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Review Paper

Ventilator-associated events in children: A review of literature

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ABSTRACT

Background: The complexity and variation in ventilator associated pneumonia (VAP) definitions in paediatrics may pose threats to the reliable identification of VAP. The revision of the surveillance definition to ventilator-associated event (VAE) has been mandated in adult populations, to overcome these issues. However, the evidence for application of the definition is unknown in children.
Objectives: To review the evidence on the application of the new VAE surveillance definition in paediatric population and examine the potential challenges in clinical practice.
Review methods: A systematic approach was used to locate and synthesise the relevant paediatric literature. Studies were appraised according to epidemiological appraisal instrument (EAI) and the grades of evidence in the National Health Medical Research Council (NHMRC) guidelines.
Results: Seven studies met the inclusion criteria. Quality of study methods was above 50% on the EAI. The overall grade of evidence was assessed as C (satisfactory). The incidence of VAE in children ranged from 1.1 to 20.9 per 1000 ventilator days as a result of variations in surveillance criteria across included studies. There is little agreement between the new VAE and PNU/VAP surveillance definition in the identification of VAP. Challenges in the application of VAE surveillance were related to; the difference in modes of ventilation used in children versus adults, inconclusive criteria tailored to paediatric samples and a lack of data that support for automatic data extraction applied in paediatric studies.
Conclusion: This review demonstrated promising evidence using the new VAE surveillance definition to define the VAE in children, but the level of the evidence is low. Before the possibility of real implementation in clinical settings, challenges related to VAE paediatric specific criteria' and the value of automated data collection need to be considered.

1. Introduction

Mechanical ventilation is a life-saving intervention for critically ill children, yet it may impose iatrogenic complications, such as ventilator-associated pneumonia (VAP). In addition to the burden on children's health, VAP has a significant impact on the healthcare system, resulting in increased lengths of stay in the paediatric intensive care unit (PICU) in line with the increased duration of mechanical support and resulting economic burden.[1,2]

VAP continues to be a challenging complication but also the diagnosis of VAP has been a debated issue. Historically, the surveillance of nosocomial pneumonia was initiated by the Centre for Disease Control and Prevention (CDC) in 1988 and relied on the combination of three criteria: (1) radiological findings; (2) subjective clinical signs and symptoms, and (3) laboratory data.[3] The CDC criteria have remained the same for several years; however, in 2003, VAP was further categorised into early and late onset.[4] In 2005, the American Thoracic Society and Infectious Diseases Society of America limited the definition of VAP to

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Table 1
Current PNU1/VAP definition: alternative criteria for infants and children.[7]

PNU1 VAP definition	Radiological criteria
For both aged categories	(a) Patient **with underlying diseases** has **two or more** imaging test results with **one** of the following; (b) Patient **without underlying diseases has one or more** imaging test results with **one** of the following: New and persistent OR progressive and persistent: 1. Infiltrate 2. Consolidation 3. Cavitation Pneumatoceles, in ≤1 year old
	Signs and symptoms
Alternate criteria for infant ≤1 year old	Worsening gas exchange (e.g., oxygen desaturations [e.g., pulse oximetry <94%], ↑ oxygen requirement or ↑ ventilation demand) and **three** of the following: • Temperature instability • Leukopenia (≤4000 WBC/mm^3) or leucocytosis (≥15,000 WBC/mm^3) and left shift (≥10% band forms) • New onset of purulent sputum, change in character of sputum, ↑ respiratory secretions, or ↑ suctioning requirements • Apnoea, tachypnoea, nasal flaring with retraction of chest wall or grunting • Wheezing, rales, or rhonchi • Cough • Bradycardia (<100 beats/min) or tachycardia (>170 beats/min)
Alternate criteria for children >1 or ≤12 year old	At least **three** of the following: • Fever (>38.0 °C/100.4 °F) or hypothermia (<36.0 °C/96.8 °F) • Leukopenia (≤4000 WBC/mm^3) or leucocytosis (≥15,000 WBC/mm^3) • New onset of purulent sputum, change in character of sputum, ↑ respiratory secretions, or ↑ suctioning requirements • New onset of worsening cough, dyspnoea, apnoea, or tachypnoea • Rales or bronchial breath sounds • Worsening gas exchange (e.g., oxygen desaturations [e.g., pulse oximetry <94%]↑ oxygen requirement or ↑ ventilation demand)

WBC, white blood cell.

pneumonia in patients with mechanical ventilation for at least 48 h.[5] The CDC further classified pneumonia into three categories (PNU1, PNU2, and PNU3) and provided alternative criteria for infants and children.[6] The current VAP criteria for children were published by the CDC (Table 1).[7] Most recently, in 2013, the CDC released a new surveillance tool to capture events extending beyond VAP. This new phenomenon is referred to as ventilator-associated event (VAE) and includes three ordinal tiers, called tier (1) ventilator-associated condition (VAC); tier (2) infection-related ventilator-associated complication (IVAC), and tier (3) Possible VAP (PVAP) (Table 2).[8] A diagnosis of VAE can be made when the patient's physiological or mechanical ventilation parameters meet all the criteria across the three tiers. The complex variability in VAP criteria and diagnosis over time is illustrated in Fig. 1.

Currently, the VAE surveillance definition applies only to adult mechanically ventilated patients and has not been systematically adopted in the paediatric population.[9] Adult studies have shown that the VAE surveillance definition is objective and based on the numerical criteria, less time consuming, and a robust predictor of outcomes.[10] It also permits the identification of other ventilator-associated complications such as pulmonary

Table 2
The VAE tiers with respective requirements and criteria.[8]

VAE tier	Requirements and criteria
1. Ventilator associated condition (VAC)	Prerequirement: patient is required to have a baseline period of stability or improvement on ventilator for ≥ 2 calendar days of stable or decreasing *daily minimum FiO_2 or PEEP values. VAC criteria: 1. Increase FiO_2 ≥ 0.20 OR PEEP ≥3 cmH_2O 2. Sustained for 2 days *Daily minimum defined by the lowest value of FiO2 or PEEP during a calendar day that is maintained for at least 1 h.
2. Infection-related ventilator-associated complications (IVAC)	Prerequirement: patient is required to meet the VAC criteria IVAC criteria: 1. Temperatures <36 °C or >38 °C **OR** abnormal white blood cell (WBC) count (≤4000 cells/mm^3 or ≥ 12, 000 cells/mm^3) **AND** 2. New antimicrobial agent(s) is started and continued for ≥4 days within 2 days of the increase in PEEP or FiO_2.
3. Possible ventilator-associated pneumonia (PVAP)	Prerequirement: patient is required to meet the IVAC criteria PVAP criteria: 1. Positive culture of respiratory secretion (via endotracheal aspirate, BAL, lung tissue, or protected specimen brush) met the quantitative or semiquantitative thresholds OR 2. Purulent respiratory secretions and positive culture via specimens in criteria 1 but not meeting those thresholds for growth **OR** 3. One positive test from pleural fluid or lung histopathology or diagnostic test for *Legionella* species or respiratory secretion positive for viral organism, within 2 calendar days of meeting the IVAC criteria

VAE, ventilator associated events; FiO_2, fraction of inspired oxygen; PEEP, positive end expiratory pressure, WBC, white blood cell; purulent secretions, ≥25 polymorphonuclear cells, ≤10 squamous epithelial cells per low-powered field; positive culture, endotracheal aspirate ≥105 colony forming units/ml.

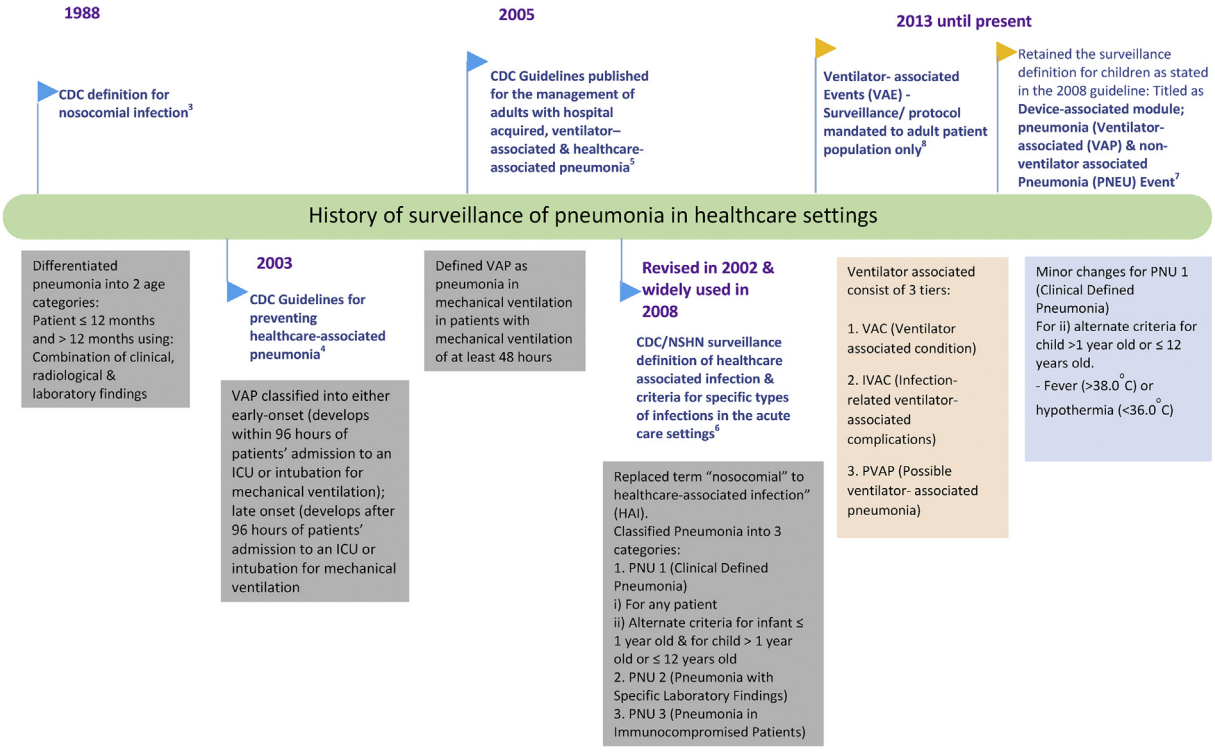

Fig. 1. History of surveillance of pneumonia in healthcare settings. CDC, Centre for Disease Control and Prevention.

oedema, atelectasis, and acute respiratory distress syndrome.[11] Additionally, the definition simplifies the surveillance process and minimises inconsistency within incidence reporting. However, information about the use of the adult VAE surveillance definition in paediatric populations is lacking; thus, this review aims to fill this clinical knowledge gap. This review will explore literature pertaining to the application of the VAE adult criteria to the paediatric population and identify potential challenges with this practice.

1.1. Aims/objectives

This literature review was conducted to synthesise the available literature on VAE to answer the following research questions:

1. Is the new VAE surveillance definition used in adults able to identify ventilator-associated complications in the paediatric population?
2. What are the potential challenges in the application of the new VAE surveillance definition in paediatric clinical practice?

2. Material and methods

A systematic literature search was conducted in the following electronic databases: PubMed, CINAHL, ScienceDirect, Cochrane Review library and Cochrane Database of Systematic Reviews, and MEDLINE. Subject headings (MeSH or CINAHL headings) were included as follows: 'pneumonia, ventilator-associated', 'complication, ventilator-associated', surveillance, and some minor/subheadings. Key search terms were 'ventilator associated pneumonia', 'ventilator associated event', 'child*', 'criteria', 'surveillance', 'p(a)ediatric', 'pneumonia', 'intensive care unit'. The Boolean operators OR, AND, and NOT were applied. The wildcard symbols were not applied in Google scholar searches. The search considered all relevant literature related to VAEs (as per the new surveillance definition) and was limited to English language publications from January 2010 to February 2018.

The reference lists from identified articles were also hand-searched to reduce the possibility of excluding relevant literature. To maximise effectiveness of search strategies, the literature search was undertaken in consultation with an expert health librarian. Screening by the title and abstract was carried out by one author; if this was insufficient to make a decision on the article, the full text was obtained. The inclusion of retrieved publications was reviewed and agreed by two authors, and there was no disagreement. The predefined inclusion criteria were the following: (1) paediatric patients aged 0–18 years and (2) received invasive mechanical ventilation.

A purpose-built data extraction form consists of study setting, aims, participant population, and outcome measure. One author extracted data from the included articles. The data were then evaluated by the first author to obtain the methodological quality using an epidemiological appraisal instrument (EAI) described by Genaidy et al.[12] There were 39 of 43 items in the EAI applicable for the purpose of review. Four items that were not applicable were the following: (1) adverse effects reported that may be consequences of the intervention, (2) newly incident cases consideration, (3) subjects randomisation, and (4) randomisation assignments' concealment. The scoring for the items was as either "yes" (2 points), "partial" (1 point), "no" (0 point), or "unable to determine" (0 point).[12] Cut-off points between high and low quartiles based on EAI scores, (more than 50% as higher quality and less than 50% as low quality) described in a study conducted by Nix et al.[13] was used. The discussions were held, and consensus was obtained for any disagreements with other two authors. Finally, grading was undertaken using the NHMRC Description of Evidence Levels, Grade of Recommendation and Body of Evidence Assessment Matrix.[14]

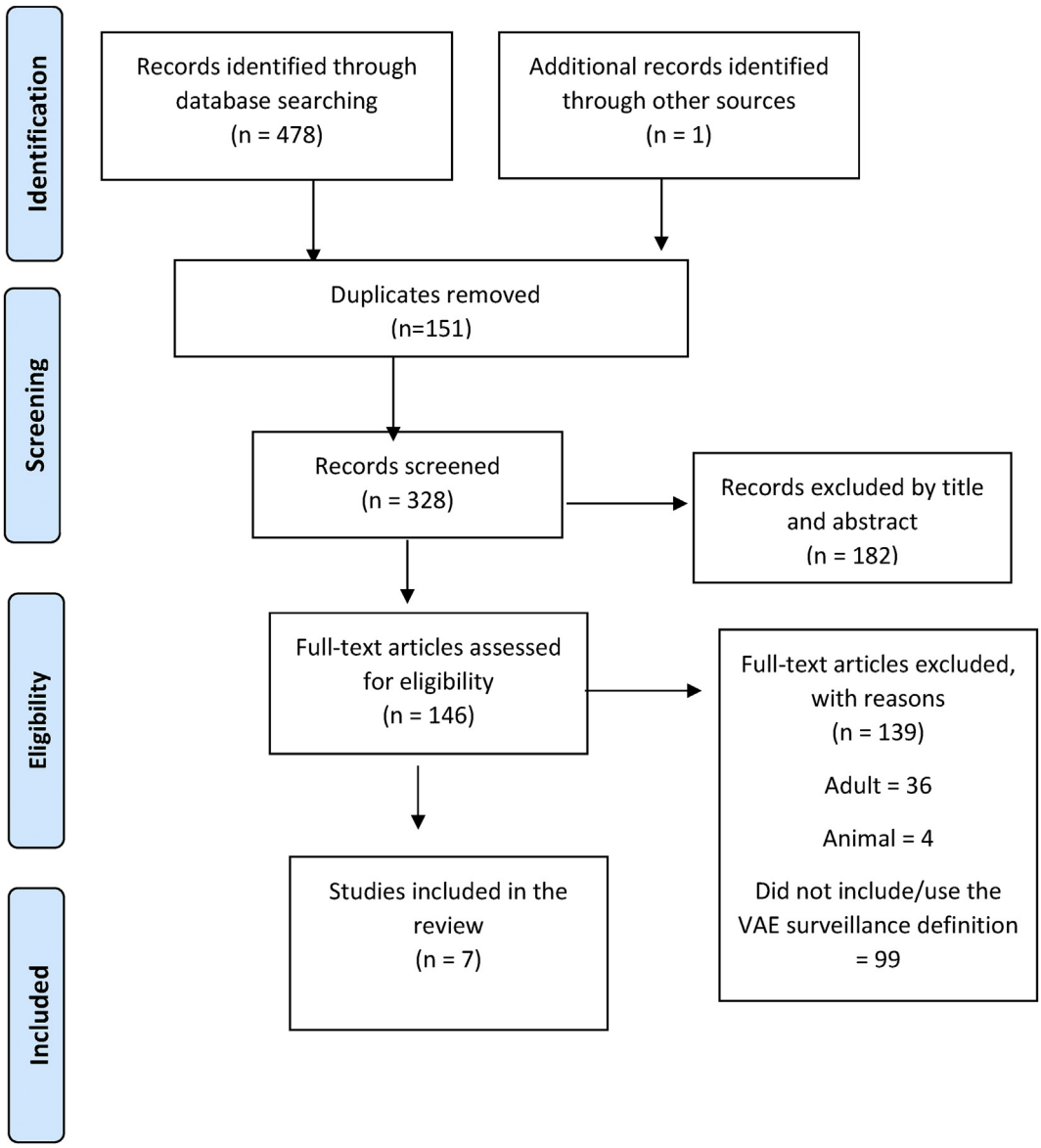

Fig. 2. PRISMA flow diagram of literature selection.[15] PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

2.1. Search results

The search retrieved a total of 328 potential articles during the initial stage of screening. The authors then excluded publications that did not use the new VAE surveillance definition, duplicates, and those studies undertaken in adults and animal models. A total of seven articles remained for inclusion in this review, which was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (Fig. 2).[15] Two included studies were conducted in Europe,[16,17] and the remaining included studies were from the United States of America.[18–22] Six included studies were retrospective in design, and one was a prospective study.[17] Overall, the level of evidence was level III-3 prognosis with a satisfactory body of evidence (grade C) based on the National Health and Medical Research Council guidelines.[14] Individual study summaries are provided in Table 3. After the data were available, the methodological quality of the studies was assessed using EAI.[12] The EAI is a reliable appraisal tool developed by epidemiologists, biostatisticians, and physicians for assessing observational studies.[12] The quality of most of the studies was more than 50% (high),[16,18–22] with only one study reporting low quality (less than 50%)[17] on the EAI. In all studies, the study design and source of population were clearly described.

3. Results

Is the new VAE surveillance definition used in adults able to identify ventilator-associated complications in the paediatric population?

Four studies adopted the new VAE surveillance definition in paediatric patients to describe the prevalence of VAE in their respective units. Iosifidis et al.[16] conducted a retrospective study to evaluate the new surveillance definition for VAC, IVAC, and PVAP and compared this with an earlier CDC VAP definition referred to as PNU1/VAP (Table 1). The study undertaken in 2011 involved 119 children admitted to the PICU. The study found that 19 patients met the VAC tier with the incidence rate of 11.2 per 1000 ventilator days. Of 19 patients meeting the VAC tier, 14 met the IVAC tier and from those 14 cases, 12 met the PVAP tier. The researchers also evaluated the same cohort of patients using the PNU1/VAP surveillance

Table 3
Study summaries and agreement between surveillance tools.

Authors	Location	Study design/ population	NHMRC level of evidence	Incidence or prevalence of VAE	Agreement between surveillance tools
Phongjitsiri et al., 2015[21]	USA	Retrospective cohort (606 patients)	III-2 aetiology evidence	VAC = 20.9/1000 ventilator days. IVAC = 12.9/1000 ventilator days. PVAP = 7.1/1000 ventilator days. PrVAP = 3.7/1000 ventilator days, 16.3% undetermined infection = 2.1/1000 ventilator days.	New VAE versus PNU/VAP = 41 patients versus 9 patients
Cocoros et al., 2016[20]	USA	Multicenter retrospective cohort (8862 patients)	III-3 prognosis evidence	VAC = 1.1–4.6/1000 ventilator days depending to ICU types.	No comparison of tools was carried out, however, attempted to test different thresholds of VAC—proposed FiO_2 of 0.25 and MAP at 4 for paediatric patients
Narayanan et al., 2016[17]	United Kingdom	Prospective cohort (258 patients)	III-3 prognosis evidence	VAC = 4.2/1000 ventilator days. PVAP = 1.8/1000 ventilator days.	New VAE versus PNU/VAP = 7 patients versus 4 patients
Beardsley et al., 2016[18]	USA	Retrospective cohort (217 patients)	III-3 prognosis evidence	IVAC = 2.16/1000 ventilator days.	New VAE versus PNU/VAP = 4 MV episodes versus 5 MV episodes Only 1 MV met both definitions
Cirulis et al., 2016[19]	USA	Retrospective cohort (119 patients)	III-3 prognosis evidence	9 patients met the new VAE surveillance definition. 22 patients identified using the modified VAE surveillance definition.	New VAE and modified new VAE versus PNU/VAP = poor sensitivity but good specificity
Iosifidis et al., 2016[16]	Greece	Retrospective cohort (119 patients)	III-3 prognosis evidence	11.2/1000 ventilator days.	New VAE versus PNU/VAP = 12 patients versus 13 patients Agreement = poor agreement (5 patients met both surveillance tools)
Taylor et al., 2014[22]	USA	Retrospective cohort (285 patients)	III-3 prognosis evidence	17 patients experienced PVAP.	New VAE versus PNU/VAP = 17 patients versus 15 (9 patients met both surveillance tools)

VAE, ventilator-associated event; VAC, ventilator-associated condition; IVAC, infection-related ventilator complication; PVAP, possible ventilator-associated pneumonia; PrVAP, probable ventilator-associated pneumonia; FiO_2, fraction of inspired oxygen; MAP, mean airway pressure; MV, mechanical ventilation.

definition, and the results demonstrate poor agreement between two surveillance definitions, despite the same incidence reported. Only five patients met the VAP criteria classified by both surveillance definitions.

Phongjitsiri et al.[21] using a similar study design with a larger cohort of patients' records (n = 606) reported that the incidence rate of VAE was 20.9 per 1000 ventilator days. Of these, the incidence of IVAC, probable VAP (probable pneumonia), PVAP, and undetermined infections was 12.9, 7.1, 3.7, and 2.1 per 1000 ventilator days, respectively. The study did not assess for the agreement of surveillance tools, but the authors mention that 41 patients met the probable VAP and PVAP tier of the new VAE surveillance versus nine patients using PNU/VAP.

A study by Taylor et al.[22] evaluating two surveillance definitions in 285 patients in a single PICU revealed that seventeen patients met the PVAP tier using the new VAE surveillance definition, and 15 met the VAP criteria using the older PNU2/VAP surveillance definition. However, only nine patients were detected by both definitions. The comparison between proportions of patients who met the PVAP tier by the new VAE surveillance definition and those who met the VAP by PNU/VAP surveillance definition was not significant ($p = 0.78$).

The prospective study by Narayanan et al.[17] demonstrated that the new VAE surveillance definition was unable to identify any additional VAP cases than those which were detected using the PNU/VAP surveillance definition. In this study, children (n = 325) were prospectively evaluated over a 6-month period, and it was found that seven met the VAC tier. Of these seven children, six met the IVAC tier and from those six, three met the PVAP tier. The incidence rate for VAC and PVAP was 4.2 and 1.8 per 1000 ventilator days, respectively, and the VAP rate using the PNU/VAP surveillance definition was 2.4 per 1000 ventilator days.

Three studies evaluated the new VAE surveillance definition but with modification of some criteria or parameters for a paediatric sample.[18–20] A multicentre retrospective cohort study undertaken by Cocoros et al.[20] involved 8862 patients across five hospitals. To detect VAC, instead of using daily minimum PEEP value increase of at least 3 cmH_2O in the adult VAE surveillance definition, they investigated/replaced the PEEP value with mean airway pressure (MAP) 4, 5, 6, and 7 cmH_2O. Furthermore, they also tested an increment of daily minimum FiO_2 into three thresholds, 0.20, 0.25, and 0.30, instead of only daily minimum FiO_2 0.20 threshold used in the adult VAE surveillance definition. Using the MAP$\geq$ 4/FiO_2 $\geq$ 0.20, the VAC incidence rates were 3.3–4.6 per 1000 ventilator days. Patients in the cardiac ICU had higher incidence rate compared with PICU and neonatal intensive care unit. Using the MAP $\geq$4/FiO_2 $\geq$ 0.20, the incidence rates were 2.9–3.2 per 1000 ventilator days. Using MAP $\geq$7/FiO_2 $\geq$ 0.30, the incidence rates were 1.1–1.3 per 1000 ventilator days.[20]

The main findings of the study supported the position that the definition was able to detect VAC, regardless of thresholds, and was associated with higher morbidity and mortality with hazard ratios ranging from 1.6 (95% confidence interval, 0.7–3.4) to 6.8 (2.9–16.0) depending on the ICU types (four PICUs, three cardiac ICUs, and one neonatal intensive care unit. The study proposed the application of FiO_2 of 0.25 and MAP of 4 cmH_2O thresholds to identify VAC in paediatric patients.[20]

Beardsley et al.[18] in their study applied daily minimum PEEP value of at least 2 cmH_2O instead of 3 cmH_2O used in the adult VAE surveillance definition to evaluate VAC in 300 episodes of mechanical ventilation (217 PICU patients). They also evaluated various ventilator-associated infections criteria, such as PNU/VAP,[6] ventilator-associated tracheobronchitis,[23,24] and lower respiratory tract infection criteria.[6] The results showed that the VAE surveillance definition used was consistent with PNU1/VAP surveillance definition. The incidence of IVAC was 2.16 per 1000 ventilator days (four mechanical ventilation episodes) that met the VAE surveillance definition versus the incidence of VAP was 2.60 per 1000 ventilator days (five mechanical ventilation episodes) that met the

PNU/VAP surveillance definition. However, only one mechanical ventilation episode met both surveillance definitions. The incidence of ventilator-associated tracheobronchitis and lower respiratory tract infection criteria was 5.19 (four mechanical ventilation episodes) and 6.92 (16 mechanical ventilation episodes) per 1000 ventilator days, respectively.

Cirulis et al.[19] found high levels of specificity of both VAE surveillance definitions—the new VAE surveillance definition described by the authors as VAC_0 and a modified VAE surveillance definition as VAC_{MP}—in paediatric traumatic brain injury patients. The VAC_{MP} used a modification of VAC/VAE criteria for PEEP value greater than or equal to 2 cmH_2O, sustained for more than or equal to one day, and retained other parameters for IVAC, and PVAP (VAC_0) was defined in the same way as the new VAE surveillance definition. Previously, they assessed 119 children using the PNU2/VAP surveillance definition and reported that 39 patients met the VAP criteria. Nine patients met the new VAE surveillance definition (VAC_0) tier, and 22 patients met the modified VAE surveillance definition (VAC_{MP}). Despite high specificity of both VAE surveillance definitions (VAC_0 and VAC_{MP}), low sensitivity was demonstrated in comparison to PNU2/VAP surveillance definition. Furthermore, patients who experienced pulmonary diagnosis in VAE or VAP using PNU2/VAP definitions had a significantly worse outcomes compared with the group who were without respiratory complications.

What are the potential challenges in the application of the new VAE surveillance definition in paediatric clinical practice?

The principal challenge in the application of the new VAE surveillance definition in the paediatric population relates to unique paediatric physiology and the resulting differences in ventilation modalities clinically required.[20] The new VAE surveillance definition excludes all patients on high-frequency oscillatory ventilation (HFOV) or extracorporeal life support.[8] Furthermore, during periods of time while the patient is on airway pressure release ventilation, the VAC should be determined by the changes in FiO_2 only.[8]

One of the benefits highlighted in the adult literature is that the definition of VAE enables automated data extraction which reduced time spent on surveillance and minimises human bias.[25] Only Phongjitsiri et al.[21] reported a locally developed and supported system that enabled automatic data extraction from electronic medical records for later analysis and with minimal workforce implications. Beardsley et al.[18] identified mechanical episodes in eligible patients using the Virtual PICU Systems from electronic medical records; however, the data were limited to demographic characteristics, Paediatric Risk of Mortality, and PICU outcomes such as duration of mechanical ventilation, PICU length of stay, and PICU mortality. While Beardsley et al. briefly explained the data retrieval for their study, other researchers used data from electronic medical records without automated data retrieval.[16,17,19,20,22] Thus, challenges remain regarding the feasibility and reliability of both automated and manual collection and documentation of clinical data.[26]

4. Discussion

Surveillance tools for assessing VAP and other associated adverse outcomes have existed since 1988. Each new iteration builds on previous models, yet none have been designed exclusively for paediatrics. This review explored the literature comparing the current VAE tool with previous iterations in paediatrics. Only one study undertook sensitivity and specificity testing between the two tools and found that although there was a high specificity, the sensitivity score indicated that underreporting of VAE may occur with the new surveillance definition.[19] Several other studies compared calculated incidence rates across two tools, and these authors concluded that there was little agreement between the two tools, although there was consistency in reporting.[16–18,22] This has significant ramifications for paediatric settings as the number of VAE cases meeting the VAE surveillance definition in children seems to be higher than those in adults. Of 1209 adult medical and surgical patients, 67 met the VAC tier, and of those, 34 met the IVAC tier with an incidence rate of 7.0 and 3.6 per 1000 ventilator days, respectively.[27] In contrast, the PICU study by Phongjitsiri et al.[21] reported an incidence rate of 20.9 and 12.9 episodes per 1000 ventilator days, respectively. Surveillance tools act not only as a means of determining the quality of care delivered and measuring patient outcomes but also as a benchmark to compare outcomes across units and countries.[11,28]

Innovation in care delivery and effectiveness in preventative strategies can be measured based on surveillance data, yet if the data are uncertain, we should question if the data are adequately robust to draw conclusions. Substantial variation exists in incidence rates with more VAE identified in a study conducted by Iosifidis et al.[16] (11.2 episodes per 1000 ventilator days), compared with a paediatric study that was published in the same year by Cocoros et al.[20] (2.9–3.2 episodes per 1000 ventilator days). Variation in case mix provides a possible explanation for this range particularly with a broader group of patients (infant and paediatric) and inclusion of all types of ICUs by Cocoros et al.[20] Adult multicentre ICU studies report similar outcomes.[29,30] Consistent results were reported in the three included studies which adopted the new VAE definition[17,21,22] compared with two studies where modifications were made to the criteria of VAE surveillance definition.[18,19]

The inclusion of positive microbiological cultures of endotracheal aspirate in PNU1/VAP by some researches is questionable as these may not reflect true infection.[31] There was consistency regarding the number of PVAP-VAP cases meeting the criteria, 12 versus 13 children using the VAE surveillance definition and the PNU/VAP surveillance definition, respectively; however, the VAE surveillance definition failed to identify eight patients with positive tracheal cultures.[16] A similar result was demonstrated in a comparison study of the traditional PNU/VAP versus VAE surveillance definition in adult patients. The VAE surveillance definition revealed the incidence of 10.0 episodes per 1000 ventilator days versus 8.0 episodes per 1000 ventilator days using the traditional PNU/VAP surveillance definition; however, the VAE surveillance definition discovered 32% more patients with VAP because the definition signalled other causes such as fluid overload.[25] The historical PNU/VAP surveillance definitions relied heavily on radiological findings and the subjective interpretation of respiratory signs and symptoms. However, the new VAE surveillance definition replaces these criteria with objective parameter definitions such as FiO_2 and PEEP, thus minimising subjectivity and potentially reducing ambiguity in the diagnosis of VAP and improving both internal and external validity.[32,33]

Another challenge unique to paediatric critical care clinicians rests on using adult-focused tools and mechanisms to assess the prevalence of iatrogenic adverse events. The review of the current evidence illustrates that this is the case with diagnosing VAEs. This suggests the merit of the new VAE surveillance definition which has broader capture of VAE in the paediatric population and opportunities to examine clinical impact and later, the specific preventative strategies.[34,35] Both definitions have merit in identification of ventilator-associated complications, but the new VAE surveillance provides other explanations for noninfectious complications that may exist apart from VAP in mechanically ventilated patients. A recent paediatric study examined the traits of VAE, finding 44% were also due to noninfectious conditions such as atelectasis and pulmonary oedema and shock[21] (compared with

pneumonia, pulmonary oedema, and acute respiratory distress syndrome in adults).[10,25,27,36]

The inclusion and exclusion of modality of ventilation and antibiotic treatment for VAE surveillance definitions in paediatrics appears somewhat uninformed. Perhaps, in the paediatric context, the difference in ventilator treatment modalities and variation in antibiotic prescribing may not be as profound as that which is evident in adult settings.[18,20] However, omitting HFOV risks excluding very sick children as this modality is one of the recommendations in children with acute respiratory failure.[37] Cocoros et al.[20] argued for the need to include patients on HFOV, considering that the usage of HFOV in paediatric patients is more frequent than in adult units, while other studies did not specify their ventilation inclusion and exclusion criteria.[16–19,22] The modification threshold of PEEP to 2 cmH_2O was also applied, and adjustment period of stability to 24 h was also tested.[18,19] However, the evidence of these modifications is limited to three studies.

The value of automated data extraction using the adult VAE surveillance definition is also worthy of further consideration in paediatric settings. In an adult study, the automated data extraction showed that it is not only efficient but also increase reliability and objectivity.[30] The potential benefit of this is also acknowledged in paediatric studies.[21,22] A recent adult study confirmed that automated data extraction is feasible with 100% sensitivity and accuracy when compared with the manual method.[38] Collaboration between clinicians and experts in medical information and systems technology may result in an innovative data extraction platform.[39]

4.1. Implications for future research

The studies identified in this review are largely from the United States where the VAP and VAE surveillance is a key clinical performance indicator. Thus, it may not be surprising that to date, there is limited research related to the application of the new VAE surveillance in paediatrics in other countries. However, discrepant VAP rates reported across the globe in adults and children may be due in part, to the lack of objectivity in the existing VAP surveillance definition,[32] and further research in investigating VAE in paediatrics is warranted. Although there is promising evidence on the benefit of using the new adult VAE surveillance definition,[26,35] there is an urgent need to conduct more studies to achieve a paediatric version of VAE surveillance definition.

4.2. Limitations

The review was restricted to English language literature, and grey literature was not included in the search strategy. This may have introduced a selection and publication biases.

5. Conclusion

This is the first review of the application of the CDC VAE surveillance definition compared with historical surveillance data in paediatrics. The strength of evidence is currently of a low level. There is substantial variation cited across studies and a lack of agreement between the old and new definitions when applied to clinical data. This suggests that the current VAE surveillance definition does not fully capture the prevalence of VAE in paediatrics, although it is adequate for monitoring. We caution against comparing the current monitoring results with historical VAP data. Although limited to only seven studies, this review provides insights into published literature related to the application of the new VAE surveillance definition and the potential implementation challenges in the paediatric population.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.aucc.2018.11.063.

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