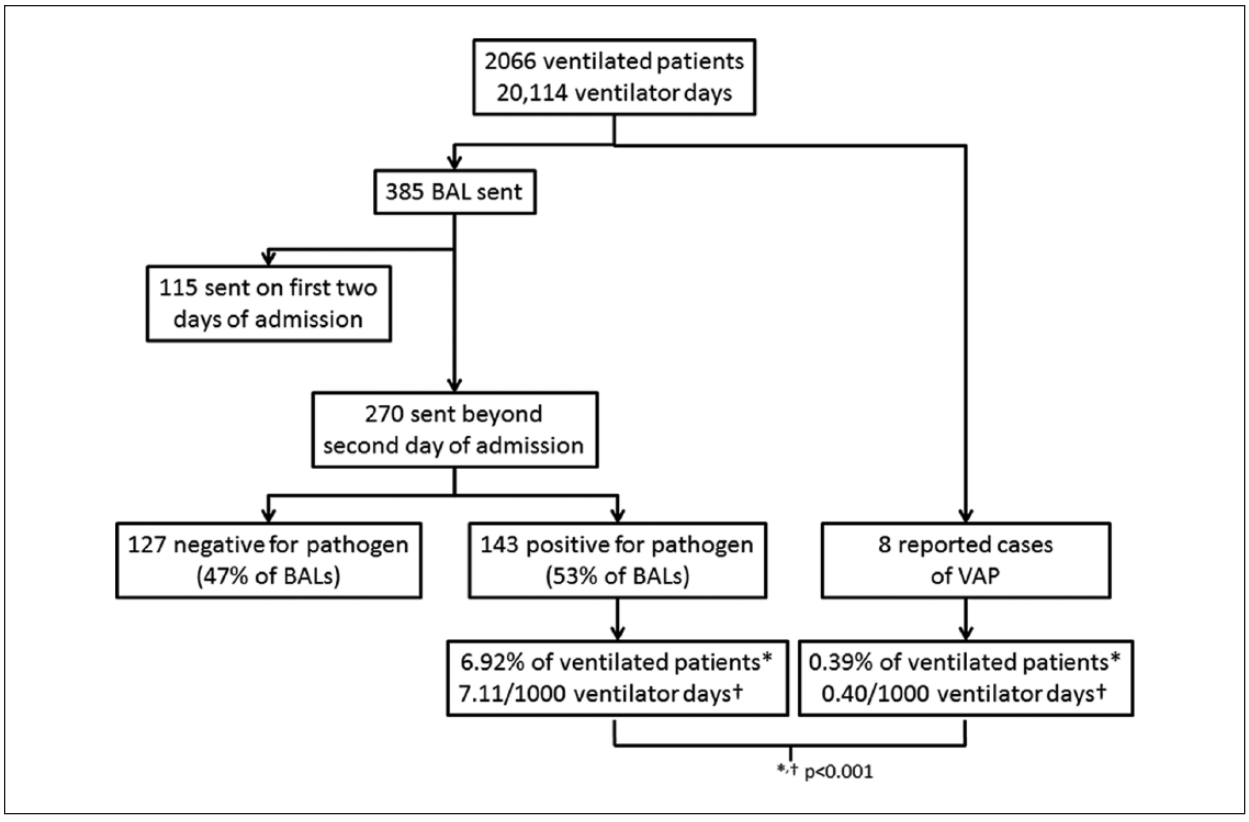


**Figure 1.** Study design and main results.
Abbreviations: BAL, bronchoscopic or non-bronchoscopic bronchoalveolar lavage; VAP, ventilator-associated pneumonia.

for ventilator-associated infection.[11] Our data support this discrepancy, which is largely due to subjectivity and interpretation of the surveillance definitions used. There was a recent change in surveillance definitions used in adult patients to various levels of "ventilator-associated events."[12] Although this new definition attempted to be more objective, there is still potential subjectivity in categorization of conditions based on practice variation in ventilation strategies and antimicrobial use. The subjectivity in VAP definitions opens the possibility of "gaming the system" in which clinically significant ventilator-associated infections are not reported as VAP due to alterations in documentation of clinical signs, interpretation of chest radiograph findings, or management of increased oxygen requirements.

Also, while VAP definitions are admittedly for surveillance use only, they cannot guide clinical diagnosis and management. A focus on developing a standardized approach to prevention, diagnosis, and management of ventilator-associated infections across institutions is warranted to improve consistency of care. More study is needed to determine the role of subjective criteria of infection and "objective" microbiology data in such a guideline. A surveillance method integrated with management guidelines may be more effective at tracking actual rates of ventilator-associated infections. We believe that an algorithm that can be used both for monitoring and also for guidance on the diagnosis and management of ventilator-associated infections would go a long way toward standardizing practice and improving patient safety.

## Author Contribution

ALB contributed to conception, design, data acquisition, analysis and interpretation and drafted and critically revised the manuscript. MRR contribued to design, data analysis and interpretation and critically revised the manuscript. TLB contributed to data acquisition and interpretation and critically revised the manuscript. MEN contributed to conception and design and critically revised the manuscript. BDB contributed to conception, design, data analysis and interpretation and critically revised the manuscript.

## Declaration of Conflicting Interests

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