

An Assessment of Critically Ill Children admitted to a General High Care Unit in a Regional Hospital in the Western Cape, South Africa

by

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Table of Contents

I. Abstract	page 4
II. Acknowledgements and Contributions	page 5
III. Abbreviations	page 6
IV. Accepted Publication:	
Article	page 7
Figures and Tables	page 25
V. Appendices:	
a. Approval letters	page 31
b. Plagiarism declaration	page 49
c. Data collection sheet	page 51
d. Informative poster	page 53

I. Abstract

Background

Many critically ill children in South Africa are cared for in regional hospitals by general Paediatricians. Critically ill adults and children are usually cared for in the same units. There is limited data on the numbers of children admitted and the outcomes of these children.

Objective

To describe the patient profile and outcomes of children admitted to a general high care unit (HCU) in a regional hospital in the Western Cape, South Africa.

Methods

This was a retrospective descriptive study of all children admitted to the HCU of George Regional Hospital during a one year period (2016). Demographic data, HIV, anthropometric data, immunisation status, diagnoses, medical interventions, length of stay, death or survival, and referral data to the tertiary paediatric intensive care unit (PICU) were collected. The PIM3 score and Standardized Mortality Ratio (SMR) was calculated.

Results

Thirty percent (144/468) of the HCU admissions were children. Most (70%) were admitted after hours. Half were under 9 months (range 3 days to 149 months). Sixty-five percent of the children required respiratory support and 45% needed inotropic support. Twenty percent of the children were transferred to the PICU. Twelve children (8,5%) died with most deaths (75%) occurring at regional level. Half of the deaths were due to sepsis with pneumonia (25%) and diarrhoea with shock (25%) accounting for the rest. The cumulative PIM3 score was 9.049 (95%CI 6.430-11.668) with an SMR of 1.326 (95%CI 1.028-1.866) observed.

Conclusion

Critically ill children accounted for a third of HCU admissions. Most children needed medical interventions. These require specific training and equipment that are often lacking. After hours admissions also put strain on limited staff. Most children were successfully discharged demonstrating a good outcome. This was achievable with good channels of communication and transport to a tertiary PICU.

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III. Abbreviations

AIDS – Acquired Immunodeficiency Syndrome
AMS – South African Red Cross Air Mercy Service
ANOVA – Analysis of Variance
BMI – Body Mass Index
Child PIP – Child Healthcare Problem Identification Programme
CI – Confidence Interval
CPAP – Continuous Positive Airway Pressure
GIT – Gastrointestinal Tract
HCU – High Care Unit
HIV – Human Immunodeficiency Virus
HREC – Human Research Ethics Committee
ICU – Intensive Care Unit
IPPV – Intermittent Positive Pressure Ventilation
IQR – Interquartile Range
L/HFA – Length/Height-for-age
MDG – Millennium Development Goal
MeSH – Medical Subheading
NICU – Neonatal Intensive Care Unit
OR – Odds Ratio
PELOD – Paediatric Logistic Organ Dysfunction
PICU – Paediatric Intensive Care Unit
PIM – Paediatric Index of Mortality
PPIP – Perinatal Problem Identification Programme
PRISM – Pediatric Risk of Mortality
PRT – Paediatric Retrieval Team
RCWMCH – Red Cross War Memorial Children’s Hospital
SD – Standard Deviation
SDG – Sustainable Development Goal
SMR – Standardized Mortality Ratio
U5MR – Under-five Mortality Rate
WFA – Weight-for-age
WFH – Weight-for-height/length
WHO – World health organisation

IV. Accepted Publication

(Accepted to the South African Journal of Child Health)

AN ASSESSMENT OF CRITICALLY ILL CHILDREN ADMITTED TO A GENERAL HIGH CARE UNIT IN A REGIONAL HOSPITAL IN THE WESTERN CAPE, SOUTH AFRICA.

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Critically ill children accounted for a third of HCU admissions. Most children needed medical interventions. These require specific training and equipment that are often lacking. After-hours admissions also put strain on limited staff. Most children were successfully discharged demonstrating a good outcome. This was achievable with good channels of communication and transport to a tertiary PICU.

Article

Introduction

Almost 34 000 children under the age of 15 years died in South Africa during 2016. This makes up 7,4% of the total deaths (n=34 000/456 612)^[1]. The number of deaths have been used to represent an estimate of people requiring critical care^[2]. Critical illness can be defined as illness or injury that acutely impairs one or more vital organ system. This leads to a high chance of life-threatening deterioration in the clinical condition which requires critical care services. These are described as medical care delivered to a critically ill or injured person^[3]. In this study we aim to describe the profiles and outcomes of children admitted to a general High Care Unit (HCU) providing critical care, in a regional hospital in the Western Cape, South Africa during 2016.

Intensive care is the highest level of patient monitoring and treatment and an intensive care unit can be defined as a designated area where resources and equipment are concentrated to care for critically ill patients. The level of care and supervision is more sophisticated than a general ward and can be subcategorised into 3 levels, namely: Category 1 – tertiary intensive care unit facility, Category 2 – specialised organ support unit, Category 3 - high care unit^[4]

Paediatric intensive care in the public sector is a very limited resource. Most severely ill children in South Africa are cared for by general paediatricians in mixed medical/surgical intensive care and high care units where both adults and children are admitted. This is observed across both public and private sectors. Of almost 4 200 critical care beds across the country,

only around 1 800 are available in the government sector and about 20% (n=815/4168) are reserved for paediatric and neonatal patients in public and private hospitals^[5].

There are no clear guidelines on the number of Intensive Care Unit (ICU) beds per population. Bed availability varies across the world and increased ICU beds per population does not necessarily mean improved mortality. The South African ratio of 8.9 beds per 100 000 people is comparable to Australia and Spain. However, the life expectancy in South Africa is only 54 years (82 years in Australia and Spain). The United States has up to 31.7 beds per 100 000 people and Sri Lanka has only 1.6 per 100 000, with similar life expectancies^[6].

The South African under-5 mortality (U5M) rate has decreased in recent years (estimated 37 - 40/1000 live births in 2015) with the Western Cape seeing a substantial decrease from 58.4/1000 (in 2008) to 31.1/1000 live births in 2015^[7,8,9]. In order to reach Sustainable Development Goal (SDG) 3 by, amongst others, reducing the U5M rate to 25 per 1000 live births by 2030, more data on the profiles and outcomes of critically ill children in regional hospitals are needed^[10]. This includes all children needing high dependency or intensive care. More data may reveal potential areas where interventions could improve survival^[11].

A higher mortality rate is observed in children cared for in mixed units and well established models from developed countries show better outcomes with centralised paediatric critical care and retrieval services^[12,13]. However, data on the implementation of these models in low or middle income countries are lacking^[14]. In addition, the transport of critically ill children to the tertiary paediatric intensive care unit (PICU) also poses a challenge with a high incidence of transfer related adverse events shown in a recent study in Cape Town^[15]. Nevertheless, another study at Worcester Hospital showed a good outcome in children admitted to a mixed regional hospital HCU^[16].

Other outcome modalities arising from paediatric critical care in the developed world are mortality prediction scores such as the Paediatric Index of Mortality (PIM) score^[17,18]. The score is used as a tool to assess mortality risk. The standardised mortality ratio (SMR) is calculated and this provides a ratio of expected to observed deaths that is used to compare different units. However, other factors such as diagnostic profiles, medical and surgical cases, unit resources, protocols, etc. affect PIM scores. The SMR, therefore, does not only compare quality of care ^[17]. Paediatric Index of Mortality 2 (PIM2) model has been validated as an

accurate comparative index of paediatric intensive care in many settings, including South Africa^[19,20,21]. In 2013 an updated Paediatric Index of Mortality 3 (PIM3) model was published^[22]. This model is currently being used and validated in PICUs across South Africa. However, in a recent study in KwaZulu-Natal, it has been shown to underpredict mortality^[23]. PIM3 has not been validated at regional hospital level. The PIM3 calculated SMR could potentially be used to compare the quality of care between different regional hospitals^[22].

Methods

This study was conducted at George Regional Hospital's High Care Unit (HCU). George Regional Hospital serves both the Eden and Central Karoo districts. The joint population consist of approximately 650 000 (11% of the Western Cape population) with almost 200 000 children under 15 years of age^[8,9]. The HCU maintains six critical care bed spaces (Category 3) for both adults and children^[4]. There are no dedicated beds exclusively reserved for children

In general, children are admitted to the HCU when intubation, inotropic support or more intensive monitoring and care is required ^[4,24]. There are four other higher care beds available in the general paediatric ward, and Continuous Positive Airway Pressure (CPAP) can be provided in the general ward. If patients admitted to the HCU require longer than 72 hours of ventilation, or tertiary sub-specialist critical care is required, patients are discussed for transfer via air ambulance to the PICU at Red Cross War Memorial Children's Hospital (RCWMCH) in Cape Town. Admission to the PICU is determined by the RCWMCH PICU admission criteria^[24,25].

Patients are cared for by a staff of ten professional nurses, four staff nurses and two nursing assistants. During a shift, two to three professional nurses and one staff nurse and/or nursing assistant are on-duty. Only one of the professional nurses is formally trained in paediatric critical care.

The management of medically and surgically ill children is overseen by the doctors of each respective specialty. The paediatric service consists of two general paediatricians, one subspecialist neonatologist, two senior medical officers, and six junior doctors including one registrar, three medical officers and two rotating medical interns. Together they serve the neonatal unit, general paediatric ward, HCU, outpatient department and emergency centre. They also provide outreach and referral services to the subdistricts. In the surgical department

there are four general surgeons, one general surgery registrar, five medical officers and two interns.

There are no doctors allocated to working solely in the HCU. After hours, admitted patients are the responsibility of one off-site consultant and one on-site junior doctor of each specialty (Surgery and Paediatrics). The after-hours team are also on-call for the rest of the hospital.

The neonatal intensive care unit (NICU) at George Regional Hospital provides care to ill neonates. It functions separately from the HCU and patients can be ventilated in the five bed NICU. This unit is reserved for neonates that have not been discharged home from a healthcare facility prior to presentation.

This study was a retrospective descriptive study of all children admitted to the George Regional Hospital HCU during 2016. All children under the age of 13 years were included in the study. Patients 13 years of age and older were excluded (fig.1). The HCU admissions register was used to identify all eligible children throughout the year and medical records were reviewed retrospectively. In the case of transfer, the PICU database was consulted.

This study was performed to determine the profiles and outcomes of children admitted to the HCU. Data were collected for all paediatric admissions and included tertiary PICU stay outcome. Deaths were defined and limited to those occurring during the critical care admission. Children were defined as younger than 13 years. Patient age, sex, immunisation status, Human Immunodeficiency Virus (HIV) infection status, anthropometry (using the World Health Organization criteria and corrected for gestational age), and diagnoses were documented^[26]. Sepsis was defined as a culture positive blood stream infection with multi-organ dysfunction. Prematurity was defined as birth gestational age of less than 37 weeks.

Other time related data collected included time of admission to George Regional Hospital, time of HCU admission (after hours/working hours), total duration of regional hospital admission, total duration of HCU admission, duration receiving critical care (including HCU, transfer and PICU stay), and transfer waiting period. After hours were defined as HCU admission after 17:00 and before 08:00 on weekdays, after 17:00 on Friday to 08:00 on Monday (weekends) and any public holiday admissions. The reason for delay in PICU transfer, if more than 24 hours, was sought.

Interventions in the form of respiratory support (CPAP/ mechanical ventilation) and inotropic support were recorded. The duration receiving these interventions was also noted.

Lastly, the PIM3 score was collected for all patient cases. The predicted mortality rate was compared to the actual mortality rate to calculate the Standardized Mortality Ratio (SMR)^[22].

The continuous variables were not normally distributed and data distribution is described using the median and ranges. The χ^2 test was used to analyse categorical variables. Continuous variables were compared to survival using the Kruskal-Wallis analysis of variance (ANOVA) test. Spearman correlation testing was performed to assess inter-observer variability in PIM3 scoring.

Ethical approval was obtained from the Human Research Ethics Committee (HREC) at the University of Cape Town (HREC Reference 700/2016). Study approval was obtained from the Western Cape Department of Health and local hospital management. A waiver of individual consent was granted by the HREC. An informative poster was displayed outside the HCU to inform staff, patients and caregivers of the study.

Results

Of the 468 HCU admissions, 144 (30%) were children. All 144 admissions were included in the study, and all patient records were available (fig. 1). Two children were readmitted within 48 hours of discharge from the HCU and recorded as separate admissions. The male to female ratio was almost equal (Table 1). The median age was 9 months (IQR 2 to 40 months). Half of the HIV infected children were diagnosed during the admission. Weights were available in 134 cases, while lengths/heights were available for 108 of the cases. More than a third of cases (37,3%, n=50/134) were underweight with 16,42% (n=22/134) being severely underweight. Stunting was also observed in a significant proportion of patients (36,1%, n=39/108). A large number of these were severely stunted (16,42%, n=24/108). Almost a quarter (23,15%, n=25/108) of cases were wasted with 10% (n=11/108) being severely wasted. Anthropometric values did not have an effect on survival. Eighteen admissions were born prematurely, including one of the deaths. Prematurity was not associated with a higher death rate (p=0.510).

Twelve patients (8,5%, n=12/142) died during admission. Half (n=6/12) of the patients who died were diagnosed with sepsis. The other deaths had pneumonia (n=3/12) and diarrhoea with shock (n=3/12). Half of the deaths occurred in children under 6 weeks of age (range less than 1 week to 7 years, IQR 3 weeks to 28 months). Most deaths (75%, n=9/12) occurred in the HCU and within 4 days of admission. Three deaths occurred at tertiary level. The exact time of death was available for 11 of the deaths. The median time-to-death was 2 days (range 7 hours to 22 days).

The median duration of admission to George Regional Hospital was 6 days (range 8 hours to 77 days). The patients who died tended to be admitted for a shorter period prior to death/transfer to the PICU (p=0.0041). The median duration of HCU admission was 1 day 17 hours (range 18 minutes to 13 days) (Table 2). The median time awaiting transfer to the PICU was 12 hours (range 3 hours to 12 days). Table 3 shows the reasons for delay in PICU transfer. There were no mortalities during transfer and no association between transfer and death (p=0.754). The median duration of PICU stay was 6 days (range 6 hours to 31 days). Data of PICU duration-of-stay was not available for 7 patients. No significant association was observed between PICU duration-of-stay and mortality (p=0.3056) in the 29 transfers.

Children who died all required respiratory and/or inotropic support (p=0.000). Table 4 summarises interventions received by the study population. This included support at George Regional Hospital, during transfer, and at the RCWMCH PICU. The median duration of respiratory support, including CPAP, Intermittent Positive Pressure Ventilation (IPPV), or both, was 4 days (range 3 hours to 33 days). The median duration receiving inotropes was 2 days (range 3 hours to 14 days).

Most of the admissions had respiratory or gastrointestinal/diarrhoeal disease (fig. 2)(Table 6). Medical patients tended to be younger (median 7 months, range 3 days to 11 years, p=0.0001), with half of the surgical patients being older than 5 years (range 3 months to 12 years).

Almost two thirds (62,71%, n=37/58) of the respiratory cases had pneumonia. Seven (11,86%, n=7/58) had bronchiolitis, 2 (3,4%, n=2/58) exacerbations of asthma, 4 (6,78%, n=4/58) laryngotracheobronchitis, 3 (5,08%, n=3/58) aspiration events, 4 (6,78%, n=4/59) subglottic

stenosis and 2 (3,39%, n=2/58) severe obstructive sleep apnoea. Almost one third (29,73%, n=11/37) of the cases with pneumonia also had associated congenital cardiac lesions.

Six patients (4,17%, n=6/144) were admitted with primary cardiac disorders, including 2 cases of probable myocarditis, 1 with cor pulmonale from obstructive sleep apnoea, 2 complex congenital cardiac lesions and 1 with mitral valve disease and heart failure.

Of the 19 (13,19%, n=19/144) cases with gastrointestinal disorders, 18 were admitted with acute diarrhoea and shock. This was defined as the recent onset (less than 2 weeks) of profuse loose, watery stools. Shock was present when a delayed capillary refill time (more than 3 seconds), weak pulse rate, decreased pulse volume, cool peripheries, decreased level of consciousness, and/or decreased blood pressure was associated with diarrhoea. One patient had chronic diarrhoea longer than 2 weeks with cytomegalovirus disease. One patient with phenotypic features of Down syndrome was admitted with acute diarrhoea and shock (karyotype not performed).

Of the patients with neurological disease, 6 (54,55%, n=6/11) presented with status epilepticus, 2 (18,2%, n=2/11) with acute flaccid paralysis, 2 (18,2%, n=2/11) with encephalitis, and 1 (9,1%, n=1/11) with bilateral intraventricular haemorrhage.

Five (3,47%, n=5/144) had diabetic keto-acidosis (DKA), 2 (1,39%, n=2/144) patients were admitted with haematologic disorders and bleeding. One (0,69%, n=1/144) patient had nephrotic syndrome and possible spontaneous bacterial peritonitis. Seven (4,86%, n=7/144) patients were admitted after toxin or drug ingestion. One (0,69%, n=1/144) patient had acute liver injury from an unknown cause and another (0,69%, n=1/144) had non-specific symptoms and signs of headache, lethargy, fever and petechiae.

The majority (59,09%, n=13/22) surgical admissions were trauma related. Other trauma cases included 1 (0,69%, n=1/144) drowning and 1 (0,69%, n=1/144) crush injury. Of the non-trauma cases, 2 (1,39%, n=2/144) had ruptured appendices, 2 (1,39%, n=2/144) bowel obstruction, 1 (0,69%, n=1/144) intussusception, 2 (1,39%, n=2/144) were observed post cleft palate repair, 1 (0,69%, n=1/144) post adenotonsillectomy, and 1 (0,69%, n=1/144) with hip septic arthritis. Of the surgical cases, 14 (63,64%, n=14/22) required mechanical ventilation and seven (31,82%, n=7/22) inotropic support. There was no difference observed between medical and

surgical category need for additional support ($p=0.611$) nor durations requiring ventilatory ($p=0.1812$) or inotropic ($p=0.3284$) support.

The cumulative PIM3 value for the study population was 9.049 (95% CI 6.430 – 11.668), with minimal interobserver variability (Spearman correlation value 0.9771, $p=0.000$). The children that were transferred to the PICU had a significantly lower PIM3 score than those who continued care at the HCU ($p=0.0495$). The expected number of deaths was thus 9 out of the 144 patient cases. The SMR was calculated as 1.326 (95%CI 1.028 – 1.866).

Discussion

This study demonstrates the relatively large proportion of children admitted to the regional hospital HCU, i.e. 30% of all admissions. Most of the children required medical interventions such as CPAP, IPPV and/or inotropic support demonstrating a need for specific equipment and training of staff. After-hours admissions in particular was proportionately higher. This puts strain on on-call staff at regional level. Most children were successfully discharged demonstrating a good outcome. This was achievable with good channels of communication and transport to a tertiary PICU.

Although not significantly associated with death, it is concerning that more than a third of the children in this study were underweight and stunted with almost a quarter being wasted. These are in keeping with trends observed in a recent meta-analysis in South Africa^[27]. Underweight children have a higher risk of poor critical care outcomes^[28]. The current trend towards increased overnutrition was not observed^[27].

The overall low mortality reflects a good outcome^[16,25]. The amount of deaths occurring in the first few days reflects the severity of critical illness in the initial period^[28]. The tendency for a younger age observed in the deaths is in keeping with other studies^[29]. HIV infection did not have a significant effect on mortality which could reflect better outcomes due to antiretroviral therapy^[30]. It is concerning to note the large proportion of undocumented HIV statuses, indicating the need for improved documentation and vigilance in testing.

Even though after-hour admission did not significantly affect outcome, it does place more strain on the on-call staff and may affect morbidity^[31]. Almost a third (29,17%, $n=42/144$) of the children were admitted for a prolonged period (>72 hours), adding to local resource use.

This is comparable to a recent study at RCWMCH PICU. During a one year period 50% of all admissions were admitted for 3 days or longer^[32]

George Regional Hospital not only serves the 3rd largest subpopulation in the Western Cape, but also provides care to the poorest (Central Karoo) and third-richest (Eden) communities, based on gross domestic product (GDP) per capita^[33]. The districts together cover almost 50% of the province's total geographical area^[34]. The distance to the nearest tertiary PICU is 427 km^[35]. This can be compared to the shorter distance to the closest PICU for other regional hospitals such as Worcester Hospital (96 km) and Paarl Hospital (48 km)^[36,37]. The air ambulance service is a necessity. The service is efficient and safe with mostly short waiting times and no mortalities during transfer^[38]. The service is delivered by a private company (EMS 24/7) and therefore service costs must be considered^[38]. Some transfers could not occur due to patient instability, making air transfer unfeasible. The median PICU stay of six days suggests that most referrals were appropriate. The RCWMCH PICU criteria for admission are based on international guidelines and incorporates local policy in order to ensure optimal use of scarce ICU services while keeping the best interest of the child and equitable access in mind. Avoidance of prolonged stays in referred cases indicate good use of critical care resources [24,25].

A relatively small proportion of the admissions (20,14%, n=29/144) required transfer to the PICU. The regional hospital team was thus responsible for the definitive management of the majority of critically ill children. This requires specific training and skills as well as equipment^[39].

CPAP and inotropic support can be provided in the general ward at George Regional Hospital. Thus, some of the children were already receiving ventilatory and/or inotropic support prior to HCU admission and even after being transferred out of the unit. This requires added expertise and vigilance from general ward staff, which is not necessarily available.

As expected, pneumonia and diarrhoea made up a large proportion of the diagnoses and demonstrated an increased risk of death. These have been shown to be the leading causes of death elsewhere in the Western Cape^[40]. Confirmed cases of sepsis is also a significant cause of death in critically ill children^[28]. The high proportion of trauma/injury related surgical admissions is concerning. More than 60% of deaths in children older than 5 years in the

Western Cape are due to trauma/injury^[41]. This number also seems to be increasing at national level^[42].

The relatively higher number of deaths observed in this study when compared to Worcester Hospital from 1 July 2008 to 30 June 2009 (n=12/185) could be explained by multiple factors^[16]. Patients that were transferred were not further assessed for survival at the tertiary centre in the Worcester based study^[16]. The relative ease of transfer to the tertiary PICU due to shorter distance and the availability of road transfer may also have contributed to a lower mortality rate^[43,44].

To our knowledge this is the first study applying the PIM3 score to a critical care unit at regional level (i.e. George Regional Hospital HCU). This score has not been validated at this level and should be interpreted with caution. A lower PIM3 score for the transferred cases could explain the low mortality rate at the PICU^[22]. The SMR shows a value that is worse than expected. This could be due to many factors including the lack of paediatric critical care training, a study population with inherently poorer health due to poverty and malnutrition, and limited on-site availability of senior doctors after hours^[23,45,46]. This observation may suggest that more regionalised critical care support such as technology-enabled remote care (telemedicine) from the PICU, as well as specialist outreach could be applicable^[47,48].

Limitations of the study are the retrospective nature of data collected with documentation discrepancies regarding times of interventions, admissions and transfers. A short study period and small population size was used. HIV exposure was also not documented. The neonatal area functions independently making this study difficult to compare to other South African studies^[16]. Further study is needed to assess neonatal critical care in the region.

The application of a scoring system that has not been validated in this setting limits the value of interpreting the SMR^[22]. Future studies could assess morbidity and long term effects of critical disease as well as validate other mortality scoring systems at regional level.

Conclusion

Critically ill children made up a large portion of the admissions to the George Regional Hospital HCU. Most of the children required medical interventions such as inotropes and

respiratory support. Only 20% of the children were referred to the tertiary PICU indicating a need for regional hospital staff to be competent in managing critically ill children. General paediatricians and surgeons working in regional hospitals should be confident in treating very ill children and must ensure that junior doctors are trained in working in this environment. Special training of nurses and adequate availability of equipment are necessary to ensure good outcomes. Most of the children in this study were successfully discharged. This reflects the good quality of care at regional level, during air transfer and at the tertiary PICU. Prompt stabilisation and care, as well as appropriate transfer to the tertiary facility is necessary to avoid mortality, however, due to tertiary bed scarcity, weather limitations and patient instability this is sometimes not feasible. More studies are needed to assess the care of critically ill children at regional level in South Africa. Mortality predictors may be relevant in regional hospital settings but more studies are needed to validate these models. These predictors could potentially be used to compare services and assist in health system planning.

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Conflicts of interest

None.

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Figures and Tables

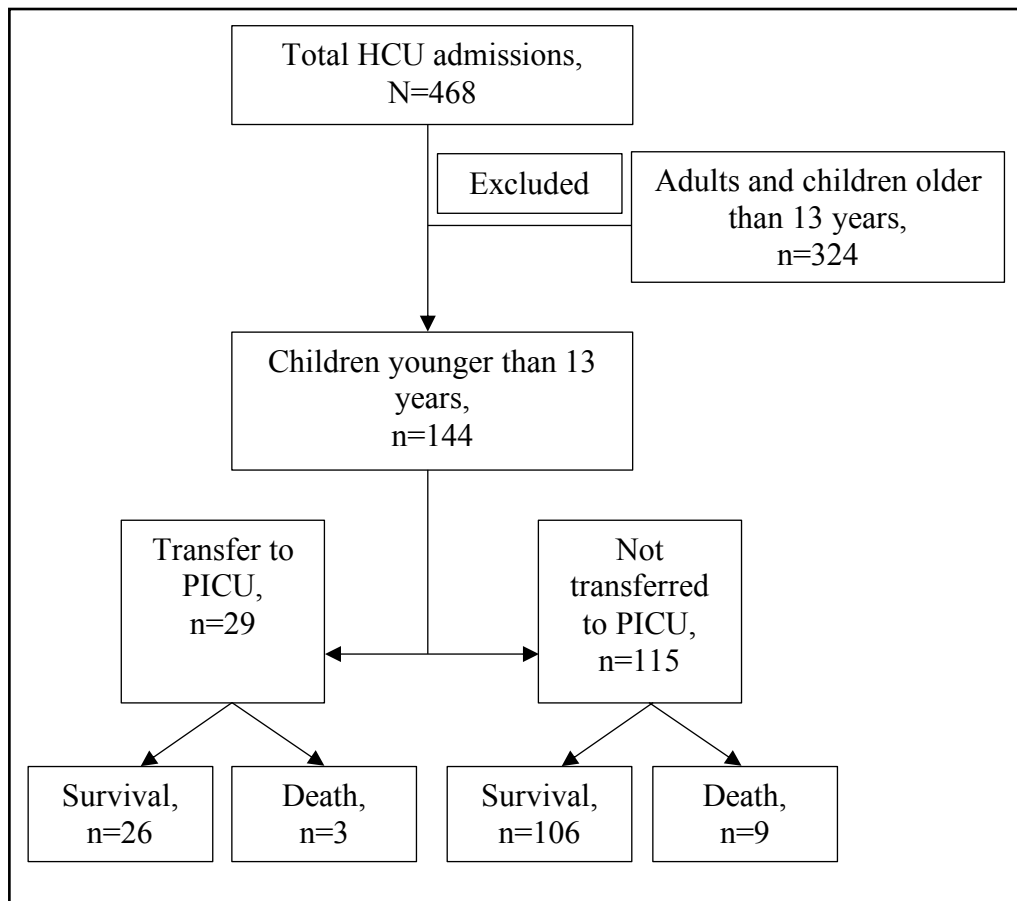


Fig. 1. Sampling strategy with transfer data and outcomes

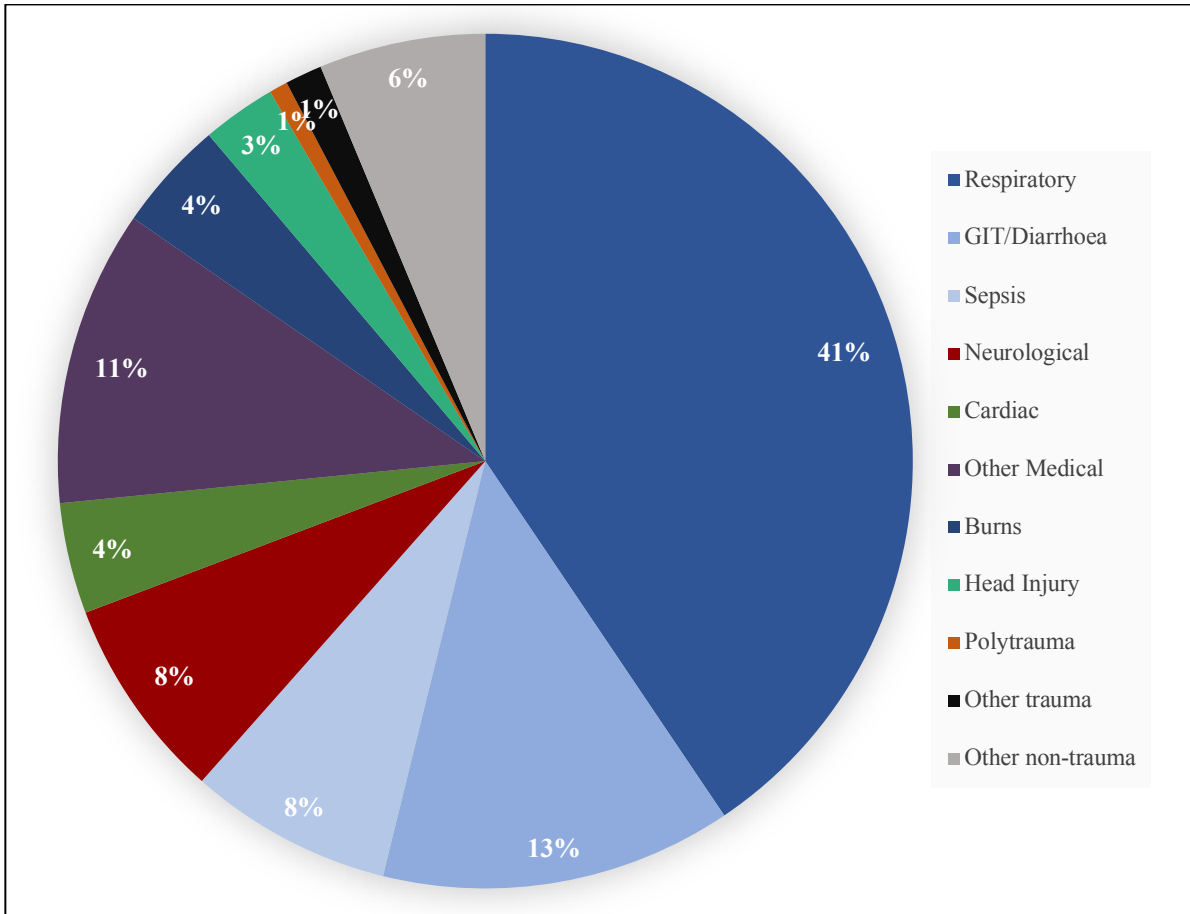


Fig. 2. Diagnostic categories represented as percentages of admissions

Table 1. Comparing sex, age ranges, immunisations, HIV status and anthropometry to mortality as well as transfers to the PICU, N=144

Data	Frequency n(%)	Transfer PICU n(%)	Mortality n(%)
Gender			
Male	74 (51,39)	14(9,72)	5(3,47)
Female	70 (48,61)	15(10,42)	7(4,86)
Age			
<1month	30 (20,83)	4(2,78)	6(4,17)
1-12 months	50 (34,72)	10(6,94)	2(1,39)
1-5ys	34 (23,61)	7(4,86)	2(1,39)
>5yrs	30 (20,83)	8(5,56)	2(1,39)
Immunisations complete			
yes	80 (55,56)	13(9,03)	7(4,86)
no	15 (10,42)	4(2,78)	2(1,39)
unknown	49 (34,03)	12(8,33)	3(2,08)
HIV status			
Infected	6 (4,17)	0	1(0,69)
Not infected	100 (69,44)	24(16,67)	9(6,25)
unknown	38 (26,39)	5(3,47)	2(1,39)
*WFA Z-score, N=134			
between -2 and +2SD**	80 (59,70)	17(12,69)	6(4,48)
between -2 and -3SD	28 (20,90)	5(3,73)	2(1,49)
below -3SD	22 (16,42)	5(3,73)	3(2,24)
between +2 and +3SD	2(1,49)	1(0,75)	1(0,75)
more than +3SD	2(1,49)	0	0
***L/HFA Z-score, N=108			
between -2 and +2SD	69(47,92)	9(6,25)	2(1,85)
between -2 and -3SD	15(10,42)	2(1,39)	0
below -3SD	24(16,67)	5(3,47)	1(0,93)
between +2SD and +3SD	3(2,08)	0	0
more than +3SD	3(2,08)	0	0
#WFH/BMI Z-score, N=108			
-2 to +2SD	81 (75,00)	9(8,33)	2(1,85)
between -2 and -3SD	14 (12,96)	4(3,70)	0
below -3SD	11(10,19)	3(2,78)	1(0,93)
between +2 and +3SD	2(1,85)	0	0
more than +3SD	0	0	0
*WFA = Weight-for-age, **SD = Standard deviation, ***L/HFA = Length/Height-for-age, #WFH/BMI = Weight-for-height/length/Body Mass Index			

Table 2. HCU admission and transfer to PICU, N=144			
Data	Frequency, n(%)	Death, n	Death p value
After-hour admission to HCU			0.275
yes	100 (69,44)	10	
no	44 (30,56)	2	
Duration of stay in HCU			0.894
<2 days	82 (56,94)	8	
2-3 days	20 (13,89)	2	
3-5 days	22 (15,28)	0	
>5 days	20 (13,89)	2	
Transfer to PICU			0.754
yes	29 (20,14)	3	
no	115 (79,86)	9	
*Waiting time until transfer			0.351
<24 hrs	17 (58,62)	1	
24 - 48 hrs	7 (24,14)	2	
>48 hrs	5 (17,25)	0	
*29/144 were transferred to RCWMCH PICU			

Table 3. More than 24 hour delay in transfer to PICU, n=12/29	
Reason for delay	Number of patients
Lack of PICU bed availability	5
Unstable patient	5
Weather conditions unsuitable for air transfer	1
No reason noted	1

Table 4. Respiratory and inotropic support at George Regional Hospital, during transport and at the PICU, N=144

Data	Frequency (%)	Deaths, n	Death p value	Odds Ratio OR(95%CI)
Ventilation			0.007(any ventilation)	
No	51 (35,42)	0		
CPAP	36 (25,00)	3		
IPPV	35 (24,30)	6		
CPAP and IPPV	22 (15,28)	3		
Inotropes			0.000(any inotropes)	
No	79 (54,86)	5		
Yes	65 (45,14)	7		
Time requiring Ventilation support*			0.022	
<1 day	14 (15,56)	4		0.4(0.125-1.275)
1-3 days	23 (25,56)	5		0.278(0.103-0.748)
3-6 days	21 (23,32)	1		0.05(0.007-0.373)
>6days	32 (35,56)	2		0.067(0.016-0.279)
Time requiring inotropes**			0.013	
<1 day	9 (14,52)	5		1.25(0.336-4.655)
1-3 days	34 (54,84)	5		0.172(0.067-0.445)
3-6 days	10 (16,12)	2		0.053(1.177)
>6days	9 (14,52)	0		0
*93/144 ventilated, information on N=90				
** 65/144 inotropes, information on N=62				

Table 5. Diagnostic categories with transfers to the PICU and deaths

Primary Diagnosis	Diagnosis Frequency, N=144 n(%)	Transfers, N=29 n(%)	Deaths N=12 n(no. of transfers)	Odds Ratio of Transfer, OR(95%CI)	Odds Ratio of Death, OR(95%CI)
<i>Medical</i>	122(84,72)	21(72,41)	12(3)	0.208(0.130-0.333)	0.109(0.060-0.198)
Respiratory	58(40,28)	14(48,28)	3(2)	0.318(0.174–0.581)	0.055(0.017 – 0.174)
GIT/Diarrhoea	19(13,19)	1(3,45)	3(1)	0	0.188(0.055-0.643)
Sepsis	11(7,64)	1(3,45)	6	0.1(0.013-0.781)	1.2(0.366-3.932)
Neurological	11(7,64)	3(10,34)		0.375(0.099-1.414)	
Cardiac	6(4,17)	2(6,90)		0.5(0.092-2.730)	
Other	16(11,11)	0		0.063(0.008-0.471)	
Toxin/drug	7(4,86)				
DKA	5(3,47)				
Haematological	2(1,39)				
Acute liver injury	1(0,69)				
Nephrotic syndrome	1(0,69)				
Not specified	1(0,69)				
<i>Surgical</i>	22(15,28)	8(27,59)	0	0.571(0.240-1.362)	0
Burns	6(4,17)	4(13,80)		2.0(0.366-10.920)	
Head Injury	4(2,78)	2(6,90)		1.0(0.141-7.100)	
Polytrauma	1(0,69)	1(3,45)			
Other trauma	2(1,39)	0		0	
Drowning	1(0,69)				
Crush injury	1(0,69)				
Other non-trauma	9(6,25)	1(3,45)		0.125(0.016-1.000)	
Appendicitis	2(1,39)				
Bowel obstruction	2(1,39)	1(3,45)		0.125(0.016-1.000)	
Intussuception	1(0,69)				
Cleft palate repair	2(1,39)				
Adenotonsillectomy	1(0,69)				
Hip septic arthritis	1(0,69)				

V. Appendices

a. Approval Letters

1. Research Protocol
2. Human Research Ethics Committee Approval
3. HREC FHS011 Study Deviation form
4. HREC FHS017 Annual Progress Renewal
5. Amendment to approval (Extended to 30 January 2020)
6. HREC FHS006 Protocol Amendment (Change to title)
7. Western Cape Department of Health Approval
8. Acceptance letter from South African Journal of Child Health
9. Form 19 Plagiarism declaration

An Assessment of Paediatric Critical Care in a Regional Hospital in South Africa

Research Protocol

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Background

Paediatric intensive care in the government sector of South Africa is a limited resource that is available to very few (1, 2). According to a national audit conducted by Bhagwanjee, et al. in 2004 and 2005, there are 337 critical care (High Care/Intensive Care) beds available in the Western Cape public sector (1). In comparison, the private sector maintains 349 critical care beds that are available to a relatively smaller population. Together this total of 686 bed spaces are available to provide critical care to the Western Cape population of 5.823 million of which 31% (1.814 million) are children under the age of eighteen (census 2011)(1).

Of these public and private critical care beds, 2.6% are maintained for both paediatric and neonatal patients, 13.2% for neonatal only, 5.3% for paediatric patients only, and 10.5% for mixed surgical/ medical (adult) and paediatric/neonatal patients(1). This means that about 21% (144) of all critical care beds in the province is exclusively available to children, with an extra 10.5% (72) available as mixed adult/paediatric beds. This comparatively small amount of dedicated paediatric critical care beds is worrying in view of research showing higher mortality in children nursed in multidisciplinary adult intensive care units (3).

In the Western Cape public sector there are two tertiary level paediatric intensive care units (excluding neonatal subspecialist intensive care units) located at Tygerberg Hospital and the Red Cross War Memorial Children's Hospital (RCWMCH) in Cape Town. Tygerberg Hospital maintains ten – and the RCWMCH twenty-two paediatric intensive care beds.

Five other public hospitals in the Western Cape also maintain critical care beds at regional level in closed critical care units. These include mixed adult and paediatric beds.

At most of these regional units the critical care of sick children remains the responsibility of the general paediatrician and intensive care nursing staff not necessarily trained in caring for critically ill children. On average half of the children requiring critical care are medical patients with mostly respiratory problems such as pneumonia. The other half are generally patients suffering from surgical, non-trauma related diseases.

Following the work by Shann et al. in the United Kingdom and Australia, it is important to note a substantial decrease in child mortality rates related to the centralization of paediatric critical care to specialist paediatric intensive care units (PICUs) (4). Early referral of children requiring more than twelve to twenty four hours of ventilation shows a definite decrease in the risk of death (4).

In order to assess the severity of illness and risk of dying, predictive mortality score models have been developed (5-9). These predicted mortality scores can be compared to a unit's actual mortality rate thereby providing a comparative analysis of the quality of care between different units.

The Paediatric Index of Mortality (PIM2) prediction model has been validated as an accurate index of the level of tertiary paediatric intensive care in many settings (10-15). When compared to the Paediatric Risk of Mortality (PRISM) score, the PIM2 score seems to be more applicable to the South African context (15, 16). The PIM2 model has also been used in mixed (adult and paediatric) intensive care units with good correlation(17-19).

In 2013 Straney et al. released an updated third generation paediatric index of mortality score prediction model (PIM3). It has been validated in multiple pediatric -, and some mixed ICUs, in New Zealand, Australia, Ireland and the United Kingdom (20). This score has shown better correlation to actual mortality than PIM2 in these countries as well as Italy (20, 21). However, PIM3 has not been validated in a developing country. A recent study by Hendricks et al. in KwaZulu–Natal has found PIM3 to underpredict mortality in their study population (22).

Purpose of the Study

This study aims to describe the patient profiles and treatment of all paediatric patients admitted to the George Regional Hospital High Care Unit (HCU) in the Western Cape over a one-year period (2016).

The assessment will include all paediatric patients admitted from January 2016 until the end of December 2016.

Patient mortality will be described using standardized mortality rates (SMR, i.e. number of deaths observed/number of expected deaths). The PIM3 mortality prediction model will be used to calculate expected deaths. Observed deaths occurring at George Regional Hospital and at the referral tertiary critical care unit, in cases of patient transfer, will be used.

Methodology

Study Design

The study will be an observational cohort study of all children admitted to the HCU from January 2016 to the end of December 2016. Data will be collected retrospectively on previous admissions and prospectively on all subsequent HCU admissions.

The paediatric admissions book available in the HCU will be used to identify all paediatric admissions (less than thirteen years old). Patient folders will be reviewed and, where applicable, the electronic content management (ECM) system containing scanned copies of all

patient notes will be consulted. The tertiary ICU databases will be consulted as well in cases of patient transfer.

Study Population

All children older than two weeks and younger than thirteen years requiring critical care for medical and/or surgical reasons will be included. We will exclude children who demised within two hours of admission from our PIM3 analysis as these mortalities are generally accepted as not reflecting the quality of critical care.

The HCU at George regional hospital admits around two to three children a week. This translates into a study population of around one hundred patients. However, if more children should be admitted, they would also be included in the study population.

Setting

George Regional Hospital is a general level two hospital as defined by the South African Health System. The hospital offers care to the local population of George in the Western Cape, including referrals from surrounding district hospitals and primary care facilities as well as private institutions in the Eden district municipality. The district consists of a population of 574,265 individuals of which 148,463 (25,85%) are children under the age of fifteen (census 2011). The HCU maintains six bed spaces for both adults and children. Patients are cared for by a staff of ten professional nurses, four staff nurses and two nursing assistants. During a shift, two to three professional nurses and one staff nurse and/or nursing assistant care for patients. Only one of the professional nurses on staff is formally trained in delivering paediatric critical care.

The management of medically and surgically ill children is overseen by the doctors of each respective speciality.

The paediatric department consists of two consultant general paediatricians, one consultant sub-specialist neonatologist, two senior medical officers, and six junior doctors including one paediatric registrar, three medical officers and two medical interns rotating through paediatrics.

In the surgical department there are four consultant general surgeons, one general surgery registrar, five medical officers and two interns.

There are no critical care doctors specifically working in the HCU. After-hours the patients are the responsibility of one off-site consultant and one on-site junior doctor of each speciality.

There are no official set admission criteria. Admission is consultant driven with the majority of patients being admitted when invasive ventilation is found necessary. Other admission scenarios include shock requiring central line placement and inotropic support, closer monitoring of critically ill children needing non-invasive ventilation and post-operative care in some children.

No official exclusion criteria are employed. However, as a general rule patients who fulfil the world health organization criteria for severe acute malnutrition due to inadequate diet are not

considered for HCU admission. Human Immunodeficiency Virus infection or TB disease does not exclude admission.

Referral to a tertiary ICU is consultant driven. Generally if patients require longer than forty-eight to seventy-two hours of ventilation, or if specific tertiary sub-specialist critical care is required, patients are discussed for transfer via fixed wing air ambulance to the tertiary centre (Tygerberg Hospital or RCWMCH) for further care if bed space at the referral unit allows.

Recruitment and enrolment

All children fulfilling the inclusion criteria and admitted to the High Care Unit during 2016 will be included.

Research procedures and data collection methods

Data will be collected by the paediatric registrar using the attached data collection sheet. The patient data will be stored in a secure, password protected document and computer. Patient anonymity will be maintained.

For each admission patient demographics, diagnoses and severity of disease identifiers according to the PIM3 scoring system will be collected. The predicted mortality score will then be compared to the actual mortality rate using standardized mortality risk ratios (SMR).

We will also document some of the aspects of critical care required during the admission. This will include ventilation requirements, inotropic support and referrals to the tertiary intensive care units for further care.

Data analysis

This will occur during 2017 after completion of the data collection. Data statistical analysis will be done using Stata 11, StataCorp. 2009. College Station, TX: StataCorp LP.

Chart review of 20 randomly selected records for the time period will be done by the on-site supervising consultant to limit inter-rater bias of the PIM3 scoring.

Numerical variables will be expressed as means and standard deviations if a normal distribution is found. If a skewed distribution of data is found the median and interquartile ranges will be noted. Categorical data will be expressed as proportions. A significance level of $p < 0.05$ will be used for all analysis. We will consult a statistician to help verify data analysis.

Budget

As this will be a descriptive study, no additional costs will be incurred. Printing costs will be borne by the researchers.

Description of risks and benefits

There are no risks to the patient population in doing this study.

It will also quantify, qualify and reflect on the burden of critically ill children in the region which in turn may motivate towards more investment in the local critical care needs of children.

By identifying and quantifying certain predictors of mortality (through PIM3), this study will provide data on the PIM3 use and applicability in a developing country.

Ethical considerations

Approval

Approval will be obtained from the Departmental Research Committee, School of Child and Adolescent Health, and the Human Research Ethics Committee of the Faculty of Health Sciences, University of Cape Town before conducting the research. Local hospital management approval will also be obtained.

Informed consent process

We will ask the Ethics committee to waive consent, as this is a non-interventional descriptive study. Assent from caregivers will be obtained for all prospective data collection.

Confidentiality and access to information

Patient confidentiality will be maintained throughout. Research data will be kept on electronic database systems on the registrar's password protected electronic notebook. The registrar, on-site consultant and mentor consultant at RCWMCH ICU will have access to this data. All research will adhere to requirements stated in the declaration of Helsinki, 2013.

At the study conclusion

This study will provide important information on critical care at a regional level. It is necessary to assess the level of care at regional level and the coordination with tertiary level care in order to identify areas that may need improvement or change in current practice.

Identifying these areas of improvement may directly help in improving patient care. Quantifying the burden of the regional critical care-requiring diseases may identify areas of care that require more support. Assessment of transfer waiting times and paediatric bed occupation may also indicate a need for more paediatric bed spaces, paediatric specialized transport units, and more paediatric critical care trained care-givers.

By reflecting on some of the critical care needs of the local population as well as conditions related to patient transfer, this study may help implement guidelines for early and safe transfer of critically ill children.

This study is limited by some factors: the clinical notes may not contain all the required information, the study will assess only admissions during a one year period, a limited regional patient population will be assessed thus limiting generalizability, and databases at different institutions may not contain all the required data.

Data will be prepared for publication in a peer-reviewed journal at the conclusion of the study.

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UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee



Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6626
Email: shuretta.thomas@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

13 October 2016

HREC REF: 700/2016

Dr S Salie
Paediatrics and Child Health/ICU
Red Cross Hospital

Dear Dr Salie

PROJECT TITLE: AN ASSESSMENT OF PAEDIATRIC CRITICAL CARE IN A REGIONAL HOSPITAL IN SOUTH AFRICA (MMED CANDIDATE - DR R VOSLOO)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study subject to the following:

- Please develop a sign in all official languages that can be placed in the ward informing parents and children regarding the research; that it has been approved and they can opt out.

Approval is granted for one year until the 30th October 2017.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval before the research may occur.

The HREC acknowledge that the student, Dr Ruan Vosloo will also be involved in this study.

Yours sincerely

Signature Removed

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.

HREC 700/2016



UNIVERSITY OF CAPE TOWN
UNIVERSITY OF CAPE TOWN

HUMAN RESEARCH
ETHICS COMMITTEE

21 JAN 2019

HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

Form FHS011: Study deviation

HREC office use only (FWA00001637; IRB00001938)			
This serves as acknowledgement of a protocol deviation as described below.			
Chairperson of the HREC signature	Signature Removed	Date	21/1/2019

Principal Investigator to complete the following:

1. Protocol Information

Date	18/01/2019
HREC REF Number	HREC REF 700/2016
Project Title	An Assessment of Paediatric Critical Care in a Regional Hospital in South Africa
Protocol number (if applicable)	
Principal Investigator	Shamiel Salie
Department / Office Internal Mail Address	shamiel.salie@uct.ac.za

2. Protocol deviation description

Please describe the deviation below, including the reason why the deviation occurred.
No ethics approval from November 2017 to December 2018 (during writing of article)

3. Follow-up actions

3.1 Please describe any follow-up action(s) taken or planned as a result of this deviation e.g. DSMB reporting, report to sponsor, informing participants.
George Regional Hospital Management notification
3.2 Please describe what action(s) have or will be taken to prevent similar deviations in future.
Timely completion of article. Planning to submit final article in 2019

4. Principal Investigator's acknowledgement of responsibility

This signature indicates the PI has reviewed the deviation, taken appropriate follow-up action and implemented or plans to implement preventative steps where possible.			
Signature of PI:	Signature Removed	Date	18/01/2019



UNIVERSITY OF CAPE TOWN
UNIVERSITEIT VAN KAPSTAD

HUMAN RESEARCH
ETHICS COMMITTEE

21 JAN 2019

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee



HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

FHS017: Annual Progress Report / Renewal

Record Reviews/Audits/Collection of Biological Specimens/Repositories/Databases/Registries

HREC office use only (FWA00001937; IRE00001935)			
This serves as notification of annual approval, including any documentation described below.			
<input checked="" type="checkbox"/> Approved	Annual progress report	Approved until/next renewal date	30.01.2019
<input type="checkbox"/> Not approved	See attached comments		
Signature Chairperson of the HREC	Signature Removed		Date Signed 21/1/2019

Principal Investigator to complete the following:

1. Protocol Information

Date (when submitting this form)	15/01/2019		
HREC REF Number	700/2016	Current Ethics Approval was granted until	30/10/2017
Protocol title	An Assessment of Paediatric Critical Care in a Regional Hospital in South Africa		
Principal Investigator	Shamiel Saie		
Department / Office Internal Mail Address	C1, PICU, Red Cross War Memorial Children's Hospital shamiel.salie@uct.ac.za		
1.1 Does this protocol receive US Federal funding?	<input type="checkbox"/> Yes	<input checked="" type="checkbox"/> No	

2. Protocol status (tick ✓)

<input type="checkbox"/>	Research-related activities are ongoing
<input checked="" type="checkbox"/>	Data collection is complete, data analysis only
Please indicate (in the block below) the titles and HREC reference numbers of any projects currently making use of the Database/registry/repository.	
An Assessment of Paediatric Critical Care in a Regional Hospital in South Africa	

3. Protocol summary

Total number of records or specimens collected, reviewed or stored since the original approval	144
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.	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

4. Signature

Signature of PI	Signature Removed		Date	15/01/2019
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UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee



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16 April 2019

HREC REF: 700/2016

Dr Shamiel Salle
Paediatric Intensive Care Unit
Child & Adolescent Health
Red Cross War Memorial Children's Hospital

Dear Dr Salle

PROJECT TITLE: AN ASSESSMENT OF PAEDIATRIC CRITICAL CARE IN A REGIONAL HOSPITAL IN SOUTH AFRICA (MMED CANDIDATE - DR R VOSLOO)

Thank you for submitting your annual progress report to the Faculty of Health Sciences, Human Research Ethics Committee dated 15/01/2019. The HREC acknowledge that we had the incorrect renewal date reflected in the signed fhs017 form.

Approval should've been reflected until 30 January 2020.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.

(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

Please quote the HREC reference number in all your correspondence.

Yours sincerely

Signature Removed

PROFESSOR M BLUCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE



Form FHS006: Protocol Amendment

HREC office use only (FWA00001637; IRB00001938)		
<input checked="" type="checkbox"/> Approved	<input checked="" type="checkbox"/> Type of review: Expedited	<input type="checkbox"/> Full committee
This serves as notification that all changes and documentation described below are approved.		
Signature Chairperson of the HREC	Signature Removed	Date <u>27/8/2019</u>
<p>Note: All <u>major</u> amendments must include a local <u>synopsis</u> justifying the changes for the amendment. Please note that incomplete amendment submissions will not be reviewed.</p>		
Comments from the HREC to the Principal Investigator:		
<p>Note: The approval of this protocol amendment does not grant annual approval. Please complete the <u>FHS016 / FHS017</u> form for annual approval at least one month before study expiration.</p>		

Principal Investigator to complete the following:

1. Protocol Information

Date (when submitting this form)	<u>27/08/2019</u>	
HREC REF Number	<u>700/2016</u>	
Protocol title	An assessment of paediatric critical care in a regional hospital in south africa	
Protocol number (if applicable)		
Principal Investigator	<u>Shamiel Salle</u>	
Department / Office Internal Mail Address	Department of Paediatrics and Child Health PICU Red Cross War Memorial Children's Hospital	
1.1 Is this a major or a minor amendment? (see <u>FHS006</u>) Major (tick box) Minor (tick box)	<input type="checkbox"/> Major	<input checked="" type="checkbox"/> Minor
1.2 Does this protocol receive US Federal funding?	<input type="checkbox"/> Yes	<input checked="" type="checkbox"/> No
1.3 If the amendment is a major amendment <u>and</u> receives US Federal Funding, does the amendment require full committee approval? Note: Any protocol amendments for Full Committee review MUST be submitted on the monthly HREC submission dates. (Please email an electronic copy to <u>hrec-enquiries@uct.ac.za</u>)	<input type="checkbox"/> Yes	<input checked="" type="checkbox"/> No





2. List of Proposed Amendments with Revised Version Numbers and Dates

Please itemise on the page below, all amendments with revised version numbers and dates, which need approval.
 This page will be detached, signed and returned to the PI as notification of approval. Please add extra pages if necessary.

An assessment of critically ill children admitted to a general high care unit in a regional hospital in the Western Cape, South Africa

Title change to above 27/08/2019

3. Protocol status (tick ✓)

<input type="checkbox"/>	Open to enrolment
<input type="checkbox"/>	No participants have been enrolled
<input type="checkbox"/>	Closed to enrolment (tick ✓)
<input type="checkbox"/>	Research-related activities are ongoing
<input type="checkbox"/>	Research-related activities are complete, long-term follow-up only
<input checked="" type="checkbox"/>	Research-related activities are complete, data analysis only

4. Proposed changes will affect: (tick ✓ all the categories that apply)

Protocol	
<input type="checkbox"/>	Study objectives, design (including Investigator's brochure, clinical activities, study length)
<input type="checkbox"/>	Study instruments, questionnaires, interview schedules
<input type="checkbox"/>	Sample size
<input type="checkbox"/>	Recruitment methods
<input type="checkbox"/>	Eligibility criteria (inclusion and exclusion criteria)
<input type="checkbox"/>	Drug/device (composition, amount, schedule, route of administration, combination with other drugs/devices, safety information)
<input type="checkbox"/>	Data collection/ analysis
<input type="checkbox"/>	Principal Investigator. (Please attach revised conflict of interest and PI declaration statements. Refer: sections 7 and 8.4 in the New Protocol Application Form FHS013)
<input type="checkbox"/>	Consent form and information sheet
<input type="checkbox"/>	Recruitment materials (e.g. advertisements)
<input type="checkbox"/>	Administrative (e.g. change in sponsor's name, change in contact information)
<input checked="" type="checkbox"/>	Other. Please specify: New name, more descriptive as outcomes in PICU also assessed



4.1 In your opinion, will there be any increase in risk, discomfort or inconvenience to participants?	<input type="checkbox"/> Yes	<input checked="" type="checkbox"/> No
If yes, please provide a detailed justification/explanation:		

4.2 What follow-up action do you propose for participants who are already enrolled in the study?	
<input type="checkbox"/>	Inform current participants as soon as possible
<input type="checkbox"/>	Re-consent current participants with revised consent/assent forms (append)
<input checked="" type="checkbox"/>	No action required
<input type="checkbox"/>	Other. Please describe:

5. Detailed description of the change(s)

Please attach, for each amendment, a summary of all changes which clearly indicates:	
i. Old wording (e.g. strikethrough text, CHANGED FROM and CHANGED TO)	
ii. New wording (e.g. <i>italicized</i> , bold , tracked)	
iii. Detailed rationale/ justification/ explanation for each change	

6. Ethics Review Levy – cost including vat

Cost for Major Amendments - R3 691.20	
(Protocols funded by UCT (e.g. departmental funding / student research) and by certain grant funding organizations (e.g. MRC, NRF, CANSA,) are exempt from charges)	
For invoicing purposes, please provide:	
Sponsor's name	
Contact person	
Address	
Telephone number	
Email Address	

7. Signature

My signature certifies that I will maintain the anonymity and/ or confidentiality of information collected in this research. If at any time I want to share or re-use the information for purposes other than those disclosed in the original approval, I will seek further approval from the HREC.			
Signature of PI	Signature Removed	Date	27/08/2019



**Western Cape
Government**

Health

STRATEGY & HEALTH SUPPORT

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www.capegateway.gov.za

REFERENCE: WC_2016RP48_224
ENQUIRIES: Ms Charlene Roderick

University of Cape Town

Anzio Road

Observatory

Cape Town

7925

For attention: Dr Shamiel Salie, Dr Ruan Vosloo, Dr Willem Breytenbach

Re: An Assessment of Paediatric Critical Care in a Regional Hospital in South Africa.

Thank you for submitting your proposal to undertake the above-mentioned study. We are pleased to inform you that the department has granted you approval for your research.

Please contact following people to assist you with any further enquiries in accessing the following sites:

George Hospital

Michael Vonk

044 802 4534

Kindly ensure that the following are adhered to:

1. Arrangements can be made with managers, providing that normal activities at requested facilities are not interrupted.
2. Researchers, in accessing provincial health facilities, are expressing consent to provide the department with an electronic copy of the final feedback (**annexure 9**) within six months of completion of research. This can be submitted to the provincial Research Co-ordinator (Health.Research@westerncape.gov.za).
3. In the event where the research project goes beyond the *estimated completion date* which was submitted, researchers are expected to complete and submit a progress report

(Annexure 8) to the provincial Research Co-ordinator

(Health.Research@westerncape.gov.za).

4. The reference number above should be quoted in all future correspondence.

Yours sincerely

Signature Removed

DR A HAWKRIDGE

DIRECTOR: HEALTH IMPACT ASSESSMENT

DATE: 12/12/2016.

8. Acceptance letter from the South African Journal of Child Health:

From: SAJCH em@editorialmanager.com

Subject: Your Submission

Date: 06 January 2020 at 10:24

To: Ruan Vosloo drruanvosloo@icloud.com

CC: "Willem J Breytenbach" willem.breytenbach@westerncape.gov.za, "Shamiel Salie" shamiel.salie@uct.ac.za

Ref.: SAJCH01706R1

An assessment of critically ill children admitted to a general high care unit in a regional hospital in the Western Cape, South Africa

South African Journal of Child Health

Dear Dr Vosloo,

We are pleased to let you know that your manuscript has now been accepted for publication in South African Journal of Child Health.

Before we send to the production team however, please could you attend to the following technical issues:

1. Please provide a clean version of the manuscript without track changes.
2. References to follow Vancouver style and provide DOIs where possible. Journal titles to be in abbreviated form, not italicised. Please refer to the SAJCH author guidelines for details
3. Figures to be provided in pdf format.
4. Include the following sections after the conclusion of your article:

- Acknowledgements
- Author contributions
- Funding
- Conflicts of interest

If there are none, then just add None.

Please send your amended manuscript to claudian@samedical.org

Also note that as per the author guidelines, page-fee charges have been implemented for all research articles. Please find payment form attached herewith. As soon as proof of payment and the completed form have been received, we will send your article into production. (Please note that we are unable to process American Express card payments). Please send proof of payment to claudian@samedical.org

Nearer the date of publication you will receive page proofs from the copy editor, please check these carefully for errors.

Thank you for submitting your work to the journal.

Best wishes

John Pettifor, MBBCh; PhD

Editor In Chief

South African Journal of Child Health

There is additional documentation related to this decision letter. To access the file(s), please click the link below. You may also login to the system and click the 'View Attachments' link in the Action column.

[View Attachments](#)

In compliance with data protection regulations, you may request that we remove your personal registration details at any time. ([Remove my information/details](#)). Please contact the publication office if you have any questions.

b. Plagiarism declaration

Plagiarism Declaration

“This thesis/dissertation has been submitted to the Turnitin module (or equivalent similarity and originality checking software) and I confirm that my supervisor has seen my report and any concerns revealed by such have been resolved with my supervisor.”

Name: Ruan Vosloo

Student number: VSLRUA001

Signature:

Signature Removed

Date:

06/05/2020

c. Data Collection Sheet

Identifying data

Patient Name:
Hospital number:
Gender:
Date of birth:
Age:
Immunizations up to date (yes, no, unknown):
HIV status (positive, negative, exposed, unknown):
Nutritional status (weight/length/MUAC/WHO Weight-for-height Z-score):

Hospital admission

Admission date and time:
Discharge date and time:
Survival (yes, no):
- If no, state whether demised in HCU, tertiary critical care unit or general ward after discharge from critical care

Critical Care admission

Admission date and time to HCU:
Discharge date and time from HCU:
Length of HCU stay:

Referral to tertiary PICU (yes, no; state Tygerberg Hospital or RCWMCH):
Length of time from decision to transfer until actual transfer:
- When applicable, state reason for delay >24hours:

Referral back from tertiary centre (yes, no):
- If no, state reason (e.g. demised at tertiary centre)
- If yes, state date and time of return to regional hospital

Length of stay at tertiary ICU:

Ventilation support (CPAP/ IPPV/ HFOV):
- Total time requiring ventilation support (first day is day 0, total length during critical care admission, both at Regional and Tertiary level):

Inotropic support (yes, no):
- If yes, state inotropes used (e.g. dobutamine, dopamine, adrenalin)
- Total time requiring inotropic support:

Primary diagnostic category (Discharge diagnosis)

- *Include description of specific diagnosis*

Medical

Central Nervous System
Cardiovascular
Respiratory
Gastrointestinal
Renal
Endocrine
Haematological/ Oncological
Infective
Other (poisoning, rheumatology)

Surgical

Surgical non-trauma

Ruptured appendix
Bowel obstruction
Intussuception
Relaparotomy
Other

Surgical trauma

Head injury
Polytrauma
Burns
Other (snake bites, gunshots, stab wounds)

PIM3 variables

Collected within 1 hour of HCU admission

- | |
|---|
| • Pupillary reaction to bright light (>3mm and both fixed = 1, other or unknown = 0): |
| • Elective admission to ICU (no = 0, yes = 1): |
| • Mechanical ventilation at any time during the first hour in ICU (no = 0, yes = 1): |

- | |
|---|
| • Base excess in arterial or capillary blood, mmol/l (unknown = 0): |
| • Systolic Blood Pressure, mmHg (0 if in cardiac arrest, 30 if shocked and BP unmeasurable, unknown = 120): |
| • FiO2 (record 0 if unknown): |
| • PaO2 (kPa) in arterial or capillary blood (record 0 if unknown): |

- | |
|---|
| • Recovery from surgery or a procedure is the main reason for ICU admission (0 – No, 1 – yes from bypass cardiac, 2 – yes from non-bypass cardiac, 3 – yes from non-cardiac procedure): |
|---|

Risk category

- | |
|--|
| • Low-risk diagnosis (if doubt record 0): 0 – none, 1 – asthma, 2 – bronchiolitis, 3 – croup, 4 – OSA, 5 – DKA, 6 – Seizure disorder: |
| • High-risk diagnosis (if doubt record 0): 0 – none, 1 – spontaneous cerebral haemorrhage, 2 – cardiomyopathy or myocarditis, 3 – hypoplastic left heart syndrome, 4 – neurodegenerative disorder, 5 – NEC: |
| • Very high – risk diagnosis (if doubt record 0): 0 – none, 1 – cardiac arrest preceding ICU admission, 2 – SCID, 3 – leukaemia or lymphoma after first induction, 4 – bone marrow transplant recipient, 5 – liver failure is the main reason for ICU admission: |

d. Informative poster

Neem asseblief kennis (Afrikaans):

Alle kinders onder dertien jaar oud wat in hierdie kritiese sorgteenheid tydens 2016 opgeneem is, sal in 'n waarnemende studie genaamd "An Assessment of Paediatric Critical Care in a Regional Hospital in South Africa" betrek word. Hierdie studie poog om die getal kritieke siek kinders wat in George Streekshospitaal opgeneem is en ook dié wat na tersiêre sentrums verwys word, te beskryf. Slegs roetine data, bv. opnamedatums, diagnose en die graad van siektetoestand sal gebruik word. Alle data sal anoniem bly.

Hierdie studie is deur die Universiteit van Kaapstad Fakulteit Gesondheidswetenskappe se menslike navorsings-etiekkomitee goedgekeur (verwysingsnommer 700/2016).

Ouers, versorgers, wetlike oppassers en pasiënte het die opsie om nie aan hierdie studie deel te neem nie. Indien so verkies, verwittig die eenheidspersoneel van hierdie besluit.

Hierdie studies al deur die volgende dokters uitgevoer word:

Dr S Salie

- *Pediatriese intensiewe sorgspesialis by Die Rooikruis Oorlogsgedenk Kinderhospitaal in Kaapstad*
- *Hoofondersoeker*

Dr R Vosloo

- *Kliniese assistent in Pediatrie by Die Universiteit van Kaapstad*
- *MMed kandidaat en mede-ondersoeker*

Dr WJ Breytenbach

- *Spesialis algemene pediater en hoof van die kliniese eenheid van pediatrie by George streekshospitaal*
- *Mede-ondersoeker en toesighouer*

Kontak gerus Dr Ruan Vosloo via epos by drruanvosloo@icloud.com of via die hospitaal se skakelbord indien daar enige navrae is.

Dankie vir u samewerking.

Please be advised (English):

All children under thirteen years of age that are admitted to this critical care unit during 2016 will be enrolled in an observational study titled "An Assessment of Paediatric Critical Care in a Regional Hospital in South Africa". The study aims to describe the number of critically ill children admitted to George Regional Hospital and those that need to be referred to Tertiary centres. Only routinely collected data will be used, e.g. dates of admission, diagnosis and severity of illness. All data will remain anonymous.

This study has been approved by The University of Cape Town Faculty of Health Sciences Human Research Ethics Committee (reference number 700/2016).

Parents, caregivers, guardians and patients have the option to opt out of this study. Please inform the unit staff of this decision.

The study will be conducted by:

Dr S Salie

- *Consultant Paediatric Intensive Care Specialist at The Red Cross War Memorial Children's Hospital in Cape Town*
- *Principal Investigator*

Dr R Vosloo

- *General Paediatrics Registrar at The University of Cape Town*
- *MMed candidate and co-investigator*

Dr WJ Breytenbach

- *Consultant General Paediatrician and Head of the Clinical Unit of Paediatrics at George Regional Hospital*
- *Local supervisor and co-investigator*

Kindly contact Dr Ruan Vosloo via email at drruanvosloo@icloud.com or via the hospital switchboard if there are any queries.

Thank you for your cooperation.

Sicela niqaphele (isiXhosa):

Bonke abantwana abaneminyaka engaphantsi kweshumi elinesithathu abalaliswa kwicandelo labagula kakhulu bazakubhaliswa kwisifundo esinesihloko esithi "An assessment of Paediatric Critical Care in a Regional Hospital in South Africa". Sizakujongana nenani labantwana abalaliswa kwisibhedlele saseGeorge kunye nabo baphele bethunyelwa kwizibhedlele eziphakamileyo. Kuzakuqokelelwa zinto ezifana nosuku lokulaliswa, isigulo, kwakunye nokuba ugula kangakananina. Yonke into iyakuba yimfihlelo.

Esi sifundo sivunyelwe yi-Dyunivesithi yaseKapa kwicala lezifundo lwezeMpilo nayiKomiti yayo (University of Cape Town Faculty of Health Sciences Human Research Ethics Committee) natsi nenombolo ebonakalisa oku (700/2016).

Abazali, abantu abanemvume yokugada umntwana, kunye nomntwana lowo (isigulana) bavumelekile ukwala ukuthatha inxaxheba.

Iyakuba isenziwa ngaba balandelayo:

Grq S Salie

- *Ugqirha wabantwana kwicandelo labagula kakhulu kwisibhedlele sabantwana i-Red Cross esiseKapa*
- *Umphandi ophetheyo*

Grq R Vosloo

- *uGqirha ofundela ukuba ngugqirha wabantwana kwiDyunivesithi yaseKapa*
- *Umphandi oncedisayo*

Grq WJ Breytenbach

- *Ugqirha wabantwana nomphathi wecandelo lezabantwana kwisibhedlele saseGeorge*
- *Umphandi oncedisayo*

Ungathetha noGqr Vosloo kwi email ethi drruanvosloo@icloud.com okanye ucele isibhedlele sikukhuphele kuye ukuba unemibuzo okanye nantonina ekukhathazayo ngalomba.

Siyabulela ngentsebenziswano yakho