Risk factors associated with unplanned ICU admissions following paediatric surgery: a systematic review

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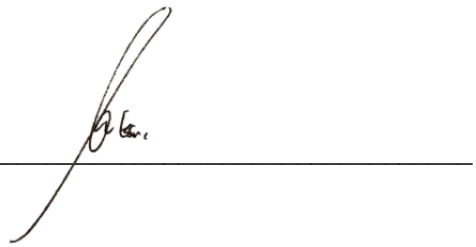
A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in the partial fulfilment of the requirements for the degree of Master of Medicine in the branch of Anaesthesiology.

Johannesburg, 2021

Declaration

I, Sameera Essa, herewith declare that this research report is my own, unaided work. It is being submitted for the degree of Master of Medicine at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.



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No publications or presentations to date

Abstract

Background

Unplanned admissions to the intensive care unit (ICU) have important implications in the general management of patients and result in unfavourable resource consequences. Research in this area has been conducted in the adult and non-surgical population. To date, there is no systematic review addressing the risk factors in the paediatric surgical population. Our aim was to synthesise the information from studies that explore the risk factors associated with unplanned ICU admissions following surgery in children.

Methods

We conducted a systematic review of published literature (PROSPERO registration CRD42020163766), adhering to the Preferred Reporting of Observational Studies and Meta-Analysis (PRISMA) statement. The Population, Exposure, Comparator, Outcome (PECO) strategy used was based on: population – paediatric population, exposure – risk factors, comparator – other, and outcome – unplanned ICU admission. Data that reported on unplanned ICU admissions following paediatric surgery were extracted and analysed. Quality of the studies was assessed using the Newcastle-Ottawa Scale.

Results

Six studies were included in the data synthesis. Three studies were of good quality with the Newcastle-Ottawa Scale score ≥ 7 points. The pooled prevalence (95% CI) estimates of unplanned ICU stay was 0.08 (0.01- 0.20) and ranged between 0 – 0.34%. General anaesthesia, together with endotracheal tube care and inappropriate intravenous fluid administration contributed to significant risk of unplanned ICU admission compared with other types of anaesthesia. Airway abnormalities were reported to be associated with risk of adverse outcome in three of the studies whereas systemic comorbid abnormalities were reported in four. Abdominal surgery and ear, nose and throat (ENT) surgery resulted in a significantly higher risk of unplanned ICU admission. Emergency surgery resulted in three times more likelihood of risk. Due to the heterogeneity of the data, a meta-analysis with risk prediction could not be performed.

Conclusion

Significant patient, surgical and anaesthetic risk factors associated with unplanned ICU admission in children following surgery have been identified in this study. A combination of these factors may direct planning toward anticipation of the need for a higher level of postoperative care. Some events which resulted in unplanned ICU admission were found to be predictable and preventable. Further work to develop a predictive score for unplanned ICU stay is desirable.

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LIST OF ABBREVIATIONS

ASA	American Society of Anaesthesiologists
DALYs	Disability-Adjusted Life Years
ENT	Ear, Nose and Throat
ICU	Intensive Care Unit
MeSH	Medical Subject Headings
MRI	Magnetic Resonance Imaging
PACU	Post-Anaesthesia Care Unit
PECO	Population, Exposure, Comparator, Outcomes
PELOD	Paediatric Logistic Organ Dysfunction
PICU	Paediatric Intensive Care Unit
PIM-2	Paediatric Index of Mortality-2
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analyses
USA	United States of America
WHO	World Health Organisation

Draft Article

Risk factors associated with unplanned ICU admissions following paediatric surgery: a systematic review

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Introduction

Unplanned admissions to the intensive care unit (ICU) have been acknowledged as a global marker of safety.[1] Awareness of this concept has encouraged research to determine the incidence and risk factors of these occurrences. This research has been interrogated in a systematic review process with beneficial conclusions drawn, however, these studies included adults and non-surgical patients.[2-4] To date, we have not been able to find a systematic review addressing the risk factors associated with unplanned ICU admissions in paediatric surgical patients.

Disease and trauma-related injuries in the paediatric surgical population have been well described,[5, 6] and if left untreated can contribute significantly to morbidity and mortality.[7] Despite this, many children have unmet needs[8, 9] although it is expected that with the Global Initiative for Emergency and Essential Surgical Care,[10] and the Global Surgery 2030 initiative,[11] there will be a gradual expansion of paediatric surgical services. To cope with the current and probable rise in patient load, efficiency by surgical and anaesthetic teams is becoming a crucial part of management.

Children require special care in the perioperative period due to their unique anatomy, physiology and the nature of disease they present with[12]- despite this knowledge, adverse events in the perioperative period do occur.[13, 14] Although they are not common, these events have far reaching effects: some of these patients may require a step up in care for monitoring, supportive or therapeutic purposes. This can result in an unexpected admission to the ICU, which has a physical impact on the child,[15] a psychological impact on the caregiver(s),[16] as well as repercussions on the medical staff, establishment and resources. Mortality and length of hospital stay are also two to three times higher in those who have adverse events warranting unscheduled ICU admissions.[17] In South Africa, a large prospective study was conducted looking at postoperative outcomes in paediatric patients.[14] In this study, 7.9% of patients were admitted to the ICU due to postoperative complications. Of these patients, 40.5% were unplanned.[14]

Identifying specific risk factors for ICU admissions post-surgery in the preoperative assessment of paediatric surgical patients will inform improved decision making by surgeons and anaesthetists. Understanding these factors allows for an improved awareness during perioperative decision making and parental counselling and consent. Resources can be efficiently allocated,[18] and high risk patients transferred to centres that have ICU availability and expertise. This is especially important in lower income settings where judicious use of resources is required.[19] We conducted a systematic review of published literature to synthesise the information from studies that explore the risk factors associated with unplanned ICU admissions following surgery in children.

Methods

Registration and reporting

This systematic review was registered with PROSPERO, registration CRD42020163766. A human research ethics committee waiver (W-CP-191108-2) from the University of the Witwatersrand was obtained. The protocol established adheres to the Preferred Reporting of Observational Studies and Meta-Analysis Protocols (PRISMA-P) statement.[20] A PRISMA flow diagram of the study is presented (Figure 1).

Database search

We conducted a search of the PubMed and Scopus medical databases. The PubMed search strategy is outlined in Table 1. The search was performed independently by two authors on the 17th of July 2020 (SE and PNM) and repeated on the 19th of July 2020, and included all papers to that date.

Our search strategy was based on the following PECO framework:

- Population: paediatric surgical patients
- Exposure: risk factors
- Comparator: other
- Outcome: unplanned ICU admission

The eligibility criteria were publications that reported on risk factors of unplanned ICU admission, cohort and case control studies, population including paediatric patients only (age

≤ 18 years). Ineligibility criteria were non-English studies, duplicate studies and studies with insufficient data that could not be obtained after communicating with authors.

Data collection

The search results were exported into Endnote, then transferred to Microsoft Excel for data management. Duplicates were removed from the spreadsheet. SE and PNM independently screened each abstract for eligibility according to the abovementioned inclusion and exclusion criteria. Where there was uncertainty about articles for inclusion, this was resolved with input from other reviewers (YM and PMC). Additionally, we performed a hand-search from the reference lists of eligible manuscripts to identify other relevant papers which might have been missed during the search of the PubMed and Scopus electronic databases.

Quality assessment

A full text review of eligible papers was done to assess study quality. This was assessed with the Newcastle-Ottawa Scale, the results of which are shown in Table 2. A score ≥ 7 points was used as a threshold to identify studies of good quality. All eligible studies were included in our final systematic review, irrespective of their quality assessment finding.

Data extraction

Data extracted from each study included geographical location, study design, sample size, whether single or multicentre, type of surgery and significant risk factors of unplanned ICU admission.

Data analysis

Descriptive statistical methods, specifically determining frequencies and percentages, and univariate analysis were used to establish the most common risk factors from all the eligible papers. No meta-analysis was performed due to the heterogeneity of the data, and it should be noted that there were varying definitions of an “unplanned ICU admission”.

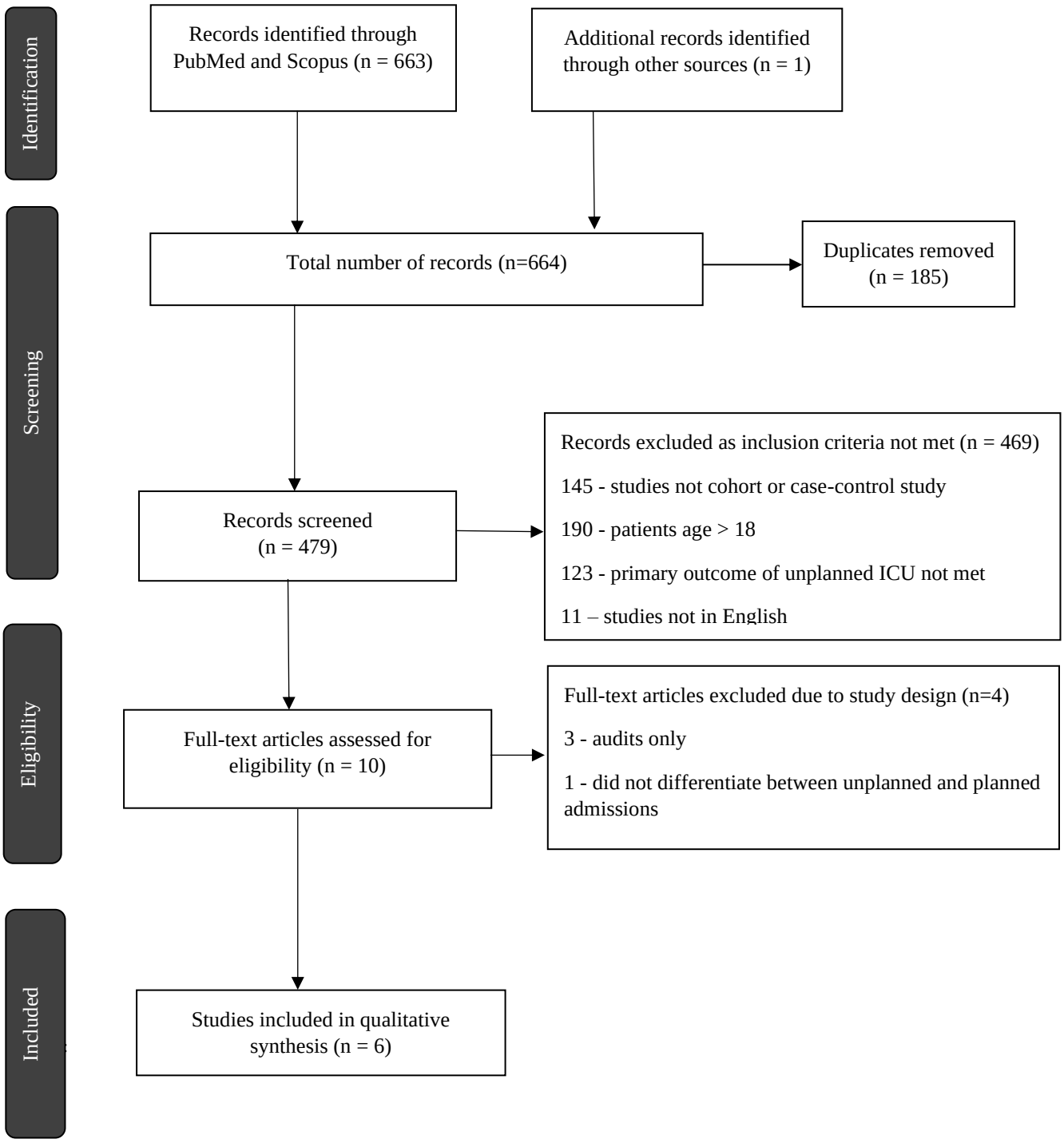

Figure 1: PRISMA Data Collection

Table 1: PubMed* Search Strategy

Query	MeSH term/Phrases
Population: Paediatric surgical patients	Paediatric* [Title/Abstract], Pediatrics [MeSH], Pediatric* [Title/Abstract], Child* [Title/Abstract], Child [MeSH], Infant* [Title/Abstract], Neonat* [Title/Abstract], Newborn* [Title/Abstract], Adolescen* [Title/Abstract] "following surgery" [Title/Abstract], Perioperative period [MeSH], Postoperative period [MeSH], Perioperative* [Title/Abstract], Postoperative* [Title/Abstract], "after surgery" [Title/Abstract], "after anaesthesia" [Title/Abstract], "after anesthesia" [Title/Abstract], "anaesthesia-related" [Title/Abstract], "anesthesia-related" [Title/Abstract], "post surgery" [Title/Abstract], surg* [Title/Abstract]
Exposure: Risk factors	"Risk factor*" [Title/Abstract], Risk factors [MeSH], Risk* [Title/Abstract], Hazard* [Title/Abstract], Odds [Title/Abstract], Morbidit* [Title/Abstract], Morbidity [MeSH], Complicat* [Title/Abstract], Complications [MeSH], Predict* [Title/Abstract], Likel* [Title/Abstract], Associat* [Title/Abstract], High* [Title/Abstract], Increas* [Title/Abstract], Factor* [Title/Abstract]
Outcome: Unplanned ICU admission	Unplanned [Title/Abstract], Unscheduled [Title/Abstract], Unintended [Title/Abstract], Unintentional [Title/Abstract], Incidental [Title/Abstract], Unexpected [Title/Abstract], Unbooked [Title/Abstract], Unanticipated [Title/Abstract] ICU [Title/Abstract], Intensive care unit [MeSH], "Intensive care" [Title/Abstract], "High dependency" [Title/Abstract], "Critical care" [Title/Abstract], "High care" [Title/Abstract], CCU [Title/Abstract], PICU [Title/Abstract], "Critical illness*" [Title/Abstract], Critical illness [MeSH], "Acute illness*" [Title/Abstract], "Acute disease*" [Title/Abstract], Acute disease [MeSH], "Catastrophic illness*" [Title/Abstract], Catastrophic illness [MeSH], "critical incident*" [Title/Abstract], "critical event*" [Title/Abstract]

* Scopus search was performed using the keywords from the [Title/Abstract] searches of the PubMed strategy

Results

The results of the literature search of PubMed and Scopus are illustrated in Figure 1. The search produced 663 papers, of which 185 were duplicates. After the title and abstracts were reviewed, nine full-text articles were included for review. The reasons for exclusion of 469 abstracts are depicted in the PRISMA flow diagram (Figure 1). Following screening of the reference lists of all full-text manuscripts, one potential paper was found that may have had relevance but was not included as the author did not respond with the requested full text after a month. Expert consultation was sought during the data collection process and attention was brought to an additional article of relevance.[21] This systematic review therefore includes six papers for analysis with a total of 327 492 patients.

Three studies were of good quality with a Newcastle-Ottawa Scale score of ≥7 points (Table 2).[21-23] The characteristics of the studies are shown in Table 3. Five of the six studies were from developed countries and were retrospective in nature.

Table 2: Newcastle-Ottawa Scale Quality Assessment Scores

Author (year)	Selection	Comparability	Outcome	Overall score	Good study quality?
Allen et al. (2020)	4	1	3	8	Yes
Arambula et al. (2018)	4	-	1	5	No
Da Silva et al. (2013)	3	1	2	6	No
Landry et al. (2017)	2	1	3	6	No
McHenry et al. (2019)	4	-	3	7	Yes
Tweedie et al. (2012)	3	1	3	7	Yes

Table 3: Characteristics of included studies

Author (year of publication)	Country	Study design	Total number of patients in study	Unplanned ICU group (n)	Number of sites	Selection bias	Surgery type
Allen et al. (2020)	USA	Retrospective cohort	338	24	Single centre	Y: Patients with known OSA or sleep disordered breathing	Adeno-tonsillectomy
Arambula et al. (2018)	USA	Retrospective cohort	133	7	Single centre	Y: Patients with known OSA or sleep disordered breathing	Adeno-tonsillectomy
Da Silva et al. (2013)	Brazil	Case-control	116	28	Single centre	Y: patients with TBI excluded	No exclusions
Landry et al. (2017)	USA	Retrospective cohort	324818	211	Multicentre	N	No exclusions
McHenry et al. (2019)	USA	Retrospective cohort	460	158	Single centre	Y: Trauma and weekend admissions not included	Urology, cardiac and orthopaedic procedures excluded
Tweedie et al. (2012)	UK	Retrospective cohort	1627	17	Single centre	N	Adeno-tonsillectomy

ICU, intensive care unit; USA, United States of America; UK, United Kingdom; OSA, obstructive sleep apnoea; TBI, traumatic brain injury; Y, Yes; N, No.

The prevalence of unplanned ICU admissions ranged from 0 – 0.34% with pooled prevalence (95%CI) estimates of 0.08 (0.01- 0.20) (Figure 2). There was significant heterogeneity in the analysis. Four studies reported a prevalence of below the pooled estimate whilst two were higher.

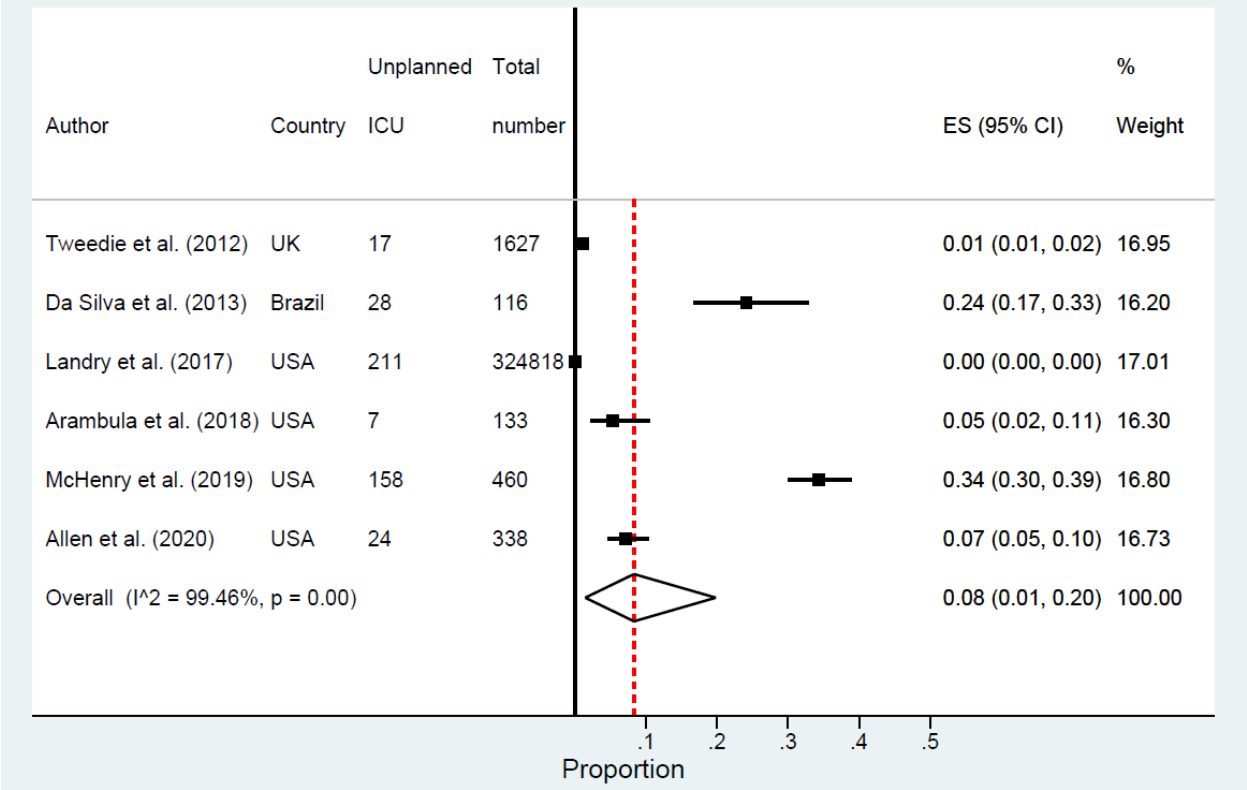

Figure 2: Prevalence of unplanned ICU admissions

Risk factors were derived from univariate analysis and categorised into unplanned ICU admissions compared to other which included: 1) no ICU admissions (adenotonsillectomy surgery), 2) planned ICU admissions or 3) a reference category. Furthermore, these were grouped as patient, anaesthetic and surgical factors.

Patient factors

Age less than one year was found to be a significant risk factor.[24] The presence of respiratory and airway abnormalities,[25] and abnormal sleep studies[22] were also seen as significant risk factors in unplanned ICU admissions (Table 5). The presence of comorbidities such as cerebral palsy and mucopolysaccharidosis[23] resulted in an increased likelihood of unplanned ICU admission.

Anaesthetic factors and other outcomes

Respiratory complications (pulmonary oedema, atelectasis and pneumonia), including the need for postoperative respiratory support in the form of supplemental oxygen or positive pressure, were significant reasons for unplanned ICU admission.[22] Patients who spent a longer time in the post-anaesthesia care unit (PACU), and who spent a longer time requiring supplemental oxygen in the PACU,[26] were more likely to undergo an unexpected escalation of care to ICU. Length of hospital stay was higher in the unplanned ICU cohort compared to those not admitted to ICU.[26] General anaesthesia[24, 25] and night shift cases[24] were also likely to have unplanned ICU admissions. Cases performed by an attending were more likely to be admitted to ICU unplanned.[24]

Surgical factors

Two studies found that general paediatric surgery including abdominal surgery, and ear, nose and throat (ENT) surgery resulted in a higher risk of unplanned ICU admission.[21, 25] Emergency surgery was almost three times more likely to result in unplanned ICU admission.[25] Events which resulted in unplanned ICU admission were found to be predictable and preventable and included issues related to endotracheal tube care and inappropriate intravenous fluid administration.[25]

Table 4: Risk factors associated with unplanned ICU admissions vs other

Author	Parameter	N (%)/Median (IQR)/ Means ± SD		UOR [95% CI]	p-value
		Unplanned ICU	Other		
Patient risk factors					
Allen et al.					
	OSA	12 (50)	46 (29)	2.39 [1.00 -5.71]	0.045
	Sleep study	12 (50)	46 (29)	2.39 [1.00 - 5.71]	0.045
	Hypoapneas	38 (40)	7 (21)	-	0.01
	RDI	12 (16)	6 (5)	-	0.03
	AHI	7 (18)	2 (3)	-	0.01
Tweedie et al.					
	Cerebral Palsy	3 (18)	50 (3)	6.58 [1.83- 23.64]	0.017
	MPS	2 (12)	20 (1)	10.44 [2.24 - 48.69]	0.022
Landry et al.					
	Age: under 1 year/13-18 years	71 (0.13)	52 (0.06)	2.25 [1.58 - 3.22]	<0.001
	ASA PS class: III / I-II	82 (0.18)	113 (0.04)	4.39 [3.3 - 5.83]	<0.001
	ASA PS class: IV / I-II	16 (0.17)	113 (0.04)	4.02 [2.38 - 6.79]	<0.001
Arambula et al.					
	Number of co-morbidities	2.1±1.4	0.9±1.1	-	0.007
	Pre-operative AHI	6.1±4.8	19.4±17.5	-	0.056
Da Silva et al.					
	Respiratory tract/airway abnormality	8 (29)	6 (7)	5.48 [1.70 - 17.54]	0.006
McHenry et al.					
	PELOD score	10 (0-11)	1 (0-10)	-	<0.01
	Presence of disability (VPSDis)	-	-	3.67	0.011
Anaesthetic risk factors and other outcomes					
Arambula et al.					
	Total PACU time on O2 (min)	176.2±133.5	43.0±57.5	-	<0.0005
	Total PACU time on O2 (%)	76.8±38.6	30.1±29.3	-	0.0001
	Total PACU time (min)	225.3±121.3	144.5±119.9	-	0.088
	Length of hospital admission (days)	4.7±2.8	1.3± 1.4	-	<0.0005
	Days requiring supplemental O_2	3.5±2.7	1.2±1.9	-	0.009
	% days requiring O_2	63.1±34.7	32.9±29.4	-	0.025
Allen et al.					
	Respiratory support	21 (88)	12 (8)	84 [21.88 - 322.55]	<0.0005
	Complications	15 (63)	12 (8)	20 [7.25 -55.17]	<0.0005
da Silva et al.					
	General anaesthetic	27 (96)	64 (73)	10.13 [1.30 - 78.68]	0.016
	SaO_2<90% at any time	10 (36)	8 (9)	5.56 [1.92 - 16.05]	0.002
	VCCAMM 1-3	24 (86)	24 (27)	16 [5.03 - 50.93]	<0.0001
	VCCAMM 4-5	17 (61)	19 (22)	5.61 [2.25 - 13.98]	0.0002
	Predictable adverse events	10 (36)	13 (15)	3.20 [1.21 - 8.47]	0.031
	Preventable adverse events	8 (29)	8 (9)	4 [1.34 - 11.97]	0.022
	Mechanical vent + hemodynamic instability	9 (32)	10 (11)	3.70 [1.32 - 10.36]	0.017
	Length of mechanical vent (days)	4.5 (3.75 - 9.5)	2 (0.82 - 5)	-	0.01
Landry et al.					
	Other anaesthetic / general anaesthetic	22 (0.03)	189 (0.07)	0.46 [0.3 - 0.71]	<0.001
	Attending anaesthetist present / not present	79 (0.05)	132 (0.08)	0.44 [0.23 - 0.83]	0.012
	Weekend cases/weekday cases	14 (0.04)	197 (0.07)	0.54 [0.31 -0.93]	0.026
	After hours shift / day shift	106 (0.11)	105 (0.05)	2.38 [1.82 - 3.12]	<0.001
McHenry et al.					
	PIM-2 score	0.4 (0.17-1.1)	0.14 (0.12-0.17)	-	<0.01
Surgical risk factors					
Da Silva et al.					
	Abdominal procedure	15 (54)	27 (31)	2.61 [1.09 - 6.22]	0.048
	Emergency surgery	12 (43)	18 (20)	2.92 [1.17 - 7.25]	0.034
McHenry et al.					
	ENT	-	-	1.15	<0.0001
	General paediatric surgery	-	-	2.19	<0.0001
Landry et al.					
	Case duration: 61-180 mins/<60 mins	73 (0.06)	17 (0.02)	3.93 [3.3 - 5.83]	<0.001

	Case duration: >180 mins/<60 mins	30 (0.12)	17 (0.02)	7.37 [4.06 - 13.36]	<0.001

ICU, intensive care unit; OSA, obstructive sleep apnoea; CI, confidence interval; IQR, interquartile range; SD, standard deviation; UOR, unadjusted odds ratio; RDI, respiratory disturbance index; AHI, apnoea-hypopnoea index; MPS, mucopolysaccharidosis; ASA PS, American Society of Anaesthesiologists physical status; PELOD, Paediatric Logistic Organ Dysfunction; VPSDis, Virtual PICU Systems disability score; min, minutes PACU, post-anaesthetic care unit; vent, ventilation; VCCAMM, The Victorian Consultative Council on Anaesthetic Mortality and Morbidity; PIM-2, Paediatric Index of Mortality Score-2; ENT, ear, nose and throat.

Two studies demonstrated that patients required mechanical ventilation and spent a longer time on oxygen compared to the planned ICU group.[25, 26] Cases longer than 60 minutes, and those involving the head, upper abdomen and radiologic procedures were significant risk factors in this group.[24]

Discussion

In this study, the prevalence of unplanned ICU admission was below 1%. Risk factors associated with unplanned ICU stay were found to be patient, surgical and anaesthetic related. Significant patient, surgical and anaesthetic risk factors associated with unplanned ICU admission reflect similar risk factors of perioperative respiratory adverse events and postoperative respiratory complications.[13, 27] This systematic review finds that age less than a year and the presence of disability resulted in a significant risk of unplanned ICU admission.[21, 24, 26]

An association between risk scores and unplanned ICU admissions was found with a higher Paediatric Index of Mortality 2 (PIM-2) score, American Society of Anaesthesiologists (ASA) status (III-IV) and Paediatric Logistic Organ Dysfunction (PELOD) score having a strong association.[21, 24] While a higher ASA status by definition suggests organ dysfunction and functional limitation, this tool may be less reliable in paediatrics.[28] The PIM-2 score constitutes a variety of variables of clinical, biochemical and other factors: it is difficult to know which variables had a greater bearing on the scores found to be significant. The PELOD score consists of 10 variables representing severity of five organ systems function (respiratory, cardiovascular,

renal, neurologic and haematological) and is validated for use in the ICU setting to indicate disease severity and predict mortality.[29]

Postoperative pulmonary complications have been well described and defined in adults, but this is lacking in the paediatric population.[27] Risk scores in adults highlight the strong association between upper abdominal surgery and a higher risk of postoperative pulmonary complications.[30] Abdominal procedures alone can cause fluid and blood loss, electrolyte disturbances which may have been present preoperatively, hypothermia and postoperative respiratory complications.[31] Poorly managed pain, which is not an uncommon occurrence in paediatrics,[32] can also result in splinting and worsen postoperative respiratory function. Da Silva et al. found that inappropriate fluid management in the emergency abdominal procedures was one of the reasons for a preventable event.[25] An increased length of surgery more than 60 minutes was found to be significant, and can relate to technical difficulties of the surgery itself, and the required increased complexity of the anaesthetic.[24]

General anaesthesia compared to monitored anaesthesia care, neuraxial or regional anaesthesia, carried a higher risk of unplanned admissions.[24, 25] Perioperative respiratory events are higher under general anaesthesia,[13] and can be due to the effects of airway manipulation, invasive ventilation, atelectasis and the effects of neuromuscular blocking agents and opioids on the respiratory system. Intraoperative hypoxia was also found to be a significant contributor to unplanned ICU admission.[25] This is a reflection of respiratory events ranging from atelectasis to more serious issues such as broncho- or laryngospasm, pulmonary oedema and aspiration. Causes of hypoxia observed were bronchial aspiration, pulmonary oedema, respiratory depression, difficult intubation, accidental extubation and endotracheal tube obstruction.[25]

Radiologic procedures were also important risk factors for unplanned ICU admissions, specifically Magnetic Resonance Imaging (MRI) of the brain.[24] Patients presenting for MRI may have significant pathology or systemic disease warranting the need for special investigation (e.g., tumours, cerebral palsy, uncontrolled seizures)[33] and coupled with the added difficulty of practice in a remote anaesthesia setting, this may lead to unanticipated complications. These patients are often treated on an outpatient basis.

A longer time in the PACU post tonsillectomy, mostly due to desaturation and requiring supplemental oxygen, was found to be significant and would indicate the potential need for an escalated level of care.[26] This finding may also direct consideration toward introducing more high care units which carry less of a resource burden than an ICU bed. At risk patients who only require closer monitoring and simple therapies rather than invasive organ support could be managed in this setting for a certain period of time and would subvert the need for ICU care.

Patients who required unplanned ICU admission postoperatively were found to need respiratory support in the form of supplemental oxygen or mechanical ventilation.[25, 26] This is in keeping with the fact that the reason for ICU admission was commonly respiratory related. Length of stay in hospital and duration of mechanical ventilation or oxygen requirement was longer even when compared with the planned ICU groups.[25, 26] Only two studies[23, 25] reported mortality outcomes of which there were none in the unplanned ICU group.

Unanticipated ICU admissions were also higher on weekdays as opposed to weekends.[24] This could be explained by the fact that elective surgery and complicated cases usually will occur in the week when specialist expertise is readily available. It may also be due to the fact that children presenting for emergency cases would be physiologically unwell and ICU would have been pre-empted; the volume of cases over the weekend would also be expected to be much lower than

during the week as noted by Landry et al.[24] This finding may be vastly different in low- and middle income countries where the pressure of emergencies is higher due to the burden of injuries[34] and delayed presentation of disease.[35] This is suggested by the South African Paediatric Surgical Outcomes Study (SAPSOS), which found that important risk factors of postoperative complications included urgency of surgery and an infective indication for surgery[14]: this possibly highlights the impact of delayed presentation of disease on postoperative outcome.

Landry et al. examined a range of facility types in all regions of the United States of America (USA), and were able to make resource comparisons.[24] Cases in the Midwest carried an increased risk of unplanned ICU admissions: the possible explanation was that they are more resource conservative regarding the use of ICU.[24] If this is the case, it can be extrapolated that unplanned ICU admissions may be increased in countries where resources are constrained and ICU bed availability is limited thus leading to cases being performed without a confirmed ICU booking. However, more research is required in this area.

Numerous scoring systems have been created and adapted over the years,[36] with the aim of assisting practice through perioperative risk stratification. While risk scores have been developed to predict paediatric mortality[37] and increased perioperative risk,[38] no formal model exists to anticipate the specific need of critical care services in the postoperative period. While there is not enough evidence from this review to establish a scoring system for escalated care in paediatric surgical patients, the knowledge of the identified risk factors can nevertheless guide decision making in the perioperative period. Rather than using the risk factors of unplanned ICU admissions individually, a combination of these factors may direct planning toward anticipation of the need for a higher level of postoperative care. Future research into this topic will also be assisted through efficient data collection based on these factors.

Limitations

Our systematic review had some limitations. Due to the paucity of papers found and the heterogeneity of the data, we could not proceed to a meta-analysis. The final articles included for review were all retrospective and had vastly varying methodologies. The studies had diverse selection criteria of cohorts and comparisons, differing definitions of an unplanned ICU admission, and different data extracted as considered relevant. This made it difficult to make suitable comparisons and broad conclusions for this research question. While some studies were large[24] and of good quality data and analysis,[21-23] it is difficult to fully extrapolate the findings to a global context given that influences of varying health care settings may impact findings much differently.

Conclusion

Identifying the risk factors associated with unplanned ICU admissions has given us more insight into which patients will require more attention, preparation and advanced care. While at risk patients should not be overlooked, unnecessary admission to an ICU can also be harmful and the two ends of the spectrum need to be balanced. In countries where patient load is high and where resources don't meet this demand, theatre efficiency is always optimised by better planning. While this study has identified significant patient, surgical and anaesthetic risk factors associated with unplanned ICU admission in children, further studies will be required to afford development of a risk stratification tool in the future.

Conflict of interest

The authors declare no conflict of interest.

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Ethics approval

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Appendix 1: Proposal

Risk factors associated with unplanned ICU admissions following paediatric surgery: a systematic review

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1. Introduction

Over two hundred million people worldwide undergo surgery yearly, with almost seven million of these cases resulting in significant complications which contribute to morbidity and mortality.[1] When looking at the burden of disease in the paediatric population, some of the top ten causes of disability-adjusted life years (DALYs) include neonatal disorders, congenital birth defects and road injuries.[2] Low and middle income countries tend to have a higher incidence of trauma-related admissions compared to high income countries where congenital defects contribute to the majority of admissions.[3] Although there is a lack of comprehensive data in Africa, in The Gambia and Somaliland the most common surgical conditions found were trauma-related, congenital anomalies or surgical infection.[4-7] Globally, congenital anomalies represent a substantial part of the burden of disease,[8, 9] and in South Africa the incidence is as high as developed and other developing countries.[10] Consequently, children often present for either lifesaving or preventative reasons for surgery, and these will require management by anaesthesia.

Despite a prevalence of paediatric surgical conditions of up to 12.2%,[4, 5] there is a significant proportion of children who have surgical needs that are not met due to lack of surgical access and expertise.[11, 12] This can contribute substantially to DALYs due to the resultant chronic disability.[13] The identification of this gap in required paediatric surgical services has prompted a move to addressing this need.[14-16] This can be achieved as essential surgical procedures have been found to be cost effective in poorly resourced countries.[15] In 2005, the World Health Organisation (WHO) launched the Global Initiative for Emergency and Essential Surgical Care.[14, 16] Part of the mandate is to develop systems and resources, and to expand the surgical, obstetric and anaesthesia health workforce.[14, 16] A Lancet report, Global Surgery 2030, likewise aims to improve access, surgical volume and surgical workforce.[15] While the current burden of paediatric surgical conditions has been acknowledged, the unmet need of surgical care being addressed as a public health issue has a further implication that many more children will present for surgery in the coming years.

Managing children presenting for surgery poses a myriad of considerations for the anaesthetist and is not without risk. Studies worldwide have examined the incidence and factors associated with perioperative adverse events in children, with varying results.[17-21] Advances in anaesthetic practice and monitoring have mostly resulted in a decline in perioperative mortality.[22, 23] Despite this, the incidence of critical events in children is up to 8%.[17, 18, 24] A study done in 2017 demonstrates a critical incident rate of 5.2% in Europe.[19] This rate is substantially higher in low income countries at up to 14.8%.[20] In South Africa, a large prospective study was conducted looking at postoperative outcomes in paediatric patients.[21] In this study, 7.9% of patients were admitted to the intensive care unit (ICU) due to postoperative complications. Of these patients, 40.5% were unplanned.[21] Therefore, during the management of critical events and postoperative complications, ICU admission may be warranted for monitoring or supportive reasons.

When a patient has an adverse event that requires a sudden step up in postoperative care, the consequences can be far reaching. On an administrative level, unexpected admissions to the ICU have costly implications due to a shift in allocated resources to deal with the unanticipated event and its sequelae.[25] The role of an intensive care unit is specific and controlled, due to it being a costly and scarce resource.[26] An ICU needs to have sufficient space, equipment, monitoring devices, specially trained staff and other human resources.[27] As a result, bed allocation must be "rationed".[26] In South Africa, the cost of an ICU stay per patient per day is estimated at R22 870, with the highest cost allocation to human resources followed by direct "patient activity" costs.[28] The difficulties that these critical incidents create can cause a significant financial burden especially in environments where resources are already constrained.

Admission to the ICU has an important impact on patient outcome. The mortality of patients admitted to the paediatric ICU (PICU) is estimated at around 2% in developed countries[29-31] and up to 13% in low and middle income countries.[32, 33] In Africa, the mortality rate is found to be considerably high, ranging from 25-50%.[34-37] In a study in Nigeria, mortality in postoperative

patients was found to be significantly elevated.[34] Morbidity is another key outcome and is generally found to be higher than mortality rates.[38, 39] This is a reflection of improvements in reducing mortality over the years, but with the added concern of patients surviving with a poorer functional status. This is not always static and can worsen over years. Pinto et al.[39] noted that the worsening in functional status was twice as much after three years. Another repercussion of ICU admission is the social and psychological effects of this stay on the parents or caregivers, some of which can be long term.[40-45]

On a background of a global goal to reduce childhood mortality,[46] it is imperative that those involved in the management of children continue to attempt improving the care of this population. The WHO has initiated another worldwide challenge called the Second Global Patient Safety Challenge: Safe Surgery Saves Lives.[47] It was agreed upon by experts that as part of this challenge, four aspects of surgical care should be improved upon, one of which is the practice of safe anaesthesia.[47] Unplanned ICU admissions have been acknowledged as a global marker of safety in patients undergoing surgery.[48] In Australia, Haller et al.[48] investigated the use of unplanned ICU admissions as a tool to infer preventable anaesthetic or surgical complications. Of the unplanned admissions in this study, 87 to 92% sustained an anaesthetic or surgical complication. Preventability was also assessed and it was found that preoperative assessment and thus intraoperative management was inadequate in 24-27% of cases. After extensive review of the eligible cases, it was then concluded that using unscheduled ICU admissions is a useful way of determining safe care of surgical patients.[48] Another similar study was conducted in Australia but looked at 30-day mortality and length of hospital stay.[49] It was found that mortality and length of hospital stay were two to three times higher in those who had adverse events warranting unscheduled ICU admissions.[49]

This concept of unplanned ICU admissions being a global indicator of safety[48] has been a motivator by establishments around the world to audit and review these cases. Many studies have

been conducted with varying methodologies, with the main outcome being the identification of the predominating risk factors leading to these ICU admissions.[25, 50-55] An unplanned ICU admission as defined by these studies vary. In a study by Downey et al.,[50] an admission was regarded as "booked" if the ICU bed was requested before the case commenced in theatre. Other studies defined an unscheduled ICU admission as occurring within 24 hours of the end of a surgical procedure in a case where the bed was not booked preoperatively.[52, 54] Gibson et al.[51] extended this cutoff period to up to 48 hours postoperatively as it was found that the surgical start time was recorded more reliably than the end time. The preoperative time within which an unplanned ICU admission was defined was also specified by Gibson et al.[51] as being requested less than 24 hours preoperatively. An audit was conducted in Australia from 1993 to 1995 which aimed to detect predictability and preventability of unplanned ICU admissions.[50] Of these patients, 20% had preventable reasons for the complications that occurred. A larger retrospective audit was conducted by Kurowski et al.[52] looking at the unplanned ICU admissions from 1998 to 2003. In this study, only anaesthetic related causes were included for analysis. The most common reasons for ICU admission were airway problems (47%), followed by respiratory (29%) and cardiovascular complications (20%). Patient factors that demonstrated greater risk were young age, showing that 68% of patients were under the age of 5 and 34% were aged less than a year. Another risk factor was the presence of one or more comorbidities (88%). The top three comorbidities were the presence of congenital heart disease, obstructive sleep apnea and intercurrent respiratory or viral infection.[52] Gibson et al.[51] included surgical as well as anaesthetic related causes for unscheduled admissions. Findings were similar to the studies in Australia where airway[52] and respiratory[50, 52] problems were the most common risk factors of anaesthetic related complications. Of the admissions caused by airway problems in the study by Gibson et al.,[51] 48% occurred following a procedure involving the upper airway. In Brazil, it was noted that factors contributing the most to unplanned ICU admissions were airway abnormalities, anaesthetic factors and intraoperative hypoxia.[25]

Although these studies on unplanned ICU admissions have differing definitions, exclusion and inclusion criteria, the results do demonstrate a pattern of risk.[25, 50-55] Circumstances around the cases were discussed including variables such as elective versus emergency surgery and where the decision to transfer patients to ICU was made. Some studies deliberated preventability and/or predictability of these events as well.[25, 50, 52] Analysing these may have benefit in determining where gaps exist in perioperative management of these patients.

The value of perioperative risk stratification has been well recognised, with numerous scoring systems created and adapted over the years.[56, 57] While risk scores have been developed to predict paediatric mortality,[58-60] no formal model exists to anticipate adverse events serious enough to require the use of critical care services specifically. The ICU is a scarce resource and needs to be managed appropriately. Clear policies need to be constructed to assist practitioners in the allocation of this resource.[61] Evaluation of critical care services demonstrates that in low income countries there is a shortage of ICU beds.[36, 62-64] ICU beds are mostly situated in large referral hospitals in urban areas.[62] A national audit conducted in South Africa similarly revealed that critical care services were mostly available in three provinces (out of nine), in predominantly level 3 hospitals.[63] It was also observed that high care units were used more as a step-down facility which increased the burden on the ICU service, and that there was a major lack of dedicated paediatric and neonatal units. The implementation of research that will assist in rationalising how and why ICU services are needed, would encourage health care managers to reconsider the distribution of this resource.[61]

Previous systematic reviews have investigated the risk factors associated with unplanned ICU admissions, but these studies included adults and non-surgical patients.[65, 66] Paediatric patients on their own present further challenges due to their unique anatomy, physiology and conditions they present with, and those requiring surgery pose further difficulties for various reasons.[67] Children have anatomical features of their respiratory system which reduce their reserves and predispose

them to hypoxia. They have a higher incidence of respiratory tract infections which also increases their risk of respiratory complications. Airway management is also challenging due to narrower airways.[67] Due to decreased circulating blood volume relative to adults, even seemingly minimal blood loss can start to impair haemodynamics much sooner. For these reasons, among many others, the paediatric population requires very careful anaesthetic planning and management.

The population of children admitted unexpectedly postoperatively can provide valuable information on the safety of each step and mode of care perioperatively. By evaluating the patient, surgical and anaesthetic factors involved in these unplanned ICU admissions, a picture of recurring risk can be constructed. Practitioners managing paediatric surgical patients can provide better care by optimising anaesthetic planning. This includes the selection of an appropriate postoperative destination, as well as improving family counselling. The evidence can also potentially be used in creating risk stratifying models and encourage health care managers to allocate and expand resources where necessary.

2. Problem statement

Literature on this topic reveals that there are numerous studies looking at the incidence and risk factors associated with unplanned ICU admissions following surgery in the paediatric population.[25, 50-55] A systematic review is a transparent method of systematically searching the literature for relevant articles, and providing a detailed analysis and synthesis of the information found.[68] While systematic reviews have been conducted on unscheduled ICU admissions in adults, there is no systematic review to elucidate the risk factors in paediatrics. This research proposes to close this gap and provide a constructive analysis of the published evidence. By guiding clinical decision making through risk stratification and enhancing the process of family preparation and counselling, perioperative management of paediatric surgical patients can be improved.

3. Aim

The aim of this research is to investigate the risk factors associated with unplanned ICU admissions following paediatric surgery by way of a systematic review of the published literature.

4. Objectives

1. To identify and describe the patient, surgical and anaesthetic risk factors associated with unplanned ICU admissions following surgery in the paediatric population
2. To describe the circumstances of these unplanned ICU admissions

5. Research question

1. What are the risk factors associated with unplanned ICU admissions in the paediatric population following surgery?

2. What are the intra- or postoperative circumstances leading to these admissions?

3. What type of support was required by these patients?

4. What was the final outcome?

6. Data collection

6.1 Research design

This research will be in the form of a systematic review with/without meta-analysis, based on the number of articles included in the review after the literature search has been done, as well as heterogeneity statistics. A systematic review as defined by Cochrane[69] is "a review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically

appraise relevant research, and to collect and analyse data from the studies that are included in the review. Statistical methods (meta-analysis) may or may not be used to analyse and summarise the results of the included studies."

6.2 Study population

The study population will include paediatric patients undergoing surgery, under the age of 18, who are admitted to ICU unexpectedly postoperatively.

6.3 Collection of data

6.3.1 Search strategy and study selection

The electronic medical databases that will be used for the systematic search are PubMed and Scopus. Articles will then be screened according to relevant inclusion and exclusion criteria, as specified below. Of the articles chosen, the reference lists of these will also be screened to identify any other relevant articles missed in the formal search. The major medical subject headings (MeSH terms) and important keywords that will be used to conduct the initial basic search are tabled in Appendix 1 and 2. Studies included will include description of unplanned ICU admission post-surgery.

6.3.2 Data extraction and quality assessment

The process of data extraction is summarised in Appendix 3. The titles and abstracts of articles obtained from the searches will be independently screened for eligibility by two reviewers. Disputes will be resolved by a deciding vote from a third independent reviewer where this may be necessary. Published peer-reviewed articles will be included. Authors of studies with unclear or incomplete data will be contacted and detailed data requested. Studies where complete data

could not be found after an attempt to contact authors will be excluded. This study will be conducted in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews.[70]

Standardised data extraction and quality assessment sheets will be used to collect data from each eligible manuscript. The data extraction sheets, which will be in an Excel spreadsheet format, will be used to collect the following information: main author and date, country of study, type of hospital, sample size, type of surgery, age and gender statistics (see Table 1). Information related to risk factors associated with the primary outcome will be extracted. Study quality will also be assessed using the Newcastle-Ottawa Scale (Appendix 4).

Table 1: Characteristics of enrolled studies

1st author, year (ref)	Sample size	Age	Male (%)	Incidence (%)	Surgery type	Reason for admission	ICU outcome	Identified risk factor(s)
							Total sample size	

6.3.3 Inclusion and exclusion criteria

Using the search strategy specified below, articles will be found on the medical databases. These will then be screened according to inclusion and exclusion criteria.

Inclusion criteria:

- Cohort and case-control studies
- Population will include paediatrics only, i.e. those under the age of 18
- Unplanned admission to the intensive care unit is the primary study outcome

Exclusion criteria:

- Non-English literature studies
- Duplicate studies

7. Data analysis

Descriptive statistics will be used to determine the most commonly reported risk factors amongst articles included in the review. We will investigate the suitability of proceeding to a meta-analysis once the final list of eligible articles has been obtained. If there are sufficient numbers of eligible articles, the extracted data will be analysed using appropriate meta-analysis statistical functions in a statistical software program. A random effects statistical model will be used to analyse the data. Odds ratios for risk factors will be computed and a pooled estimate of risk will be presented in the form of a Forest Plot. The I-squared value (measure of heterogeneity or variability between studies/papers) will be taken into account when deciding whether to include the results from the meta-analysis in the final report. As a rule of thumb, an I-squared value of <40% is considered a sign of low heterogeneity. Meta-analyses with higher levels of heterogeneity are generally not included in a systematic review report, as these results are often deemed unreliable.

8. Project outline

Activity	Sep 2019	Oct 2019	Nov 2019	Dec 2019	Jan 2020	Feb 2020	Jun 2020	Jul 2020	Oct 2020	Nov 2020
Proposal preparation										
Literature review										
Proposal submission										
Ethics approval										
Postgraduate approval										
Data collection										
Data analysis										
Draft article										
Submission										

9. Study limitations

1. The study will not include data/findings from the grey literature. This decision was related to concerns around the strength of the peer-review process in the grey literature, as well as the amount of data which could potentially be extracted from conference abstracts.

2. Only English articles will be included in the study.

10. Financial plan

The Department of Anaesthesiology will bear the cost of printing and paper for the postgraduate approval.

Item	Price per page	Number of pages	Copies	Total
Proposal	1	25	8	200
Ethics	1	4	2	8
Postgraduate form	1	2	6	12
Complete report	1	100	4	400
Grand total				**R620**

10. Ethical considerations

As this is a pure systematic review of literature, there is no patient involvement and no potential harm to patients. A request will thus be made to waiver the full ethics process.

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Appendix 1: PubMed Search Strategy

Population

#1	Search term/s	And
	Paediatric* (title/abstract)	"following surgery" (title/abstract)
or	Pediatrics (MesH)	Perioperative period (MesH)
or	Pediatric* (title/abstract)	Perioperative* (title/abstract)
or	Child* (title/abstract)	Postoperative* (title/abstract)
or	Child (MesH)	Postoperative period (MesH)
or	Infant* (title/abstract)	"after surgery" (title/abstract)
or	Neonat* (title/abstract)	"after anaesthesia" (title/abstract)
or	Newborn* (title/abstract)	"after anesthesia" (title/abstract)
or	Adolescen* (title/abstract)	"anesthesia-related" (title/abstract)
or		"anaesthesia-related" (title/abstract)
or		"post surgery" (title/abstract)
or		surg* (title/abstract)

Exposure

#2	Search term/s
	"Risk factor*" (title/abstract)
or	Risk factors (MeSH)
or	Risk* (title/abstract)
or	Hazard* (title/abstract)
or	Odds (title/abstract)
or	Predict* (title/abstract)
or	Likel* (title/abstract)
or	Associat* (title/abstract)
or	High* (title/abstract)
or	Increas* (title/abstract)
or	Factor* (title/abstract)

Control

Not applicable for observational studies

Outcome

#3	Search term/s	And
	ICU (title/abstract)	Unplanned
or	Intensive care unit (MeSH)	Unscheduled
or	“Intensive care” (title/abstract)	Unintended
or	“High dependency” (title/abstract)	Unintentional
or	“Critical care” (title/abstract)	Incidental
or	“High care” (title/abstract)	Unexpected
or	CCU (title/abstract)	Unbooked
or	PICU (title/abstract)	Unanticipated
or	“Critical illness*” (title/abstract)	
or	Critical illness (MeSH)	
or	“Acute illness*” (title/abstract)	
or	“Acute disease*” (title/abstract)	
or	Acute disease (MeSH)	
or	“Catastrophic illness*” (title/abstract)	
or	Catastrophic illness (MeSH)	
or	“critical incident*”	
or	“critical event*”	
or	Morbidit* (title/abstract)	
or	Morbidity (MeSH)	
or	Complicat* (title/abstract)	
or	Complications (MeSH)	

Appendix 2: Scopus search strategy

Population

#1	Search term/s	And
	Paediatric*	"following surgery"
or	Pediatric*	"Perioperative period"
or	Child*	Perioperative*
or	Infant*	Postoperative*
or	Neonat*	"Postoperative period"
or	Newborn*	"after surgery"
or	Adolescen*	"after anaesthesia"
or		"after anesthesia"
or		"anesthesia-related"
or		"anaesthesia-related"
or		"post surgery"
or		surg*

Exposure

#2	Search term/s
	"Risk factor*"
or	Risk*
or	Hazard*
or	Odds
or	Predict*
or	Likel*
or	Associat*
or	High*
or	Increas*
or	Factor*

Control

Not applicable for observational studies

Outcome

#3	Search term/s	And
	ICU	Unplanned
or	“Intensive care unit”	Unscheduled
or	“Intensive care”	Unintended
or	“High dependency”	Unintentional
or	“Critical care”	Incidental
or	“High care”	Unexpected
or	CCU	Unbooked
or	PICU	Unanticipated
or	“Critical illness*”	
or	“Acute illness*”	
or	“Acute disease*”	
or	“Catastrophic illness*”	
or	“critical incident*”	
or	“critical event*”	
or	Morbidit*	
or	Complicat*	

Appendix 3: PRISMA data collection

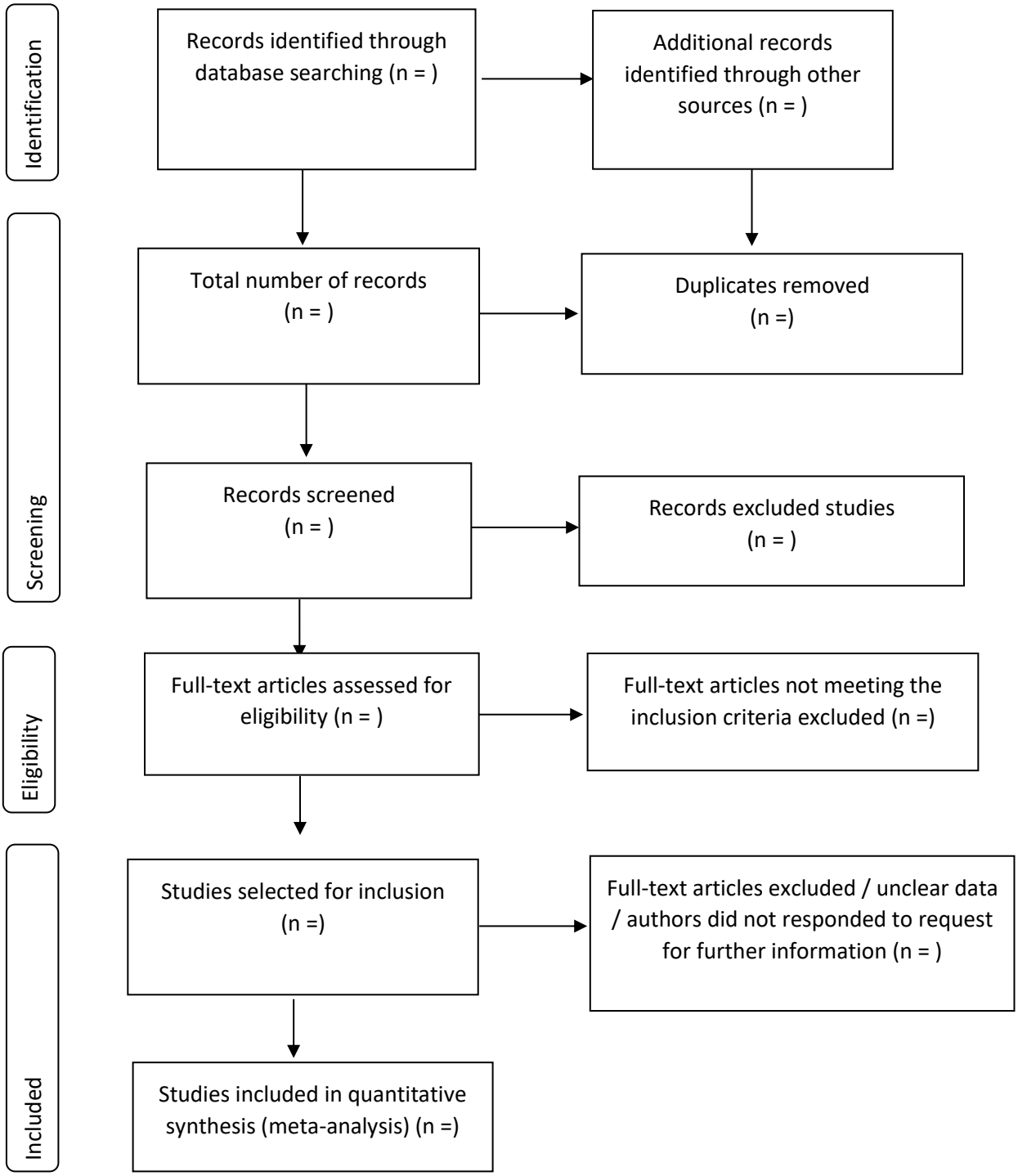


Figure 1: PRISMA 2009 flow diagram

Appendix 4:

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE
CASE CONTROL STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

Selection

1) Is the case definition adequate?
   a) yes, with independent validation ✵
   b) yes, eg record linkage or based on self reports
   c) no description

2) Representativeness of the cases
   a) consecutive or obviously representative series of cases ✵
   b) potential for selection biases or not stated

3) Selection of Controls
   a) community controls ✵
   b) hospital controls
   c) no description

4) Definition of Controls
   a) no history of disease (endpoint) ✵
   b) no description of source

Comparability

1) Comparability of cases and controls on the basis of the design or analysis
   a) study controls for _____ (Select the most important factor.) ✵
   b) study controls for any additional factor ✵ (This criteria could be modified to indicate specific control for a second important factor.)

Exposure

1) Ascertainment of exposure
   a) secure record (eg surgical records) ✵
   b) structured interview where blind to case/control status ✵
   c) interview not blinded to case/control status
   d) written self report or medical record only
   e) no description

2) Same method of ascertainment for cases and controls
   a) yes ✵
   b) no

3) Non-Response rate
   a) same rate for both groups ✵
   b) non respondents described
   c) rate different and no designation

NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE
COHORT STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

Selection

1) Representativeness of the exposed cohort
   a) truly representative of the average _____ (describe) in the community ✵
   b) somewhat representative of the average _____ in the community ✵
   c) selected group of users eg nurses, volunteers
   d) no description of the derivation of the cohort

2) Selection of the non exposed cohort
   a) drawn from the same community as the exposed cohort ✵
   b) drawn from a different source
   c) no description of the derivation of the non exposed cohort

3) Ascertainment of exposure
   a) secure record (eg surgical records) ✵
   b) structured interview ✵
   c) written self report
   d) no description

4) Demonstration that outcome of interest was not present at start of study
   a) yes ✵
   b) no

Comparability

1) Comparability of cohorts on the basis of the design or analysis
   a) study controls for _____ (select the most important factor) ✵
   b) study controls for any additional factor ✵ (This criteria could be modified to indicate specific control for a second important factor.)

Outcome

1) Assessment of outcome
   a) independent blind assessment ✵
   b) record linkage ✵
   c) self report
   d) no description

2) Was follow-up long enough for outcomes to occur
   a) yes (select an adequate follow up period for outcome of interest) ✵
   b) no

3) Adequacy of follow up of cohorts
   a) complete follow up - all subjects accounted for ✵
   b) subjects lost to follow up unlikely to introduce bias - small number lost - > ____ % (select an adequate %) follow up, or description provided of those lost) ✵
   c) follow up rate < ____% (select an adequate %) and no description of those lost
   d) no statement

Appendix 2: Human research ethics committee clearance certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

Ref: W-CP-191108-2

08 November 2019

TO WHOM IT MAY CONCERN:

Waiver: This certifies that the following research does not require clearance from the Human Research Ethics Committee (Medical).

Investigator:	**Dr Sameera Essa (student no 2097216)**
Supervisor:	**Palesa Mogane, Palesa Motshabi and Yoshan Moodley**
Faculty:	Health Sciences
School:	Clinical Medicine
Department:	Anaesthesiology
Project title:	**Risk factors associated with unplanned Intensive Care Unit admissions following paediatric surgery: a systematic review**
Reason:	Literature Review

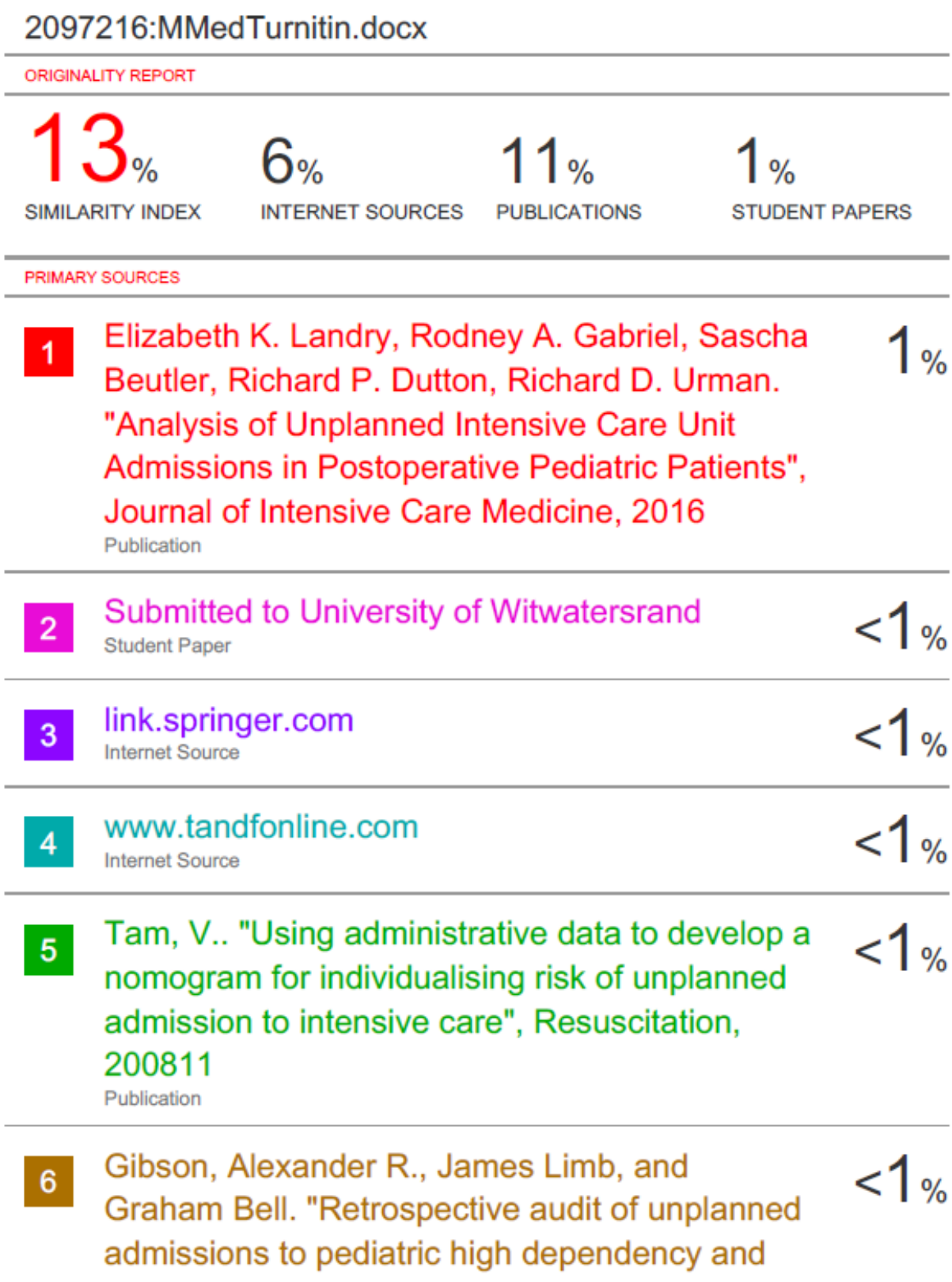
Dr Clement Penny

Chair: Human Research Ethics Committee (Medical)

Copy – HREC (Medical) Secretariat: Zanele Ndlovu, Rhulani Mkansi,Iain Burns, Mapula Ramaila

Research Office Secretariat: Faculty of Health Sciences, Phillip Tobias Building, 3rd Floor, Office 301, 29 Princess of Wales Terrace, Parktown, 2193 Tel +27 (0)11-717-1252 /1234/2656/2700 Private Bag 3, Wits 2050, email: zanele.ndlovu@wits.ac.za Office email: hrec-medical.researchoffice@wits.ac.zaWebsite:

Appendix 3: Plagiarism/ Turnitin report cover page



2097216:MMedTurnitin.docx

ORIGINALITY REPORT

13%	6%	11%	1%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Elizabeth K. Landry, Rodney A. Gabriel, Sascha Beutler, Richard P. Dutton, Richard D. Urman. "Analysis of Unplanned Intensive Care Unit Admissions in Postoperative Pediatric Patients", Journal of Intensive Care Medicine, 2016 Publication	1%
2	Submitted to University of Witwatersrand Student Paper	<1%
3	link.springer.com Internet Source	<1%
4	www.tandfonline.com Internet Source	<1%
5	Tam, V.. "Using administrative data to develop a nomogram for individualising risk of unplanned admission to intensive care", Resuscitation, 200811 Publication	<1%
6	Gibson, Alexander R., James Limb, and Graham Bell. "Retrospective audit of unplanned admissions to pediatric high dependency and	<1%

Appendix 4: Journal guidelines to authors

Southern African Journal of Anaesthesia and Analgesia
(http://www.sajaa.co.za/index.php/sajaa/about/submissions)

Submitted manuscripts that are not in the correct format and without the required supporting documentation specified in these guidelines will be returned to the author(s) for correction and will delay publication.

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Named authors must consent to publication by signing a covering letter which should be submitted as a supplementary file. Authorship should be based on substantial contribution to:

(i) conception, design, analysis and interpretation of data;

(ii) drafting or critical revision for important intellectual content; and

(iii) approval of the version to be published. These conditions must all be met (uniform requirements for manuscripts submitted to biomedical journals; refer to www.icmje.org); and

(iv) exact contribution of each author must be stated.

Declaration of conflict of interest

Authors must declare all sources of support for the research and any association with a product or subject that may constitute a conflict of interest. If there is no conflict of interest to declare please include the following statement: The authors declare no conflict of interest.

Funding source

All sources of funding should be declared. Also define the involvement of study sponsors in the study design, collection, analysis and interpretation of data; the writing of the manuscript;

the decision to submit the manuscript for publication. If the study sponsors had no such involvement, this should be stated as follows: No funding source to be declared.

Research ethics committee approval

The submitting author must provide written confirmation of Research Ethics Committee approval for all studies including case reports. The ethics committee as well as the approval number should be included.

Statistical analysis

Authors are advised to involve medical statisticians at the protocol stage of their research project: to plan sample size, and the selection of appropriate statistical tests for analysis and presentation.

Protection of patient's rights to privacy

Identifying information should not be published in written descriptions, photographs, and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) gives informed written consent for publication. The patient should be shown the manuscript to be published. Refer to www.icmje.org.

Ethnic classification

The rationale for analysis based on racio-ethnic-cultural categorisation should be indicated.

Categories of submissions

Shorter items are more likely to be accepted for publication, owing to space constraints and reader preferences.

Original articles

Original articles on research relevant to anaesthesia and analgesia should not exceed 3 200 words, no more than 30 references, with up to 6 tables or figures. A structured abstract under the following headings, Background, Methods, Results, and Conclusions is a requirement and should not exceed 300 words.

Clinical Review articles

Review articles relevant to anaesthesia and analgesia should not exceed 2 400 words, with a maximum of 20 references and no more than 6 tables or figures. A summary of 300 words or less is required.

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Case reports should not exceed 1 800 words with no more than 10 references. Figures are limited to 2 figures and may include images or photographs. The case report should have three headings: Summary (not exceeding 100 words), Case report (with no introduction) and Discussion. Case reports will be published online only. The summary and the URL will appear in the printed version.

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Scientific Letters should not exceed 2 400 words with a maximum of 10 references. Only one table or illustration is permissible. A structured abstract under the following headings, Background, Methods, Results, and Conclusions, is a requirement and should not exceed 250 words.

Letters to the editor

Letters to the editor should be 800 words or less with only one image or table.

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Refer to articles in recent issues for the presentation of headings and subheadings. If in doubt, refer to 'uniform requirements' - www.icmje.org. Manuscripts must be provided in UK English.

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This information must be provided for ALL authors and must be submitted as a supplementary file.

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ORCID number of ALL authors must be provided – if authors do not have ORCID, please register at https://orcid.org/

Abbreviations

All abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.

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Scientific measurements must be expressed in SI units except blood pressure (mmHg) and haemoglobin (g/dl). Litres is denoted with a lowercase 'l' e.g. 'ml' for millilitres). Units should be preceded by a space (except for %), e.g. '40 kg' and '20 cm' but '50%'. Greater/smaller than signs (> and 40 years of age) should also be preceded by a space e.g. > 20 years. No spaces should precede ± and °, i.e. '35±6' and '19°C'.

Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160...

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General formatting

The manuscript must be in Microsoft Word or RTF document format. Text must be 1,5-spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes, except for Tables). The manuscript must be free of track changes.

Disclaimers should follow the Conclusion and it should be in the following order: Acknowledgements, Declaration conflict of interest, Funding source, Ethics declaration and ORCID.

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If tables or illustrations submitted have been published elsewhere, the author(s) should provide consent to republication obtained from the copyright holder.

Tables may be embedded in the manuscript file and provided as 'supplementary files'. They must be numbered in Arabic numerals (1,2,3...) and referred to consecutively in the text (e.g. 'Table 1'). Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged. Tables must be cell-based (i.e. not constructed with text boxes, tabs or enters) and accompanied by a concise title and column headings. Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

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Journal references:

Jun BC, Song SW, Park CS, Lee DH. The analysis of maxillary sinus aeration according to aging process: volume assessment by 3-dimensional reconstruction by high-resolutional CT scanning. Otolaryngol Head Neck Surg. 2005 Mar;132(3):429-34.

Polgreen PM, Diekema DJ, Vandeberg J, Wiblin RT, et al. Risk factors for groin wound infection after femoral artery catheterization: a case-control study. Infect Control Hosp Epidemiol [Internet]. 2006 Jan [cited 2007 Jan 5];27(1):34-7. Available from: http://www.journals.uchicago.edu/ICHE/journal/issues/v27n1/2004069/2004069.web.pdf.

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 jun, 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: World Health Organization, 2002. http://www.who.int/whr/2002 (accessed 16 January 2010).

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Appendix 5: PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	iv
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	2
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	2-5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	2
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	3-5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	2-5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	2-5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	2-5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	2-5

Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7-10
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	2-5

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	4
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	4
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	7
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	6
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	6-11
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	6-11
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	6
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	6-11
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	11-14
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	14-15
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future	15

		research.	
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	15

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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