Minor Dissertation, Publication-ready format:

Ventilator Associated Pneumonia (VAP):

a retrospective review of all children diagnosed with a VAP during 2017 and 2018, in the PICU, Red Cross War Memorial Children's Hospital.

By

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DECLARATION

I, Liana van Wyk, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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Abbreviations

BAL	Broncho-alveolar lavage
CDC	Centres for Disease Control and Prevention
CPIS	Clinical Pulmonary Infection Score
DVT	Deep vein thrombosis
FiO_2	Fraction of inspired oxygen
HAI	Hospital acquired infection
IHI	Institute of Healthcare Improvement
IQR	Interquartile range
MAP	Mean airway pressure
MeSH	Medical Subject Headings
PaO_2	Partial pressure of oxygen
PDSA	Plan, Do, Study, Act
pedVAE	Paediatric ventilator-associated event
PEEP	Positive end-expiratory pressure
PICU	Paediatric Intensive Care Unit
SOD	Selective Oropharyngeal Decontamination
USA	United States of America
VAE	Ventilator Associated Event
VAI	Ventilator Associated Infections
VAP	Ventilator Associated Pneumonia

Abstract:

Background: Ventilator Associated Pneumonia (VAP) is a common hospital acquired infection in children leading to an increase in morbidity and mortality. A study conducted in our PICU in 2013, showed that VAP rates decreased dramatically after implementation of a VAP bundle and appointing a VAP coordinator, to 4/1000 ventilator days. As part of a "Plan, Do, Study, Act" cycle, it was necessary to evaluate the efficacy of these interventions.

Objectives: To evaluate the VAP rate in the PICU over a two year period from 2017 - 2018, and secondly to describe the causative organisms and antibiotic sensitivity/resistance patterns during this period.

Methods: This was a retrospective, descriptive study using the existing PICU VAP database to identify cases. Additional information was retrieved from the PICU admission database as well as clinical folders.

Results: Over the 2 years, 31 VAP cases were identified. The VAP rate in 2017 was 4.0 /1000 ventilator days and 5.4 /1000 ventilator days in 2018. Compliance with the VAP bundle was 68% in 2017 and 70% in 2018. The median(IQR) duration of ventilation in 2017 was 9 (6-12) days and 15 (11-28) days in 2018. The median(IQR) length of PICU stay in 2017 was 11 (8 – 22) days and 25 (17-37) days in 2018. The most common cultured organism was an ESBL *Klebsiella pneumoniae* sensitive to Amikacin and carbapenems.

Conclusion: Our VAP rate has not decreased further since 2013. The VAP rate was slightly higher in 2018, and it is imperative that we improve compliance with the VAP bundle, in order to reduce VAP rates. *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* were the commonest organisms causing VAPs and empiric use of Piptazobactam and Amikacin is still appropriate.

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Chapter 1: Literature review

Background

The paediatric intensive care unit (PICU) at the Red Cross War Memorial Children's Hospital, in Cape Town, South Africa, is a 22 bed multi-disciplinary unit, admitting approximately 1400 children annually. About two thirds of patients require intubation and ventilation during their admission, which places them at risk for developing a ventilator associated pneumonia (VAP). A study in this unit done in 2011, using the clinical pulmonary infection score (CPIS) to diagnose VAPs, reported VAP rates as high as 50/1000 ventilator days[1]. Subsequently, the VAP rate decreased to 19/1000 ventilator days, in the first 5 months after implementation of a care bundle[2].

To improve compliance, a VAP-coordinator was nominated whose responsibilities included: teaching, one-on-one training, implementation of the bundle, assessing compliance to the bundle, addressing obstacles, collecting CPIS forms and identifying new VAP cases. This resulted in a further decrease of VAPs to 4/1000 ventilator days in July 2013.
In addition, ventilator circuits which were previously re-used after a decontamination process, was changed to disposable circuits[2].

There have been no changes to the VAP care bundle in this PICU over the last 5 years, but there have been several staff changes, including 3 different VAP co-ordinators.
As part of an ongoing health improvement initiative and "Plan, Do, Study, Act" (PDSA) cycle, it was thought necessary to evaluate the efficacy of the previously introduced interventions and the VAP rate during 2017 and 2018.

Objectives:

The objective of this literature review is to appraise the current literature on ventilator associated pneumonia in children, with regards to incidence, diagnosis, prevention and causative organisms.

Search Strategy:

An electronic Pubmed search was undertaken using the Medical Subject Headings (MeSH) 'ventilator associated pneumonia", "VAP", "children" and "PICU". Results were screened

based on relevance of the title and review of the abstract. Further studies were identified from the references in relevant articles.

VAP rates:

VAP refers to a nosocomial pneumonia in patients who are ventilated for more than 48 hours[3]. VAPs are, second to bloodstream infections, the most common hospital acquired infection (HAI) in children[4-6], and some studies report that up to 30% of ventilated patients develop a VAP[4]. The consequences of a child developing a VAP include an increase in both mortality and morbidity, a longer duration of mechanical ventilation and an increased duration of PICU as well as overall hospital stay[4, 5, 7].

According to recent literature, the incidence of VAP in paediatrics are still very variable, with much higher rates in developing countries compared to developed countries. Galal et al reported a VAP rate of 21.3/ 1000 ventilator days over the 12 months from September 2014 to September 2015 at Cairo University Hospital, which is among the highest in the literature[4]. A paediatric hospital in Montreal, Canada had a VAP rate of 7/1000 ventilator days over a two year period from November 2013 – November 2015[8], while Hatachi et al reported a VAP rate of 3.5 / 1000 ventilator days in Japan during 2013[9]. Patrick et al described much lower rates as well as a further decrease in the incidence among hospitals in the United States of America 2007-2012 from 1.9 to 0.7 / 1000 ventilator days[10].

Prevention

Infection control by means of hand washing and decontamination of surfaces remains the mainstay of prevention of any hospital acquired infection[11, 12]. In addition, and more specifically in VAP, a 'bundle' approach has been developed by the Institute of Healthcare Improvement (IHI) for adult patients, which has also been introduced in too paediatric intensive care units[13].

The 5 components of the IHI's adult VAP bundle is as follows:

(1) Elevation of the head of bed
(2) Determining readiness for extubation by stopping sedation
(3) Prevention of peptic ulcer disease
(4) Prevention of deep vein thrombosis (DVT)
(5) and lastly, oral hygiene, using chlorhexidine[13].

However, in paediatrics not all of these approaches are applicable. For example, it is not recommended to stop sedation on a daily basis to review the child's extubation readiness. Although one study in a meta-analysis by de Neef et al found no safety issues with daily sedation interruption, it poses a high risk for accidental extubation, with the process of re-intubation potentially increasing the risk of developing a VAP[11, 13, 14]. Furthermore, the use of H_2 Antagonists and antacids are not recommended in children. The natural acidity of stomach contents play a role in decreasing colonisation with harmful bacteria. Increasing the pH of stomach content pose the risk of possible colonisation with pathogenic bacteria and increasing the risk of VAP[12, 15-17]. In adults, however, Sucralfate, which does not alter stomach pH, showed a significant decrease in VAP rates[13, 18]. DVT prophylaxis is not routinely recommended in children[14]. It is advisable to assess every child individually and not routinely make DVT prophylaxis part of the VAP-prevention bundle[11].

A recently published meta-analysis in 2019 by De Neef et al, as well as a systematic review by Niedzwiecka et al in 2019, reviewed the effectiveness of VAP bundles in ventilated children and they concluded that the implementation of a ventilator care bundle can help reduce the incidence of VAP in ventilated children[13, 19].

Other strategies to prevent VAPs in paediatrics include using cuffed endotracheal tubes, and checking cuff pressures regularly[12, 14, 20] , minimizing aspiration; changing ventilator circuits when visibly soiled or malfunctioning[14, 20]; allowing condensate to drain away from patient[14]; and selective oropharyngeal decontamination, which entails the application of topical antibiotics to the oropharynx, but at the risk of causing increased antimicrobial resistance [21, 22].

There is insufficient literature regarding the effect of oral vs nasal intubations on the incidence of VAPs in the paediatric population. However, taking into account staff shortages in developing countries such as our own, one should take into account the higher potential for accidental extubations with oral endotracheal tubes[11].

Successful and effective ventilator care bundles are dependent on good compliance, but this remains a challenge. Accountability forms a crucial component of VAP prevention as it bridges the gap between science and outcome and includes leadership, education, execution, evaluation and feedback[13, 14].

Diagnosing VAP: Guidelines, challenges, modifications

Diagnosis as well as surveillance of VAPs in the paediatric population has proven to be challenging due to a lack of objective and reliable definitions[3, 12].
The Centre for Disease Control (CDC) and prevention regularly update their definition and criteria for diagnosing VAPs. The 2018 guidelines defined a ventilator associated pneumonia as "*A pneumonia where the patient is on mechanical ventilation for >2 calendar days on the date of event, with the day of ventilator placement being Day 1 AND the ventilator was in place on the date of event or the day before."* The "pneumonia" part of the definition depends mainly on radiological and clinical findings, with subtle differences in criteria for infants <12months old, and children 1-12years old[3]. See Table A [3].

Table A:

Clinical criteria for VAP in infants <12 months old	Clinical criteria for VAP in children 1-12 years old
• At least 2 serial chest radiographs showing new or progressive infiltrates, consolidation, cavitation or pneumatocele **Plus** • Worsening gas exchange with at least 3 of the following: - Temperature instability without other recognised cause - White blood cell count <4 000/mm3 or >15 000/mm3 and band forms >10% - New-onset purulent sputum or change in character of sputum or increased respiratory	• At least 2 serial chest radiographs showing new or progressive infiltrates, consolidation, cavitation **Plus** • At least 3 of the following - Temperature >38.4 or <37°C without other recognised cause - White blood cell count <4 000/mm3 or >15 000/mm3 - New-onset purulent sputum or change in character of sputum or increased respiratory secretions

Internationally, the CDC's algorithm for VAP has been widely acceptable for surveillance and research purposes, but the backbone being radiological findings pose to be problematic due to inter-observer variability as well as other factors such as high positive end expiratory pressure (PEEP) levels, which might give a false impression of resolving infiltrates; cardiac failure or excessive fluid retention; a lack of radiograph findings in immunocompromised children; as well as different radiograph exposures. In developing countries, routine chest xrays are not performed daily and the repeated radiation exposure from chest x-rays may also be harmful due [11, 23].

Other components of the CDC's VAP criteria are not without challenges and limitations. For instance, the site of temperature measurement influences accuracy. Sputum quality and quantity are influenced by many factors including humidification, time of day and suction frequency. Auscultation and interpretation of breath sounds are subjective and dependant on the clinician's experience. Endotracheal aspirates have poor specificity and blood cultures in children with pneumonia are often negative[11].

In 2011 the CDC proposed a new approach to the surveillance of ventilator associated infections (VAI's) in the adult population. Their intention was to develop more objective criteria to report complications arising from mechanical ventilation. Adult critical care has adopted the new "Ventilator Associated Event" (VAE) paradigm in 2013 and they have been modifying the criteria for paediatric use [24].

Willson et al conducted a study to compare the newly proposed VAE criteria with clinician-diagnosed Ventilator Associated Infection (VAIs) and found that only 5 of the 89 clinical VAI's would have fulfilled the new "infective ventilator associated condition" - criteria according to the new VAE criteria[24].
Cirulis et al compared the current CDC criteria with new adult VAE criteria as well as modified paediatric VAE criteria and found 100% specificity but only 23% and 56% sensitivity for adult and modified paediatric criteria respectively [25].

In 2020 the CDC officially released the "pediatric ventilator-associated event (PedVAE)" criteria which mainly focusses on an increase in fraction of inspired oxygen (FiO2) and mean airway pressure (MAP). It is important to note that this is strictly a surveillance tool and not a clinical definition[26].

The definition of VAP as described by the CDC is complex and difficult to apply in our South African context, but the modified Clinical Pulmonary Infection Score (CPIS) has proved to be both sensitive and specific in diagnosing VAP in our setting[1]. The CPIS is a tool that was developed to facilitate the diagnosis of ventilator-associated pneumonia and works on the basis of assigning points for various signs and symptoms of pneumonia [27].

The CPIS uses five different parameters and then calculates a score based on the indices of the previous 24hours. The parameters include minimum and maximum temperature, leucocyte count, chest radiography, characteristics of pulmonary secretions, results of bronchioalveolar lavage (if done) as well as the P/F ratio (PaO2 in mmHG / fiO2).

See Table B (next page)

Table B: CPIS indices and scores		
PARAMETER	CPIS range	SCORE
Temperature (^{o}C)	36.0 – 38.4 38.5 – 39.0 <36.0 or > 39	0 1 2
Leucocyte count (x 10^{9}/l)	4.0 – 11 ≤3.9 ≥ 11.1 and no bands Or 11.1-17.0 and no differentiation done ≥11.1 with bands Or ≥ 17.1 and no differentiation done	0 1 2
Chest Radiography	No CXR taken or no infiltrate New or progressive diffuse or patchy infiltrate New or progressive lobar infiltrate	0 1 2
Pulmonary secretions	Absent or minimal Present and non-purulent (creamy) Present and purulent (yellow or green)	0 1 2
PaO_2 (Kpa) x 7.5 / FiO_2	>240 ≤240	0 2
Organism isolated on BAL within the last 24hrs	Yes No	0 2

The CPIS uses five different parameters and then calculates a score based on the indices of the previous 24hours. The parameters include minimum and maximum temperature, leucocyte count, chest radiography, characteristics of pulmonary secretions, results of bronchioalveolar lavage (if done) as well as the P/F ratio (PaO_2 in mmHG / fiO_2).

A CPIS score of ≥6 was considered diagnostic of a VAP if:

1. The patient is ventilated for more than 48hours
2. But, if the patient had a high CPIS score on admission, the score must have dropped by at least 3 points for 1 day, or 2 points for 2 consecutive days before rising to ≥6;
3. if a patient was diagnosed with a VAP previously, the score must have decreased to. < 5 for at least 2 days before rising to ≥6 [2].

See Appendix1 for complete CPIS form.

Treatment

Understanding the microbiology of VAPs is of utmost importance in order to guide empiric antibiotic therapy, aid antibiotic stewardship and prevent antibiotic resistance[5]. Internationally, *Pseudomonas aeruginosa* is the most frequently isolated organism causing VAPs [4-6, 8, 23, 28]. Other common organisms that cause VAPs are *Haemophilus influenzae* [5, 8], *Acinetobacter baumanii* [4, 23], *Staphylococcus aureus* [4, 28] and *Klebsiella pneumoniae* [6].

The literature on pathogens such as viruses in paediatric VAP is very limited. However, under the broader umbrella of nosocomial pneumonias, a recent study at a children's hospital in Mexico found that almost two thirds of children with hospital acquired pneumonias was positive for respiratory viruses, with Respiratory syncytial virus and Parainfluenza on top of the list[29]. Older studies recognised Respiratory syncytial virus as well as outbreaks of Adenovirus as important causes of nosocomial infection in children[30, 31].

Conclusions

Ventilator associated pneumonias are one of the commonest hospital acquired infections in PICU and significantly adds to mortality and morbidity. Despite seeing an initial decrease in VAPs in our unit after implementing the VAP bundle as previously published[2], ongoing evaluation remains necessary to identify areas where improvement are required.

In an era of increasing antibiotic resistance, it is vital that each PICU monitor the organisms causing nosocomial infections and determine their antibiotic susceptibility patterns.

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Chapter 2: Publication-ready Article:

Ventilator Associated Pneumonia (VAP): a retrospective review of all children diagnosed with a VAP during 2017 and 2018, in the PICU, Red Cross War Memorial Children's Hospital.

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Introduction

Ventilator Associated Pneumonia (VAP) refers to a nosocomial pneumonia in patients who are ventilated for more than 48 hours and are second to bloodstream infections, the most common hospital acquired infection (HAI) in children[1-3] and some studies report that up to 30% of ventilated patients develop a VAP.[1]

The consequences of a VAP leads to both an increase in mortality and morbidity, which includes longer duration of ventilation and increased duration of paediatric intensive care unit (PICU) as well as overall hospital stay[1, 2, 4].

According to recent literature, the incidence of VAP in paediatrics is still very variable, with much higher rates in developing countries compared to developed countries. Galal et al reported a VAP rate of 21.3/ 1000 ventilator days over the 12 months from September 2014 to September 2015 at Cairo University Hospital, which is among the highest in the literature[1]**.** A paediatric hospital in Montreal, Canada had a VAP rate of 7/1000 ventilator days over a two year period from November 2013 – November 2015[5], while Hatachi et al reported a VAP rate of 3.5 / 1000 ventilator days in Japan during 2013[6]. Patrick et al described rates as low as 1.9 to 0.7 / 1000 ventilator days[7],as well as a further decrease in the incidence, among hospitals in the United States of America during 2007-2012.

A local study done in the PICU at Red Cross War Memorial Children's Hospital in 2011, reported a very high VAP rate of 55/1000 ventilator days [8]. The VAP rate decreased to

19/1000 ventilator days in the first 5 months after the implementation of a care bundle which consisted of the following 5 elements:

a) Elevating the head of the bed to 30 º (exception made in cases where this was medically contraindicated for eg. post-operative cardiac and neurosurgical patients as well as children nursed prone and patients on High Frequency Oscillation, who were nursed at 10 º elevation.)
b) Age appropriate mouthcare.
c) Marking of oro- / nasogastric tubes after confirmation of placement and checking their position 3-4 hourly, to allow early detection of displacement and thereby reducing the risk of aspiration.
d) No saline to be used routinely in endotracheal tube before suctioning.
e) Positioning of ventilator tubing in such a manner that condensed water runs away from the patient into the water trap[8].

A VAP-coordinator was appointed to improve bundle compliance and whose responsibilities included: one-on-one training, implementation of the bundle, assessing compliance to the bundle, addressing obstacles and identifying new VAP cases. This resulted in a further decrease of VAPs to 4/1000 ventilator days in July 2013[8].
In addition, ventilator circuits which were previously re-used after a decontamination process, was changed to disposable circuits. There have been no changes to the VAP care bundle in PICU over the last 5 years, but there have been several staff changes, including the appointment of 3 different VAP co-ordinators.

In an era of increasing antibiotic resistance, it is vital to understand and monitor the organisms causing nosocomial infections and to determine their antibiotic susceptibility patterns in order to guide empiric therapy, aid antibiotic stewardship and prevent antibiotic resistance.[2]. Internationally, the most frequently isolated organism causing VAP is *Pseudomonas aeruginosa.* [1-3, 5, 9, 10] Other organisms include *Haemophilus influenzae* [2, 5], *Acinetobacter baumanii* [1, 9], *Staphylococcus aureus* [1, 10] and *Klebsiella pneumoniae.* [3]
The current antibiotic protocol in our PICU for treating children with a suspected VAP is Piptazobactam and Amikacin or using a carbapenem for children with renal failure.

As part of an ongoing health improvement initiative and “Plan, Do, Study, Act” (PDSA) cycle, it was thought necessary to evaluate the efficacy of the previously introduced

interventions. Therefore, the objectives of this study were firstly to re-evaluate the VAP rate in the PICU over a two-year period from 1 January 2017 to 31 December 2018, in order to compare it with the previously published data in 2013; and secondly to describe the organisms isolated, the bacterial resistance patterns and the appropriateness of the current empiric antibiotic therapy for VAPs.

Methods

The PICU at Red Cross War Memorial Children's Hospital (RCWMCH), Cape Town, South Africa, is a 22 bed multi-disciplinary unit, admitting approximately 1400 children annually. About two thirds of patients require intubation and ventilation during their admission, which place them at risk of developing a VAP. This was a retrospective, descriptive study using the existing PICU VAP database to identify all patients with confirmed VAPs during 2017 and 2018.

The definition of VAP as described by the CDC is complex and difficult to apply in our South African context, but the modified Clinical Pulmonary Infection Score (CPIS) has proved to be both sensitive and specific in diagnosing VAP in our setting[11]. The Clinical Pulmonary Infection Score (CPIS) is a tool that was developed to facilitate the diagnosis of ventilator-associated pneumonia (VAP) and works on the basis of assigning points for various signs and symptoms of pneumonia[12].

During the study period CPIS forms were completed on a daily basis by doctors working in the PICU. Patients with high CPIS scores were flagged as possible VAPs. These suspected cases were then reviewed by the VAP co-ordinator and a PICU consultant in order to make the diagnosis of VAP. The ultimate diagnosis of a VAP was made by one of the five PICU consultants based on the CPIS data and bacterial cultures, thus diagnosis was not made by only one person. Once a patient was diagnosed as having a VAP, the VAP information was anonymised and entered onto our local PICU VAP database by the VAP coordinator. A separate list was kept with stored CPIS forms containing the names of patients as well as VAP information for discussion at the weekly PICU morbidity and mortality meeting. The VAP coordinator was also responsible to monitor compliance to the bundle by completing checklists twice a week on every ventilated patient, thereby covering both nursing shifts. Compliance with the VAP bundle was scored by the VAP co-ordinator and reported as a percentage.

All children admitted to the PICU who were diagnosed with a VAP between 2017 – 2018 were included in the study. Additional clinical information was obtained from the PICU admission database and from the patient's clinical folders.

Approval was obtained from the Departmental Research Committee, School of Child and Adolescent Health, as well as the Human Research Ethics Committee of the Faculty of Health Sciences, University of Cape Town and local hospital management before conducting the research. The study was developed and carried out in accordance with the Declaration of Helsinki, 2013

As this was a retrospective folder review of routinely collected data and the study posed minimal risk, informed consent was not sought. Every child's parent/ caregiver receives an information leaflet upon admission to PICU explaining that routinely collected data may be used for research purposes and that data will be anonymized.

Patient confidentiality was maintained by anonymising all recorded data as well as by storing paper records in a locked cupboard, and electronic records in a password-protected spreadsheet. No patient will be identifiable in any output arising from this study.

Statistical analysis was done using Microsoft Excel and Stata 11, StataCorp. 2009, College Station, TX: StataCorp LP.
Data distribution did not have normal distribution, and therefor presented and summarized using median, interquartile percentiles and ranges.

Results

Over the 2-year period, 31 cases of VAP were identified. The VAP rate for 2017 was 4.0/1000 ventilator days and for 2018 was 5.4/1000 ventilator days.

The characteristics of the children with VAPs are shown in Table 1.

Table 1: Children diagnosed with VAPs for 2017 and 2018

	2017	2018
Total PICU admissions	1342	1441
Total VAPs	14	17
Female (%)	5 (36)	7 (41)
Median age in months (IQR)	5 (2–94)	3 (0-8)
Median length of ventilation in days (IQR)	9 (6-12)	15 (11-28)
Median length of PICU stay in days (IQR)	11 (8-22)	25 (17-37)
Median day of ventilation when VAP diagnosed in days (IQR)	5 (3-6)	8(6-13)
Deaths (%)	2 (14)	4 (24)
VAP compliance	68%	70%

The primary diagnosis of the children, who developed VAPs in PICU, were varied and ranged across all disciplines. The top 5 primary diagnoses included traumatic brain injury due to pedestrian vehicle accidents (4 cases), severe pneumonia (2 cases), congenital diaphragmatic hernia (2 cases), total anomalous pulmonary venous drainage (TAPVD) post repair (2 cases) and ventricular septal defect (VSD) post repair (2 cases).

Of the children who developed VAPs, 8 (26%) patients were electively admitted post cardiac surgery, there were 13 (42%) emergency surgical admissions and 10 (32%) emergency medical admissions.

The most common cultured organisms are shown in Table 2 .

Table 2: Organisms isolated over the 2-year study period.	
Organism	**Number (%)**
Klebsiella pneumoniae (ESBL)	10 (31)
Pseudomonas aeroginosa	7 (22)
Staphylococcus aureus	4 (13)
Acinetobacter baumanii	3 (9)
Candida albicans	1 (3)
Escherichia coli	1 (3)
Klebsiella oxytoca	1 (3)
Rhinovirus	1 (3)
Serratia marcescens	1 (3)
Stenotrophomonas	1 (3)

In two VAP cases no organisms were cultured and the diagnoses was made on clinical grounds.

Looking at the sensitivity patterns: *K. pneumoniae* were 100% sensitive to Amikacin but had intermediate sensitivity to Piptazobactam in 2 isolates; in these cases carbapenems showed 100% sensitivity. *P. aeruginosa* had 100% Aminoglycocide sensitivity, and in one case showed intermediate resistance to Piptazobactam. *S. aureus* was 75% sensitive to Cloxacillin, with only 1 case methicillin resistant. In our study, *A. baumanii* has shown 100% sensitivity to Gentamycin but 66% resistance to Piptazobactam – in these cases of resistance the bacteria were sensitive to carbapenems.

Overall, 90% of the VAP organisms in our study were sensitive to the combination of Piptazobactam and Amikacin.

Discussion

The ventilator associated pneumonia rate of 4/1000 ventilator days in 2017 was the same as the last published data in 2013, whilst the VAP rate in 2018 was slightly higher at 5.6 /1000 ventilator days. This is still higher than developed countries like Japan and the United States of America[6, 7], where rates are less than 3.5/1000 ventilator days. Children developed a

VAP after a median of 5 days ventilation in 2017 and after a median of 8 days ventilation in 2018. The longer median duration of ventilation in 2018, could potentially explain the increase in VAP rates during 2018, as it is well described that longer duration of ventilation leads to increased risk for developing VAP[13]. Prolonged ventilation in paediatrics have been defined as mechanical ventilation for more or equal to 21 days and more than 6 hours/ day [14]. In our study, 9 of the 31 patients (30%) fulfilled that definition. In 2018, patients who required ventilation longer than 21 days, were admitted with the following conditions: Hypoplastic lung (39 days), encephalitis (37 days), double outlet right ventricle post op (35 days), status dystonicus (34 days), necrotising enterocolitis (NEC)/sepsis (28 days), and tracheoesophageal fistula (24 days). Encephalitis is well described in the literature to require prolonged ventilation in the paediatric population[15, 16].

Unfortunately, the patients with pulmonary hypoplasia, necrotising enterocolitis and tracheoesophageal fistula demised, accounting for 3 out of the 4 deaths in 2018.

Internationally, the CDC's algorithm for VAP has been widely acceptable for surveillance and research purposes, but their diagnostic criteria is radiological findings, which is problematic due to inter-observer variability. Other factors affecting the efficiency of chest radiographs include high positive end expiratory pressure (PEEP) levels, which might give a false impression of resolving infiltrates; cardiac failure or excessive fluid retention can wrongly be interpreted as infiltrates; a lack of radiograph findings in immunocompromised children; as well as a difference in radiograph exposures. Repeated chest x-rays may also be harmful due to radiation exposure[9, 11]. Other challenges with the CDC VAP definition is that they rely on clinical signs and symptoms which are mostly subjective and often poorly documented in clinical notes[17].

Proper surveillance definitions are needed in order to effectively determine prevention strategies. Therefore, the CDC recently developed an objective surveillance algorithm called "pediatric ventilator-associated event (PedVAE)", which mainly focusses on an increase in fraction of inspired oxygen (FiO2) and mean airway pressure (MAP). It is important to note that this is strictly a surveillance tool and not a clinical definition[17].

In order to reduce morbidity and mortality in PICU, the prevention of VAPs should be a priority. The low VAP bundle compliance rate of 68% in 2017 and 70% in 2018 is worrying and a reduction in our VAP rate can only be achieved by improving these compliance rates.

Infection control by means of hand washing and decontamination of surfaces remains the mainstay of prevention of any hospital acquired infection[18, 19]. In addition, and more specifically in VAP, a 'bundle' (a set of practices to improve patient outcomes) approach has been developed by the Institute of Healthcare Improvement (IHI) for adult patients, and a modified version has been introduced in too paediatric intensive care units[20].

In paediatrics, not all of the adult approaches are applicable. For example, it is not recommended to stop sedation on a daily basis to review the child's extubation readiness. Although one study in a meta-analysis by de Neef et al found no safety issues with daily sedation interruption. Sedation breaks poses a high risk for accidental extubation, with the process of re-intubation potentially increasing the risk of developing a VAP[18, 20, 21]. Furthermore, the use of H_2 Antagonists and antacids are not recommended in children. The natural acidity of stomach contents play a role in decreasing colonisation with harmful bacteria. Increasing the pH of stomach content pose the risk of possible colonisation with pathogenic bacteria and increasing the risk of VAP[19, 22-24]. In adults, however, Sucralfate, which does not alter stomach pH, showed a significant decrease in VAP rates[20, 25]. DVT prophylaxis is not routinely recommended in children[21]. It is advisable to assess every child individually and not routinely make DVT prophylaxis part of the VAP-prevention bundle[18].

A recently published meta-analysis in 2019 by De Neef et al, as well as a systematic review by Niedzwiecka et al in 2019, reviewed the effectiveness of VAP bundles in ventilated children and they concluded that the implementation of a ventilator care bundle can help reduce the incidence of VAP in ventilated children[20, 26].

Other strategies to prevent VAPs in paediatrics include using cuffed endotracheal tubes, and checking cuff pressures regularly[19, 21, 27] minimizing aspiration; changing ventilator circuits when visibly soiled or malfunctioning[21, 27]; allowing condensate to drain away from patients[21]; and selective oropharyngeal decontamination, which entails the application of topical antibiotics to the oropharynx, but at the risk of causing increased antimicrobial resistance [28, 29].

There is insufficient literature regarding the effect of oral vs nasal intubations on the incidence of VAPs in the paediatric population. However, taking into account staff shortages in developing countries such as our own, there is a higher potential for accidental extubations with oral endotracheal tubes[18].

Successful and effective ventilator care bundles are dependent on good compliance, but this remains a challenge. Accountability forms a crucial component of VAP prevention as it bridges the gap between science and outcome and includes leadership, education, execution, evaluation and feedback[20, 21].

By far the most commonly cultured organism in our study was an extended spectrum beta-lactamase producing *Klebsiella pneumoniae* (30%), which is in contrast to international data where *Pseudomonas aeruginosa* is described as the most common causative agent [1-3, 5, 9, 10].

Empiric use of Amikacin and Piptazobactam in children with suspected VAPs, who do not have renal impairment, is still appropriate as 90% of the causative organisms showed sensitivity to either the one or the other. This is crucial in view of the increasing concerns about carbapenem resistant Enterobacteriaceae (CRE) colonisation and infection. Of major concern, is the developing intermediate resistance pattern seen with carbapenems, as these are the alternative drugs of choice for children with renal impairment.

The study unfortunately has several limitations. The data was extracted from existing databases. The CPIS forms were completed by varying junior doctors, and these forms were often filled in retrospectively. Leucocyte counts and chest X-rays were not performed routinely each day on ventilated patients. Inter-observer variability in interpretation of X-rays; and bacterial cultures results from tracheal aspirates instead of bronchioalveolar lavage could further play a role in missing or over diagnosing VAPs.

Recommendations

Maintaining and improving VAP compliance is of utmost importance and could include more regular checks, keeping staff motivated, informed and educated[20], as well as ongoing audits.

Conclusion

Despite seeing an initial decrease in VAPs in our unit after implementing the VAP bundle in 2013, our VAP rate has not decreased further. The VAP rate is slightly higher in 2018, but need to be followed up in subsequent years. It is also imperative that we improve compliance with the VAP bundle, in order to improve VAP rates.

Klebsiella pneumoniae and *Pseudomonas aeruginosa* were the commonest organisms causing VAPs and empiric use of Piptazobactam and Amikacin in combination is still appropriate.

Contributors

I would like to thank sister Joanne Applegate, current VAP coordinator in PICU, for her assistance with access to the data from the VAP database.

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Appendix 1:

CPIS form :

VAP identification: Clinical Pulmonary Infection Score (CPIS)

Please circle appropriate box (worst value over previous 24 hours) *(always fill in retrospectively e.g. on Sat fill in Fri's info)*

PARAMETER	CPIS RANGE	CPIS SCORE						
		Fri Date	Sat Date	Sun Date	Mon Date	Tues Date	Wed Date	Thur Date
Temperature (°C)	36.0-38.4	0	0	0	0	0	0	0
	38.5-39.0	1	1	1	1	1	1	1
	<36.0 or >39.0	2	2	2	2	2	2	2
Leukocyte count (X 10^9/l)	4.0-11	0	0	0	0	0	0	0
	≤3.9 ≥11.1 and no bands or ≥ 11.1 ≤17.0 and no differentiation done	1	1	1	1	1	1	1
	≥11.1 with bands or no differentiation done and leukocytes ≥17.1	2	2	2	2	2	2	2
Chest radiography	No CXR taken or no infiltrate	0	0	0	0	0	0	0
	New or progressive diffuse or patchy infiltrate	1	1	1	1	1	1	1
	New or progressive lobar infiltrate	2	2	2	2	2	2	2
Pulmonary secretions	Absent or minimal	0	0	0	0	0	0	0
	Present and non-purulent (creamy)	1	1	1	1	1	1	1
	Present and purulent (yellow or green)	2	2	2	2	2	2	2
PaO_2 (Kpa) X 7.5 /FiO_2 eg 14.4 X 7.5 / 0.4 = 270	>240	0	0	0	0	0	0	0
	≤ 240	2	2	2	2	2	2	2
Organism isolated on BAL within last 24 hours	No or Not Done	0	0	0	0	0	0	0
	Yes	2	2	2	2	2	2	2
TOTAL SCORE								
CPIS ≥6		YES	YES	YES	YES	YES	YES	YES
		NO	NO	NO	NO	NO	NO	NO
CPIS increased by ≥2		YES	YES	YES	YES	YES	YES	YES
		NO	NO	NO	NO	NO	NO	NO
NEW VAP		YES	YES	YES	YES	YES	YES	YES
		NO	NO	NO	NO	NO	NO	NO
Intubated ≥ 48 hours		YES	YES	YES	YES	YES	YES	YES
		NO	NO	NO	NO	NO	NO	NO

Patient sticker

Thursday CPIS :

DATE INTUBATED: _____

BACKGROUND

Ventilator-associated pneumonia (VAP) is a nosocomial lower respiratory tract infection which occurs in mechanically ventilated patients 48 hours or more after starting ventilatory support.

- **In C1 PICU the incidence of VAP has been about 22% of ventilated patients / 45 infections per 1000 ventilated days. Patients who develop VAP are likely to have longer PICU stay and ventilation and almost double the mortality than those who do not develop VAP. This is an unacceptable situation and we are therefore engaged in a process of practice improvement (the Best Care Always [BCA] initiative) to reduce the VAP incidence.**

- The most common VAP pathogens in C1 PICU are *Acinetobacter baumannii, Klebsiella pneumonia, Staph. Aureus, Pseudomonas aeruginosa.*
- Preventive measures include: adherence to standard infection control measures; early weaning and extubation, limiting sedation and ventilator "bundles".
- The **ventilator bundle** comprises: head of bed elevation; oral hygiene; ensuring that ventilator tubing runs away from the patient; accurate NGT positioning; and not using saline routinely when suctioning.
- In order to determine whether these measures are being effective it is essential that we measure our VAP rates on an ongoing basis.
- We have validated the Clinical Pulmonary Infection Score (CPIS) in the PICU. It measures and scores five clinical and radiographic signs with a total score ≥6 being suggestive of VAP.
- A score of ≥6 is only diagnostic of VAP when:
    - The patient has been ventilated for >48 hours
    - In a patient who had a high CPIS in the first 48 hours of admission, the CPIS must first drop by at least 3 points for one day or by 2 points for 2 days before increasing to ≥6 again (ie. it must be a new infection)
    - For a patient to be diagnosed with more than one VAP infection, the CPIS has to be <5 for at least 2 days before increasing to ≥6 again.

- Forms are provided for each patient per week.
- Please tick the appropriate box next to each CPIS measure.
- **You do not need to fill in the culture results (highlighted), we will do that for you each week.**
- Please keep the form in the patients' medical folder from where it will be collected each week.

THIS IS AN IMPORTANT INITIATIVE WHICH WILL IMPROVE PATIENT OUTCOME
PLEASE HELP FACILITATE THE PROCESS
WE CAN'T DO IT WITHOUT EVERYONE'S BUY- IN!

Appendix 2: ***DATA SHEET***

General Information

Study ID: _____

Folder Nr: _____

Date Of Birth: _____

Age in Months: _____

Gender: □ Male (0) □ Female (1)

Admission Information

PICU admission date: _____

Reason for PICU admission: Elective: □ Cardiac surgery

□ General Surgery

□ ENT surgery

□ Neurosurgery

□ Other:

Emergency: □ Surgical: Specify

□ Medical: Specify

Date of Discharge from PICU/ Date of Death: _____

Days in PICU: _____

VAP info:

Reason for Intubation/Ventilation: □ Elective / Post op

□ Airway protection/ Decreased LOC

□ Respiratory failure

□ Circulatory failure/shock

Date of Intubation (of VAP episode): _____

Date of Extubation: _____

Length of Ventilation: (days) _____

Date of diagnosis of VAP: _____

Organism Cultured: _____

Sensitivity Of Organism: _____

Appropriate Antibiotics at the time of Diagnosis: □ Yes □ No

Appendix 3: HREC approval (renewed)

UNIVERSITY OF CAPE TOWN
HUMAN RESEARCH ETHICS COMMITTEE
REC REG 0001
HEALTH SCIENCES FACULTY
UNIVERSITY RECORDS

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

FHS017: Annual Progress Report / Renewal

Research Involving Records/Audits/Collection of Biological Specimens/Repositories/Databases/Registries

HREC office use only (FWA00001637; IRB00001938)			
This serves as notification of annual approval, including any documentation described below.			
☑ Approved	Annual progress report	Approved until/next renewal date	30-12-21
☐ Not approved	See attached comments		
Signature Chairperson of the HREC/ Designee		Date Signed	7/12/2020

Note: Please note that incomplete submissions will not be reviewed.
Please email this form and supporting documents (if applicable) in a combined pdf-file to hrec-enquiries@uct.ac.za.

Please clarify your plan for research-related activities during COVID-19 lockdown

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)	02/12/2020		
HREC REF Number	319/2019	Current Ethics Approval was granted until	30/6/2020
Protocol title	**Ventilator Associated Pneumonia (VAP): a retrospective review of all children diagnosed with a VAP during 2017 and 2018, in the PICU, Red Cross War Memorial Children's Hospital.**		
Principal Investigator	Dr Shamiel Salie		
Department / Office Internal Mail Address	Paediatrics – Paediatric Intensive Care Unit, Red Cross Childrens Hospital shamiel.salie@uct.ac.za		
1.1 Does this protocol receive US Federal funding?			X No

2. Protocol status (tick ✓)

☐	Research-related activities are ongoing
✓	Data collection is complete, data analysis only

Please indicate (in the blank below) the titles and HREC reference numbers of any projects currently making use of the Database/registry/repository.

3. Protocol summary

Total number of records or specimens collected, reviewed or stored since the original approval		31
Total number of records or specimens collected, reviewed or stored since last progress report		
Have any research-related outputs (e.g. publications, abstracts, conference presentations) resulted from this research? If yes, please list and attach with this report.	☐ Yes	✓ No

4. Signature

Signature Removed

Appendix 4

Southern African Journal of Critical Care

http://www.sajcc.org.za/index.php/sajcc/about/submissions

Author Guidelines

Author Guidelines

Please take the time to familiarise yourself with the policies and processes below. If you still have any questions, please do not hesitate to ask our editorial staff (tel.: +27 (0)21 532 1281, email: submissions@hmpg.co.za).

Scope of the Journal.

This Journal publishes scientific articles related to multidisciplinary critical and intensive medical care and the emergency care of critically ill humans.

To submit a manuscript, please proceed to the *SAJCC* Editorial Manager website:

www.editorialmanager.com/sajcc

Please view the Author Tutorial for guidance on how to submit on Editorial Manager.

Authorship

Named authors must consent to publication. Authorship should be based on: (*i*) substantial contribution to conceptualisation, design, analysis and interpretation of data; (*ii*) drafting or critical revision of important scientific content; or (*iii*) approval of the version to be published. These conditions must all be met for an individual to be included as an author (uniform requirements for manuscripts submitted to biomedical journals; refer to www.icmje.org)

If authors' names are added or deleted after submission of an article, or the order of the names is changed, all authors must agree to this in writing.

Please note that co-authors will be requested to verify their contribution upon submission. Non-verification may lead to delays in the processing of submissions. Author contributions should be listed/described in the manuscript.

Conflicts of interest

Conflicts of interest can derive from any kind of relationship or association that may influence authors' or reviewers' opinions about the subject matter of a paper. The existence of a conflict – whether actual, perceived or potential – does not preclude publication of an article. However, we aim to ensure that, in such cases, readers have all the information they need to enable them to make an informed assessment about a publication's message and conclusions. We require that both authors and reviewers declare all sources of support for their research, any personal or financial relationships (including honoraria, speaking fees, gifts received, etc) with relevant individuals or organisations connected to the topic of the paper, and any association with a product or subject that may constitute a real, perceived or potential conflict of interest. If you are unsure whether a specific relationship constitutes a conflict, please contact the editorial team for advice. If a conflict remains undisclosed and is later brought to the attention of the editorial team, it will be considered a serious issue prompting an investigation with the possibility of retraction.

Research ethics committee approval

Authors must provide evidence of Research Ethics Committee approval of the research where relevant. Ensure the correct, full ethics committee name and reference number is included in the manuscript an accompanying documentation. A copy of the ethics approval letter must be uploaded as a supplementary file.

If the study was carried out using data from provincial healthcare facilities, or required active data collection through facility visits or staff interviews, approval should be sought from the relevant provincial authorities. For South African authors, please refer to the guidelines for submission to the National Health Research Database. Research involving human subjects must be conducted according to the principles outlined in the Declaration of Helsinki (2013), and should include a statement on independent ethical review. Where appropriate, a statement must be made that informed consent was taken from human participants, and/or whether the need for informed consent was waived.

Please also refer to the National Department of Health's guideline on Ethics in Health research: principles, processes and structures to ensure that the appropriate requirements for conducting research have been met, and that the HPCSA's General Ethical Guidelines for Health Researchers have been adhered to.

Protection of rights to privacy

Research Participants

Information that would enable identification of individual research participants should not be published in written descriptions, photographs, radiographs and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) has given informed written consent for publication and distribution. We further recommend that the published article is disseminated not only to the involved researchers but also to the patients/participants from whom the data was drawn. Refer to Protection of Research Participants. The signed consent form should be submitted with the manuscript to enable verification by the editorial team.

Other individuals

Any individual who is identifiable in an image must provide written agreement that the image may be used in that context in the *SAJCC.*

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Ethnic/race classification

Use of racial or ethnicity classifications in research is fraught with problems. If you choose to use a research design that involves classification of participants based on race or ethnicity, or discuss issues with reference to such classifications, please ensure that you include a detailed rationale for doing so, ensure that the categories you describe are carefully defined, and that socioeconomic, cultural and lifestyle variables that may underlie perceived racial disparities are appropriately controlled for. Please also clearly specify whether race or ethnicity is classified as reported by the patient (self-identifying) or as perceived by the investigators. Please note thatit is not appropriate to use self-reported or investigator-assigned racial or ethnic categories for genetic studies.

Manuscript preparation

Preparing an article for anonymous review

To ensure a fair and unbiased review process, submissions may include an anonymized version of the manuscript.

Submitting a manuscript that needs additional blinding can slow down your review process, so please be sure to follow these simple guidelines as much as possible:

- An anonymous version should not contain any author, affiliation or particular institutional details that will enable identification.
- Please remove title page, acknowledgements, contact details, funding grants to a named person, and any running headers of author names.
- Mask self-citations by referring to your own work in third person.

General article format/layout

Submitted manuscripts that are not in the correct format specified in these guidelines will be returned to the author(s) for correction prior to being sent for review, which will delay publication.

General:

- Manuscripts must be written in UK English (this includes spelling).
- The manuscript must be in Microsoft Word or RTF document format. Text must be 1.5 line spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes). Pages and lines should be numbered consecutively.
- Please make your article concise, even if it is below the word limit.
- Qualifications, ***full*** affiliation (department, school/faculty, institution, city, country) and contact details of ALL authors must be provided in the manuscript and in the online submission process.
- Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.
- Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160.
- Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'
- Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.
- Medical drugs should be referred to by their generic name although the trade name may be used in brackets in the text once if unique.

If you wish material to be in a box, simply indicate this in the text. You may use the table format –this is the *only* exception. Please DO NOT use fill, format lines and so on.

Preparation notes by article type

Research

Guideline word limit: 3 000 words (excluding abstract and bibliography)

Research articles describe the background, methods, results and conclusions of an original research study. The article should contain the following sections: introduction, methods, results, discussion and conclusion, and should include a structured abstract (see below). The title of the manuscript should concisely describe the study but should not include the outcome. The introduction should be concise – no more than three paragraphs – on the background to the research question, and must include references to other relevant published studies that clearly lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill a gap in the literature, a logical extension of previous work, or to answer an important question. If other papers related to the same study have been published previously, please make sure to refer to them specifically. At the end of the introduction clearly state the aim or objective of the study. The primary and secondary outcomes should be specified.

In the Methods section describe in sufficient detail so that others would be able to replicate the study should they need to. Sections of the methods that have been described in previous publications need only be referenced. The statistical methods should be described. Where appropriate, sample size calculations should be included to demonstrate that the study is not underpowered.

Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

The discussion should be confined to an interpretation of your results with respect to your stated aim and if applicable, a comparison to the results of similar studies. The strengths and weaknesses of your study should be discussed.

The conclusion should be confined to an interpretation of the results of the study and a recommendation if applicable.

- May include up to 6 illustrations or tables.
- References should only include the most recent and relevant articles. A maximum of 30 references is advised.

Structured abstract

- This should be no more than 250 words, with the following headings:
    - **Background:** why the study is being done and how it relates to other published work.
    - **Objectives:** what the study intends to find out
    - **Methods:** must include study design, number of participants, description of the research tools/instruments, any specific analyses that were done on the data.
    - **Results:** first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.
    - **Conclusion:** must be supported by the data, and be aligned with the conclusion in the main text.
    - Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors. It should be able to be intelligible to the reader without referral to the main body of the article.
    - Do not include any references in the abstracts.

Here is an example of a good abstract.

Scientific letters/short reports

These are shorter length, scholarly research articles of no more than 1500 words, and include case reports.

Guideline word limit: 1500 words

- Abstract: Structured, maximum 250 words, with the following headings: Background, Objectives, Methods, Results, and Conclusion.
- May include only one illustration or table
- A maximum of 15 references

Editorials

Guideline word limit: 1 000 words

These opinion or comment articles are usually commissioned but we are happy to consider and peer review unsolicited editorials. Editorials should be accessible and interesting to readers without specialist knowledge of the subject under discussion and should have an element of topicality (why is a comment on this issue relevant now?) There should be a clear message to the piece, supported by evidence.

Please make clear the type of evidence that supports each key statement, e.g.:

- expert opinion
- personal clinical experience
- observational studies
- trials
- systematic reviews.

Review articles

Narrative review articles should always be discussed with the Editor prior to submission. (Structured reviews or meta-analyses' need not be).

Guideline word limit: 4 000 words

These are welcome, but should be either commissioned or discussed with the Editor before submission. A review article should provide a clear, up-to-date account of the topic and be aimed at non-specialist hospital doctors and general practitioners. They should be aligned to practice in South and/or sub-Saharan Africa and not a précis of reviews published in the international literature

Please ensure that your article includes:

- Abstract: unstructured, of about 100-150 words, explaining the review and why it is important
- Methods: Outline the sources and selection methods, including search strategy and keywords used for identifying references from online bibliographic databases. Discuss the quality of evidence.
- When writing: clarify the evidence you used for key statements and the strength of the evidence. Do not present statements or opinions without such evidence, or if you have to, say that there is little or no evidence and that this is opinion. Avoid specialist jargon and abbreviations, and provide advice specific to southern Africa.
- Personal details: Please supply your qualifications, position and affiliations address, telephone number and fax number, and your e-mail address; and a short personal profile (50 words) and a few words about your current fields of interest.

Correspondence (Letters to the Editor)

Guideline word limit: 400 words

Letters to the editor should relate either to a paper or article published by the SAJCC or to a topical issue of particular relevance to the journal's readership

- May include only one illustration or table
- Must include a correspondence address.

Obituaries

Guideline word limit: 400 words

Should be offered within the first year of the practitioner's death, and may be accompanied by a photograph.

Illustrations/photos/scans

- If illustrations submitted have been published elsewhere, the author(s) should provide evidence of consent to republication obtained from the copyright holder.
- Figures must be numbered in Arabic numerals and referred to in the text e.g. '(Fig. 1)'.
- Each figure must have a caption/legend: Fig. 1. Description (any abbreviations in full).
- All images must be of high enough resolution/quality for print.
- All illustrations (graphs, diagrams, charts, etc.) must be in PDF form.
- Ensure all graph axes are labelled appropriately, with a heading/description and units (as necessary) indicated. Do not include decimal places if not necessary e.g. 0; 1.0; 2.0; 3.0; 4.0 etc.
- Each image must be attached individually as a 'supplementary file' upon submission (not solely embedded in the accompanying manuscript) and named Fig. 1, Fig. 2, etc.

Tables

- Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged.
- Embed/include each table in the manuscript Word file - do not provide separately as supplementary files.
- Number each table in Arabic numerals (Table 1, Table 2, etc.) consecutively as they are referred to in the text.
- Tables must be cell-based (i.e. not constructed with text boxes or tabs) and editable.
- Ensure each table has a concise title and column headings, and include units where necessary.
- Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

References

NB: *Only complete, correctly formatted reference lists in Vancouver style will be accepted. If reference manager software is used, the reference list and citations in text are to be unformatted to plain text before submitting.*

- Authors must verify references from original sources.
- Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by the World Health Organization,[2] and others.[3,4-6]
- All references should be listed at the end of the article in numerical order of appearance in the Vancouver style (not alphabetical order).
- Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus.
- Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al.
- Volume and issue numbers should be given.
- First and last page, in full, should be given e.g.: 1215-1217 **not** 1215-17.
- Wherever possible, references must be accompanied by a digital object identifier (DOI) link). Authors are encouraged to use the DOI lookup service offered by CrossRef:
    - On the Crossref homepage, paste the article title into the 'Metadata search' box.
    - Look for the correct, matching article in the list of results.
    - Click Actions > Cite
    - Alongside 'url =' copy the URL between { }.
    - Provide as follows, e.g.: https://doi.org/10.7196/07294.937.98x

Some examples:

- *Journal references:* Price NC, Jacobs NN, Roberts DA, et al. Importance of asking about glaucoma. Stat Med 1998;289(1):350-355. DOI:10.1000/hgjr.182
- *Book references:* Jeffcoate N. Principles of Gynaecology. 4th ed. London: Butterworth, 1975:96-101.
- *Chapter/section in a book:* Weinstein L, Swartz MN. Pathogenic Properties of Invading Microorganisms. In: Sodeman WA, Sodeman WA, eds. Pathologic Physiology: Mechanisms of Disease. Philadelphia: WB Saunders, 1974:457-472.
- *Internet references:* World Health Organization. The World Health Report 2002 - Reducing Risks, Promoting Healthy Life. Geneva: WHO, 2002. http://www.who.int/whr/2002 (accessed 16 January 2010).
- Legal references
- Government Gazettes:

National Department of Health, South Africa. National Policy for Health Act, 1990 (Act No. 116 of 1990). Free primary health care services. Government Gazette No. 17507:1514. 1996.

In this example, 17507 is the Gazette Number. This is followed by :1514 - this is the notice number in this Gazette.

- Provincial Gazettes:

Gauteng Province, South Africa; Department of Agriculture, Conservation, Environment and Land Affairs. Publication of the Gauteng health care waste management draft regulations. Gauteng Provincial Gazette No. 373:3003, 2003.

- Acts:

South Africa. National Health Act No. 61 of 2003.

- Regulations to an Act:

South Africa. National Health Act of 2003. Regulations: Rendering of clinical forensic medicine services. Government Gazette No. 35099, 2012. (Published under Government Notice R176).

- Bills:

South Africa. Traditional Health Practitioners Bill, No. B66B-2003, 2006.

- Green/white papers:

South Africa. Department of Health Green Paper: National Health Insurance in South Africa. 2011.

- Case law:

Rex v Jopp and Another 1949 (4) SA 11 (N)

Rex v Jopp and Another: Name of the parties concerned

1949: Date of decision (or when the case was heard)

(4): Volume number

SA: SA Law Reports

11: Page or section number

(N): In this case Natal - where the case was heard. Similarly, (C) woud indicate Cape, (G) Gauteng, and so on.

NOTE: no . after the v

- *Other references (e.g. reports) should follow the same format:* Author(s). Title. Publisher place: Publisher name, year; pages.
- Cited manuscripts that have been accepted but not yet published can be included as references followed by '(in press)'.
- Unpublished observations and personal communications in the text must **not** appear in the reference list. The full name of the source person must be provided for personal communications e.g. '...(Prof. Michael Jones, personal communication)'.

From submission to acceptance

Submission and peer-review

To submit an article:

- Please ensure that you have prepared your manuscript in line with the SAJCC requirements.
- All submissions should be submitted via Editorial Manager
- The following are required for your submission to be complete:
    - Anonymous manuscript (unless otherwise stated)
    - Author Agreement form
    - Manuscript
    - Ethics Approval form (for research articles)
    - Any supplementary files: figures, datasets, patient consent form, permissions for published images, etc.
    - Once the submission has been successfully processed on Editorial Manager, it will undergo a technical check by the Editorial Office before it will be assigned to an editor who will handle the review process. If the author guidelines have not been appropriately followed, the manuscript may be sent back to the author for correcting.

Peer Review Process

All manuscripts are reviewed initially by two of the editors and only those that meet the scientific and editorial standards of the journal, and fit within the aims and scope of the journal, will be sent for external peer review. Each manuscript is reviewed by two reviewers selected on the basis of their expertise in the field.

A double blind review process is followed at SAJCC. The time period of the entire review process may vary however depending upon the quality of the manuscript submitted, reviewers' responses and the time taken by the authors to submit the revised manuscript.

Manuscripts from review may be accepted, rejected or returned to the author for revision or resubmission for review. Authors will be directed to submit revised manuscripts within two months of receiving the editor's decision, and are requested to submit a point by point response to the reviewers' comments. Manuscripts which authors are requested to revise and resubmit will be sent for a second round of peer review, often to the original set of reviewers. All final decisions on a manuscript are at the Editor's discretion

Article Processing Charges

There is currently no article-processing charge (APC), also known as page fees, for the publication of manuscripts. The publication costs are supported by the Critical Care Society of Southern Africa and advertisements in the print version.

Please refer to the section on 'Sponsored Supplements' regarding the publication of supplements, where a charge is currently applicable.

Production process

The following process should usually take between 4 - 6 weeks:

1. An accepted manuscript is passed to a Managing Editor to assign to a copyeditor (CE).
2. The CE copyedits in Word, working on house style, format, spelling/grammar/punctuation, sense and consistency, and preparation for typesetting.
3. If the CE has an author queries, he/she will contact the corresponding author and send them the copyedited Word doc, asking them to solve the queries by means of track changes or comment boxes.
4. The authors are typically asked to respond within 1-3 days. Any comments/changes must be clearly indicated e.g. by means of track changes. Do not work in the original manuscript - work in the copyedited file sent to you and make your changes clear.
5. The CE will finalise the article and then it will be typeset.
6. Once typeset, the CE will send a PDF of the file to the authors to complete their final check, while simultaneously sending to the 2nd-eye proofreader.
7. The authors are typically asked to complete their final check and sign-off within 1-2 days. No major additional changes can be accommodated at this point.
8. The CE implements the authors' and proofreader's mark-ups, finalises the file, and prepares it for the upcoming issue.

Changing contact details or authorship

Please notify the Editorial Department of any contact detail changes, including email, to facilitate communication.

Errata and retractions

Errata

Should you become aware of an error or inaccuracy in yours or someone else's contribution after it has been published, please inform us as soon as possible via an email to publishing@hmpg.co.za,including the following details:

- Journal, volume and issue in which published
- Article title and authors
- Description of error and details of where it appears in the published article
- Full detail of proposed correction and rationale

We will investigate the issue and provide feedback. If appropriate, we will correct the web version immediately, and will publish an erratum in the next issue. All investigations will be conducted in accordance with guidelines provided by the Committee on Publication Ethics (COPE).

Retractions

Retraction of an article is the prerogative of either the original authors or the editorial team of HMPG. Should you wish to withdraw your article before publication, we need a signed statement from all the authors.

Should you wish to retract your published article, all authors have to agree in writing before publication of the retraction.

Send an email to publishing@hmpg.co.za, including the following details:

- Journal, volume and issue to which article was submitted/in which article was published
- Article title and authors
- Description of reason for withdrawal/retraction.

We will make a decision on a case-by-case basis upon review by the editorial committee in line with international best practices. Comprehensive feedback will be communicated with the authors with regard to the process. In case where there is any suspected fraud or professional misconduct, we will follow due process as recommended by the Committee on Publication Ethics (COPE), and in liaison with any relevant institutions.

When a retraction is published, it will be linked to the original article.

Indexing

Published articles are covered by the following major indexing services. As such articles published in the *SAJCC* are immediately available to all users of these databases, guaranteed a global and African audience:

- DOAJ
- AIM
- AJOL
- Scopus
- EBSCO
- EMBASE
- Crossref
- Sabinet
- Scielo

Sponsored supplements

Contact the editor for information on submitting ad hoc/commissioned supplements, including guidelines, conference/congress abstracts, Festschrifts, etc.

Submission Preparation Checklist

As part of the submission process, authors are required to check off their submission's compliance with all of the following items, and submissions may be returned to authors that do not adhere to these guidelines.

1. The submission has not been previously published, nor is it before another journal for consideration.
2. The text complies with the stylistic and bibliographic requirements in **Author Guidelines**.
3. The manuscript is in Microsoft Word format. The text is single-spaced, in 12-point Times New Roman font, and contains no unnecessary formatting.
4. Illustrations/figures are high resolution/quality (not compressed) and in an acceptable format (Jpeg). These must be submitted as 'supplementary files' (not in the manuscript).
5. For illustrations/figures or tables that have been published elsewhere, the author has obtained written consent to republication from the copyright holder.
6. Where possible, references are accompanied by a digital object identifier (DOI) and PubMed ID (PMID)/PubMed Central ID (PMCID).
7. An abstract has been included where applicable.
8. The research was approved by a Research Ethics Committee (if applicable)
9. Any conflict of interest (or competing interests) is indicated by the author(s).