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Paediatric patients ventilated in a high care area in a low resource setting: their characteristics and mortality outcomes

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PAEDIATRIC PATIENTS VENTILATED IN A HIGH CARE AREA IN A LOW RESOURCE SETTING: THEIR CHARACTERISTICS AND MORTALITY OITCOMES

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This research report is submitted in partial fulfilment of requirements for the degree of Master of Medicine in the Department of Paediatrics and Child Health, Faculty of Health Sciences, University of Witwatersrand, Johannesburg

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DECLARATION

I, Shannon Kim Cawood declare that this research report is my own work. It is being submitted for the degree of Masters of Medicine at the University of Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

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Dr Shannon Kim Cawood

.....day of ..... 20 .....

PUBLICATIONS AND PRESENTATIONS

ABSTRACT

Background. The paediatric department at Chris Hani Baragwanath Academic Hospital (CHBAH) in South Africa is able to ventilate patients in a high care area (HCA). Studies have shown that this practice increases patient mortality.

Objectives. To describe patients ventilated in the HCA and their outcomes.

Methods. Retrospective descriptive record review of all children (0-16 years) receiving mechanical ventilation in the HCA of CHBAH between 01 February 2015 and 31 October 2015.

Results. 214 patients were admitted to the HCA for mechanical ventilation. The majority of patients, 116 (54.2%) were infants with a median age of 2.35 months *(IQR*: 28 days - 8.6 months). Eight-point-nine percent of patients were HIV positive. 28.4% of patients were severely underweight, 29.6% severely stunted and 15.7% severely wasted. Acute lower respiratory tract infections were the most common cause for ventilation. In terms of intensive care unit (ICU) candidacy, there was no significant difference in terms of weight-for-age, height-for-age, weight-for-height or HIV status

Of the 214 patients, 69% were ultimately accepted into an ICU. Reasons for ICU refusal included lack of beds or poor candidacy. Sixty-eight (31.8%) patients died, with 36 of these deaths (52.9%) occurring in HCA. The mortality rate in HCA was higher than ICU (45.57% vs. 23.70%).

Conclusions. Mortality is increased when patients are ventilated outside of an ICU.

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Lastly to the patients we serve - may this information assist in continuing to improve services and quality of health care.

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ABBREVIATIONS

CHBAH	Chris Hani Baragwanath Academic Hospital
HCA	High care area
ICU	Intensive care unit
WFA	Weight-for-age
HFA	Height-for-age
WFH	Weight-for-height
USA	United States of America
PICU	Paediatric intensive care unit
HIV	Human Immunodeficiency Virus
PRISM	Paediatric Risk of Mortality Score
PIM	Paediatric Index of Mortality Score
SMR	Standard Mortality Ratio
HAART	Highly active antiretroviral treatment
OPD	Outpatients' department
SSW	Shortstay ward
AW	Admitting ward
NICU	Neonatal intensive care unit
NHLS	National health Laboratory Services
M	Mean
Mdn	Median
SD	Standard deviation
IQR	Interquartile range
NEC	Necrotising enterocolitis
SMR	Standard mortality rate

CHAPTER 1

1.0 INTRODUCTION

Background

Intensive care has become an integral aspect of medical care with the ongoing development of medical strategies to treat medical conditions and prolong life [1]. The management of patients within an ICU environment has been shown to reduce morbidity and mortality [1]. Studies have demonstrated that intensive care in both developed and developing countries is not always used optimally [2]. In developed countries, overuse of ICU results in depletion of resources and extended ICU stays, whilst in developing countries, children who require ICU do not always have access to it [2]. Studies in the United States of America (USA) have shown that paediatric ICUs (PICU) with high volumes of patients have higher mortality rates and longer duration of stay of patients in ICU [3, 4]. Volume was measured by total number of admissions to the unit and did not factor in duration of stay or turnover rates. Rather, duration of stay was assessed as an outcome. [3, 4]

In South Africa, increasing patient numbers, the high burden of disease and the human immunodeficiency virus (HIV) have greatly increased the demand on PICU beds. South Africa has been shown to have limited number of critical care beds including PICU beds [5]. The limited number of PICU beds often results in paediatric patients requiring mechanical ventilation being managed in a general paediatric ward, outside the PICU setting. Studies

have shown that the practice of providing intensive care services in a general paediatric ward outside the ICU setting increases morbidity and mortality and that this practice should be avoided [2]. These studies have also shown an increased mortality in patients admitted to ICU after have been ventilated in general paediatric wards in comparison to patients admitted to ICU directly from the emergency room or operating theatre [6]. One would expect mortality to be lower when patients are admitted from a high care area (HCA) but studies specifically relating to high care areas rather than general paediatric wards have not previously been done.

There are concerns with ventilating patients in a high care area in a general paediatric ward, outside the PICU setting. Firstly, the HCA is run by general paediatricians, not intensivists. Secondly, the ratio of nursing staff to patient is much lower in the HCA and the nursing staff are not trained in critical care. Factors associated with increased mortality in patients admitted from the general ward could also apply to HCA patients. These factors include an increased incidence of comorbidities, prior hospital stay with colonisation of infective organisms, delay in transfer to ICU until clinical deterioration, hemodynamic instability and post-cardiac arrest care [6].

South Africa, a low-middle income country has limited critical care beds and human resources despite having a high burden of diseases, resulting in limitations in the number of ICU beds available [5, 7]. Contributing to this problem is the fact that there is a vast discrepancy between the availability of resources in the public and the private health care systems. The public health system serves more than 80% of the country's population (approximately 40 million people) but only approximately 30% of doctors work in the public

sector [7]. An audit of critical care resources carried out in 2004/2005 showed that there were 4168 ICU and HCA beds in South Africa. Of the 256 private hospitals 216 (84%) had ICU beds while only 92 (23%) of the 396 public hospitals have intensive care units or high care units [5]. Eighteen percent of these intensive care/high care beds were high care beds. This translates to 1783 and 2385 high care and ICU beds in public and private hospitals respectively. The majority of ICUs are within Gauteng, KwaZulu-Natal and the Western Cape [5]. Gauteng, the province in this study hosts 176 ICUS of which 117 are private, holding 1311 beds and 59 ICUS are public, holding 627 beds. ICU beds should comprise 5-12% of hospital beds [5]. Private hospitals reach this target easily at 8.9% but public hospitals fall far short at 1.7% [5]. In Gauteng, the number of ICU beds per population is approximately 1:15 000. The ideal ICU bed to population ratio is that capable of ensuring that all patients likely to benefit from critical care can be admitted to an ICU. The exact figure is difficult to determine as there are many contributing factors. However, this ratio is below that of the estimated 3-25 per 100 000 in developed countries[5]. Of concern, is the finding that a large proportion of ICU/HCA beds were found in public level one hospitals. Level one hospitals are the first level of referral, offering basic diagnostic and therapeutic services. They are staffed by general practitioners, with no specialist services being offered. While these hospitals may have the structural facility, they often do not have the resources or the appropriately trained staff to run ICU units [5].

Due to the aforementioned resource limitations, many children requiring ICU might be denied access to it. Decisions are made daily by medical practitioners regarding the patients' access to intensive care facilities. The imbalance between demand and availability of resources has resulted in the need for strict admission criteria to ICUs. Priority setting is an important and difficult issue faced by health policy makers, where decisions need to be made

regarding use of resources [8, 9]. Practitioners providing the primary care to patients are often not involved in decisions regarding health policies and resource management and the primary decision makers often deliberate without appropriate information [8, 9]. Decisions have to be made at multiple levels as to how healthcare resources should be best allocated to address the vast discrepancies in public health related to demand for paediatric intensive care. These decisions may include whether ICU facilities should be increased or whether stricter admission guidelines should be implemented [10].

The decision regarding acceptance of cases to ICU is very difficult and a physician's subjective opinion often lacks accuracy and reliability [10]. Prognostication of mortality and risk-stratification of patients is very valuable in terms of allocating ICU resources and evaluating the patient's and the ICU's progress. Many factors not related to quality of care influence patients' mortality risk. These include diagnosis, baseline health status and severity of disease [11]. A number of countries have employed the use of objective scoring systems such as the Paediatric Risk of Mortality Score (PRISM) or Paediatric Index of Mortality Score (PIM) to predict mortality accurately while adjusting for case factors and disease severity [12]. These scores cannot be used to determine whether or not a patient is an ICU candidate but instead are used to predict mortality in a patient already admitted into ICU. The PIM score is a point-of-care score looking at eight variables collected within the first hour of contact with the patient in ICU. The PRISM score looks at fourteen variables collected over the first 24 hours following the patient's ICU admission. As the PIM score collects variables within the first hour, it is a better reflection of the patient's status prior to ICU admission. The PIM score also allows for earlier identification of high-risk patients than the PRISM score and has greater usefulness [12]. Neither score has been shown to be very accurate in predicting mortality, with both scores underestimating mortality. The usefulness

of such scores has also not been established in developing countries [10]. These scores were developed in the USA and validated in Europe and studies done on these scoring systems in developing countries have not shown good concordance with outcome. This may be due to different patient demographics, disease patterns and severity of disease in patients from developing countries [10, 13]. The performance of PIM scores has been shown to be marginally more acceptable and relatively better than PRISM scores [14]. Until better scores are formulated, the PIM and PRISM scores are the preferred scores for predicting mortality in patients requiring critical care. Probability of mortality scores can be calculated through online PIM calculators or using the equation "exp(PIM score)/(1+exp(PIM score))" to estimate risk of death[11]. In conjunction with mortality scores, a standard mortality ratio (SMR) is used to assess the performance of a unit. The SMR is calculated by dividing the number of 'observed deaths' by the number of 'expected deaths'. 'Expected deaths' data is gained from the PIM or PRISM score. If the unit SMR is equal to 1 then the mortality outcome of that unit is as expected. If the SMR is more than 1 then the mortality outcome is worse than expected and if less than 1 it is better than expected[11].

Decision-making regarding access to intensive care is made even more challenging in South Africa due to the high burden of disease in an already resource-limited healthcare system. The burden of disease is compounded by the high incidence of HIV and malnutrition. South Africa holds 0.7% of the world's population but 17% of the worldwide HIV burden [15]. Recent surveys have found the incidence of HIV in South African children aged 0 to 14 years to be 2.4% [16]. Recent surveys on nutritional status in children under 5 years of age showed that in South Africa 9% of children are underweight, 24% are stunted and 5% are wasted [17]. In the past, both HIV and malnutrition were seen as limiting factors for admission to ICU, as these patients have a higher incidence of infection and mortality [18]. However, a

study carried out in Brazil between 2006 and 2008 showed that malnutrition in critically ill patients was not an indicator of increased mortality, though these patients did have a longer duration of stay in ICU [18].

The morbidity and mortality rates of HIV infected patients have been greatly reduced by the availability of highly active antiretroviral treatment (HAART). Prior to the rollout of HAART in public health care facilities HIV infected patients admitted to ICU had poor outcomes [19-21]. HAART has resulted in a marked improvement in paediatric morbidity and mortality in HIV-infected children and HIV infection in itself should no longer be considered a limitation to ICU admission [2, 19-21].

Chris Hani Baragwanath Academic Hospital in Soweto, South Africa has the unique ability to ventilate paediatric patients in a high care area outside of an ICU for a period of time. The outcomes of such patients had not been studied previously. This study aimed to describe the characteristics of these patients and their indications for ventilation. It aimed to determine whether the hypothesis that ventilating outside of an ICU increased mortality was applicable to patients ventilated in a high care area.

1.1 AIMS AND OBJECTIVES

This aim of the study was to describe the clinical features and outcomes of critically ill neonates and paediatric patients requiring mechanical ventilation managed outside the ICU setting in a HCA placed in a general paediatric ward at Chris Hani Baragwanath Academic Hospital (CHBAH) in Soweto, South Africa.

The objectives of this study are listed below.

1. To describe the patients ventilated in the high care area at CHBAH between 01 February 2015 and 31 October 2015 with regards to age, sex, nutritional status, HIV status, clinical diagnosis, area of origin, indication for ventilation and need for inotropic support.
2. To determine the proportion of patients accepted to an ICU and to compare characteristics of those accepted with those not accepted.
3. To describe the course of events following ventilation in a HCA with regards to length of stay; time to acceptance to an ICU and time to transfer to an ICU once accepted
4. To compare mortality rates of patients ventilated in the high care area with mortality rates of those transferred to an ICU.

CHAPTER 2

2.0 MATERIALS AND METHODS

2.1 Study Population

The study was a retrospective descriptive record review of all children (0-16 years) who received mechanical ventilation in the high care area of CHBAH between 01 February 2015 and 31 October 2015.

2.1.1 Inclusion criteria

1. All children under 16 years of age admitted to the high care area of CHBAH who received mechanical ventilation between 01 February 2015 and 31 October 2015 on whom data was collected.

2.1.2 Exclusion Criteria

1. Patients who were intubated at the request of ICU and transported immediately to ICU, with no time spent ventilated in the high care area

2.2 Study Setting

The study took place at CHBAH, a tertiary level institution and the third largest hospital in the world, situated in Soweto in the south of Johannesburg, South Africa. It serves the community of Soweto with over 1.2 million people, as well as serving as a referral hospital for surrounding provinces as well as from neighbouring African states [22]. More than 2000 patients are attended to in the hospital's facilities daily [22].

The paediatric department manages a high number of patients with a variety of conditions and in a variety of specialised paediatric fields. The paediatric wards admit on average 15-30 patients daily. Paediatric patients attending the hospital are initially assessed in the paediatric out-patients' department (OPD), where they are assessed and triaged, with the decision made to discharge the patient, send them to a short-stay ward (SSW) or send them to the admitting ward (AW). Once in the AW, they are seen by a paediatric registrar and admitted to the general paediatric wards. Patients may also be transferred to the AW from other areas of the hospital such as the surgical wards, or from other primary or secondary level hospitals.

A small percentage of paediatric patients, on admission or at a point during their admission, may require mechanical ventilation and intensive care services. These patients are admitted to the HCA in the AW at the discretion of the admitting paediatric registrar. There is currently no formal protocol or criteria as to which patients may be admitted into the HCA. The HCA has the capacity to ventilate two patients at a time and accommodate up to ten

non-ventilated patients. One qualified nursing sister manages the unit with two to three staff nurses at her assistance. Paediatric patients requiring mechanical ventilation may be ventilated for a time in this HCA before being accepted into one of the ICU's. The protocol guiding these admissions state that the period of ventilation should not exceed 48 – 72 hours. The HCA area should be used as a holding area for patients prior to transfer to ICU or as a step-down area for patients discharged from ICU. However, the limited number of ICU beds available, coupled with the ICUs' admission criteria often result in patients being ventilated for longer than the stipulated 48-72 hours or in some instances, more than two patients being ventilated in the HCA at a time. Additionally, once a patient is accepted to ICU, delays in ICU admission may occur for multiple reasons including lack of ICU beds, shortage of ICU staff and prolonged waiting time for transport.

The paediatric department is supported by a paediatric intensive care unit (PICU) and a neonatal intensive care unit (NICU). The PICU has the capacity for 8 paediatric beds that are managed by paediatric intensivists with a nurse-to-patient ratio of 1:1. A minimum of two medical officers or registrars and one consultant are on duty for 24 hours with more staff on site in daytime hours. The NICU has the capacity of 18 beds, run by neonatologists with a nurse-to-patient ratio of 1:2. Two registrars and one consultant are on duty for 24 hours with more staff on site in daytime hours. Both ICUs accept patients from general paediatrics as well as from other paediatric specialities. Both ICUs have requests daily that outnumber the number of beds available. Currently, each ICU has its own criteria for admission. The NICU only specifies that the patient must be under 3.5kg, irrespective of age. This is due to the fact that the PICU's ventilating equipment is only appropriate for patients weighing more than 3.5kg and so, smaller paediatric patients need to be managed in the NICU. Admission is subject to assessment by the neonatologist in charge of the NICU at that time. The criteria

for the PICU are attached as Appendix D. Each patient is discussed with, and where possible, assessed by, an intensivist from PICU or a neonatologist from NICU upon request for an ICU bed.

Patients may be denied ICU admission for any number of reasons. The lack of ICU beds is a frequent problem. In these circumstances the paediatric registrar will attempt to find an ICU bed in another hospital. If unsuccessful, the patients are ventilated for a period of time in high care that should not exceed 48-72 hours until either clinical improvement occurs and the patient is extubated, a bed becomes available in an ICU, the decision is taken to withdraw support or the patient demises. Such decisions are made at the discretion of the attending paediatrician. Once a patient has been assessed as a poor ICU candidate, delays in withdrawal of treatment usually occur whilst families are undergoing counselling.

2.3 Data Collection

Data on all the patients was gathered from an existing database that is collected in the HCA for statistical purposes. A copy of this database is shown in Appendix A. The database identified all patients ventilated in the HCA during this period and recorded patient characteristics as well as data regarding their acceptance and transfer to an ICU, as well as the patient's outcome. Individual patient hospital clinical records were reviewed and laboratory results were accessed from the National Health Laboratory Services (NHLS) to gain further necessary data.

Data collected included patient demographic characteristics, nutritional status, HIV status, medical diagnosis, indication for mechanical ventilation, need for inotropic support, consultation of ICU, acceptance to ICU, time to transfer to ICU and outcome. Data necessary to calculate a PIM score was also collected. Admission books in the paediatric outpatients' department, were accessed to record the total number of patients seen and number admitted. Admission books in the AW, were also accessed to record the number of patients admitted to HCA compared to the total number of patients admitted. In the ICUs, admission books were accessed to gather data on admission time as well as date and time of death if death had occurred in the ICU.

Data was captured into REDCap electronic data capture tool hosted at the University of Witwatersrand [23]. Anthropometrical Z-scores were calculated using a World Health Organisation calculator Anthro, version 3.2.2, January 2011. Diagnosis was captured according to ICD-10 coding as per the attending paediatrician's assessment.

Certain patient details were considered to be missing if the original patient hospital records could not be retrieved. In such cases, data recorded in the existing database was relied upon.

2.4 Statistical Analysis

Statistical analysis was performed using STATISTICA version 12 software (StatSoft, Inc, Tulsa, OK, USA; 2012. Available from: http://www.statsoft.com). Categorical variables were described using frequencies and percentages. Continuous variables were described

using means and standard deviations for normally distributed data, and medians, interquartile ranges and ranges for data not normally distributed. Bivariate statistical analysis was performed to compare differences in characteristics between patients who were deemed good candidates for ICU and those who were deemed poor candidates. Differences in frequency of acceptance as well as time to transfer between PICU and NICU were also compared. PIM scores and probability of mortality scores were compared in patients who were assessed as either good or poor ICU candidates; in patients who died versus patients who survived; and in patients who died in HCA versus patients who died in ICU. Standard mortality rates were calculated for good versus poor ICU candidates; and in patients who died in HCA versus who died in ICU. Chi-squared tests were used for the comparison of categorical variables. Student t-tests and Mann-Whitney tests were used for the comparison of continuous variables for parametric and non-parametric data respectively. A p-value of less than 0.05 was considered to be statistically significant.

2.5 Ethical Considerations

As this was a retrospective study, informed consent from patients or their parents was not required. Ethical clearance was obtained from the University of the Witwatersrand Human Research Ethics Committee: (Medical) (reference: M150821, Appendix B). Permission to conduct research at CHBAH was obtained from the Medical Advisory Committee at CHBAH (Appendix C). Permission to access the database in the paediatric high care was obtained from the head of the HCA in the paediatric department of CHBAH. All information identifying patients was kept confidential and was only available to the primary investigator. Patients' personal details were not included in the study. As the study was retrospective there

was no direct risk to the participants. There was also no direct benefit to the participants of the study, although the outcome of the study may beneficially influence future management of patients requiring intensive care if more resources are made available.

2.6 Funding

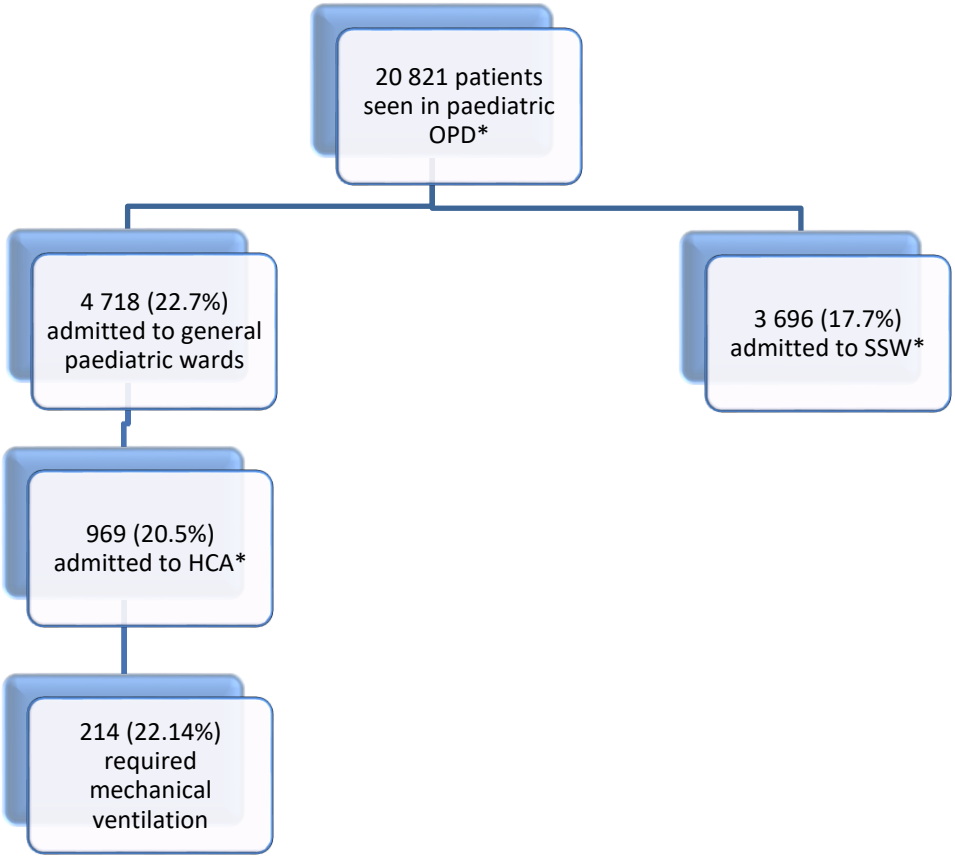
All funds required during the study period were covered by the researcher. No external funding was obtained.

CHAPTER 3

3.0 RESULTS

3.1 Demographics and Patient Characteristics

During the 9 months of the study 20 821 patients were seen in the paediatric outpatients' department of CHBAH. Figure 3.1 outlines the number of patients admitted from OPD. The 214 patients requiring mechanical ventilation makes up 4.5% of all patients admitted to the paediatric medical service.



*OPD – outpatients' department, *SSW – short stay ward, *HCA – high care area

Figure 3.1. Patients admitted to the paediatric service

Male patients constituted 115 (53.7%) of the ventilated cases and 195 (91.1%) were HIV negative. Table 3.2 further outlines HIV status of the patients. The median age of patients ventilated in HCA was 2.35 months *(IQR*: 28 days - 8.57 months) with a range of one day to 15.42 years. The majority of patients (n = 116; 54.2%) were infants between 28 days and 1 year. Twenty-five patients (11.7%) were between 1 and 5 years, 18 patients (8.4%) were between 5 and 13 years and only 3 patients (1.4%) were older than 13 years. There were 52 neonates of which 14 (26.9%) were premature births, with 11 still not having reached term for corrected gestational age. Gestational ages of premature babies were not always available thus anthropometry was described in groups with neonates (0-28days) analysed separately. The median weight for all children was 4.17kg (*IQR*: 3.00 - 7.30kg) with a range of 1.53kg

to 70.00kg. Heights were available for only 149 (69.6%) of the cases. Median height was 56.00cm (*IQR*: 50.00 - 64.00cm) with a range of 35.00cm to 160.00cm. Weight for height (WFH) could only be calculated in 149 (69.6%) of cases. See Table 3.1 for stratified Z-scores and HIV status.

Table 3.1 Anthropometry and HIV status of paediatric patients ventilated in HCA

Variable	**0-28 days (*n*=52**	**≥ 28 days (*n*=162)**
Weight (kg), *Mdn (IQR)*	2.95 (2.17;3.40)	5.03 (3.73;9.86)
Height (cm), *Mdn (IQR)*	50.00 (47.75;52.00)	58.00 (52.00;73.00)
Weight for age Z-score, *Mdn (IQR)*	-1.49 (-3.44;-0.84)	-1.89(-3.41:-0.54)
Height for age Z-score, *Mdn* (IQR)	-1.02 (-2.24;0.34)	-1.66 (-2.97:0.39)
Weight for height Z-score, *Mdn (IQR)*	-2.04 (-3.64;-0.14)	-0.86 -2.51:0.72)
Weight for age Z-score, *n* (%)		
≤ -3	18 (34.6)	46 (28.4)
-3 → -2	6 (11.5)	33 (20.4)
-2 → +2	28 (53.9)	81 (50.0)
+2 → +3	0 (0.0)	2 (1.2)
≥ +3	0 (0.0)	0 (0.0)
Height for age Z-score *n*=149, (%)	***n*=34**	***n*=115**
≤ -3	5 (14.7)	34 (29.6)
-3 → -2	7 (20.6)	17 (14.8)
-2 → +2	20 (58.8)	59 (51.3)
+2 → +3	2 (5.9)	1 (0.9)
≥ +3	0 (0.0)	4 (3.4)
Weight for height Z-score *n*=149, (%)	***n*=34**	***n*=115**
≤ -3	13 (38.2)	18 (15.7)
-3 → -2	4 (11.8)	20 (17.4)
-2 → +2	17 (50.0)	62 (53.9)
+2 → +3	0 (0.0)	6 (5.2)
≥ +3	0 (0.0)	9 (7.8)
HIV status, *n* (%)		***n*=214**
Negative	**195 (91.1)**	
Unexposed, uninfected		120 (61.5)
Exposed, uninfected		75 (38.5)
Positive	**19 (8.9)**	
Positive, on HAART		3 (15.8)
Positive, not on HAART		16 (84.2)

Of the 214 cases 167 (78.0%) were admitted to the HCA for ventilation from the paediatric admissions ward. Table 3.2 outlines the referral site of the cases.

Table 3.2 Referral site of paediatric patients admitted to HCA for ventilation

Area admitted from (*n*=214)	**Cases *n* (%)**
Paediatric admissions	167 (78.0)
General paediatric wards	16 (7.5)
Specialty wards (cardiac, haematology/oncology)	1 (0.5)
Short-stay ward	3 (1.4)
Adult medical casualty	1 (0.5)
Surgical casualty	7 (3.2)
Outside hospital	19 (8.9)

Indication for mechanical ventilation was also grouped into categories. The majority of patients, 88 (41.1%) required ventilation for type 1 respiratory failure. See Table 3.3 for further breakdown of these characteristics. Seventy-seven (36.0%) required additional inotropic support.

Table 3.3 Indication for mechanical ventilation

Indication for ventilation, *n* = 214	**Cases** *n* (%)
Respiratory	**160 (74.8)**
Type 1 respiratory failure	88 (55.0)
Type 2 respiratory failure	34 (21.3)
Apnoeas	34 (21.3)
Upper airway obstruction	4 (2.4)
Circulatory	**37 (17.3)**
Cardiorespiratory arrest	10 (27.0)
Cardiac failure	1 (2.7)
Shock - cardiogenic	3 (8.1)
Shock - septic	8 (21.6)
Shock - hypovolaemic	1 (2.8)
Severe metabolic acidosis	14 (37.8)
Neurological	**13 (6.0)**
Airway protection	13 (100.0)
Pre-/post-surgery/-intervention	**4 (1.9)**

The patients' diagnoses were grouped into broad categories. The majority of patients [111 (51.9%)] presented with acute lower respiratory tract infections. Infections (including lower respiratory tract infections, meningitis, sepsis and acute gastroenteritis) accounted for 74.3% of all admissions to HCA requiring mechanical ventilation (see Table 3.4).

Table 3.4 Diagnosis

Diagnosis, *n* = 214	**Cases** *n* (%)
Respiratory	**115 (53.7)**
Lower respiratory tract infection	111 (96.5)
Upper airway obstruction	4 (3.5)
Cardiac	**12 (5.6)**
Congenital heart disease	5 (41.7
Dilated cardiomyopathy/Myocarditis	7 (58.3)
Renal	**7 (3.3)**
Nephrotic syndrome	4 (57.1)
Chronic kidney disease	3 (42.9)
Neurology	**19 (8.9)**
Seizures	7 (36.8)
Encephalopathy	3 (15.8)
Acute flaccid paralysis	1 (5.3)
Meningitis	8 (42.1)
Endocrine	**1 (0.5)**
Diabetic ketoacidosis	1 (100.0)
Infectious	**40 (18.7)**
Sepsis (including neonatal sepsis)	30 (75.0)
Acute gastroenteritis	10 (25.0)
Neonatal (excluding neonatal sepsis)	**6 (2.8)**
NEC*/Malrotation/Volvulus	4 (66.7)
Jaundice	2 (33.3)
Other	**14 (6.5)**
Poisoning	7 (50.0)
Malignancy	5 (35.8)
Burns	1 (7.1)
Near-drowning	1 (7.1)

*NEC - necrotising enterocolitis

3.2 Evaluation of patients for ICU admission

In 197 (92.0%) of the 214 ventilated cases an ICU (either PICU or NICU) was consulted. PICU was consulted in 119 (60.4%) cases, NICU in 69 (35.0%) and both were consulted in nine (4.6%) cases where weight was approximately 3.5kg (the differentiation between patients for NICU or PICU). Of the 17 cases where an ICU was not consulted, nine were deemed to be poor candidates by the general attending paediatrician in the HCA, one died before ICU could be consulted and seven patients had clinically improved with extubation imminent before an ICU was consulted.

Of the 197 patients where an ICU was consulted, 82 (41.6%) cases were accepted on the day of consultation, 64 to PICU and 18 to NICU. One of the 64 patients accepted by PICU had been referred to both ICU's but accepted by PICU (see Table 3.5). One hundred and fifteen (58.4%) patients were not accepted initially to an ICU, 56 denied by PICU, 51 denied by NICU and 8 denied by both (see Table 3.5). Ninety-two (80.0%) of these 115 patients were not accepted due to no beds being available and 22 (19.1%) were due to them being assessed as poor candidates by the ICU team. One (0.9%) of the patients was assessed by the ICU team as being ready for extubation and thus not needing ICU care. Of the 115 patients not accepted initially, beds subsequently became available in a CHBAH ICU in 21 (18.3%), 15 in PICU and 5 in NICU. Three of these patients had initially been deemed to be poor candidates but had improved clinically and had been reassessed. Beds were found in an outside ICU for 33 patients (28.7%) although one of these patients died before transfer. Therefore 136 (69.0%) patients of the 197 referred to an ICU were ultimately accepted to an ICU, with 103 (52.3%) of these patients being accepted to a CHBAH ICU. Sixty-one (53.0%) patients stayed in HCA, 18 of these having been deemed poor candidates for ICU.

Of these 18 patients, 7 had treatment withdrawn with 3 of these patients surviving and 4 dying. Eight patients died without withdrawal. One patient had ventilation withdrawn and survived. Two patients continued to be ventilated at the discretion of the attending paediatrician and recovered. Figure 3.2 outlines the overall outcome of all 214 patients.

Table 3.5 Number of patients referred to and initially accepted by the different ICUs

ICU consulted, *n* = 197	**Cases (*n*, %)**
PICU	**119 (60.4)**
Accepted	63 (52.9)
Denied	56 (47.1)
NICU	**69 (35.0)**
Accepted	18 (26.1)
Denied	51 (73.9)
Both	**9 (4.6)**
Accepted (by PICU)	1 (11.1)
Denied	8 (88.9)

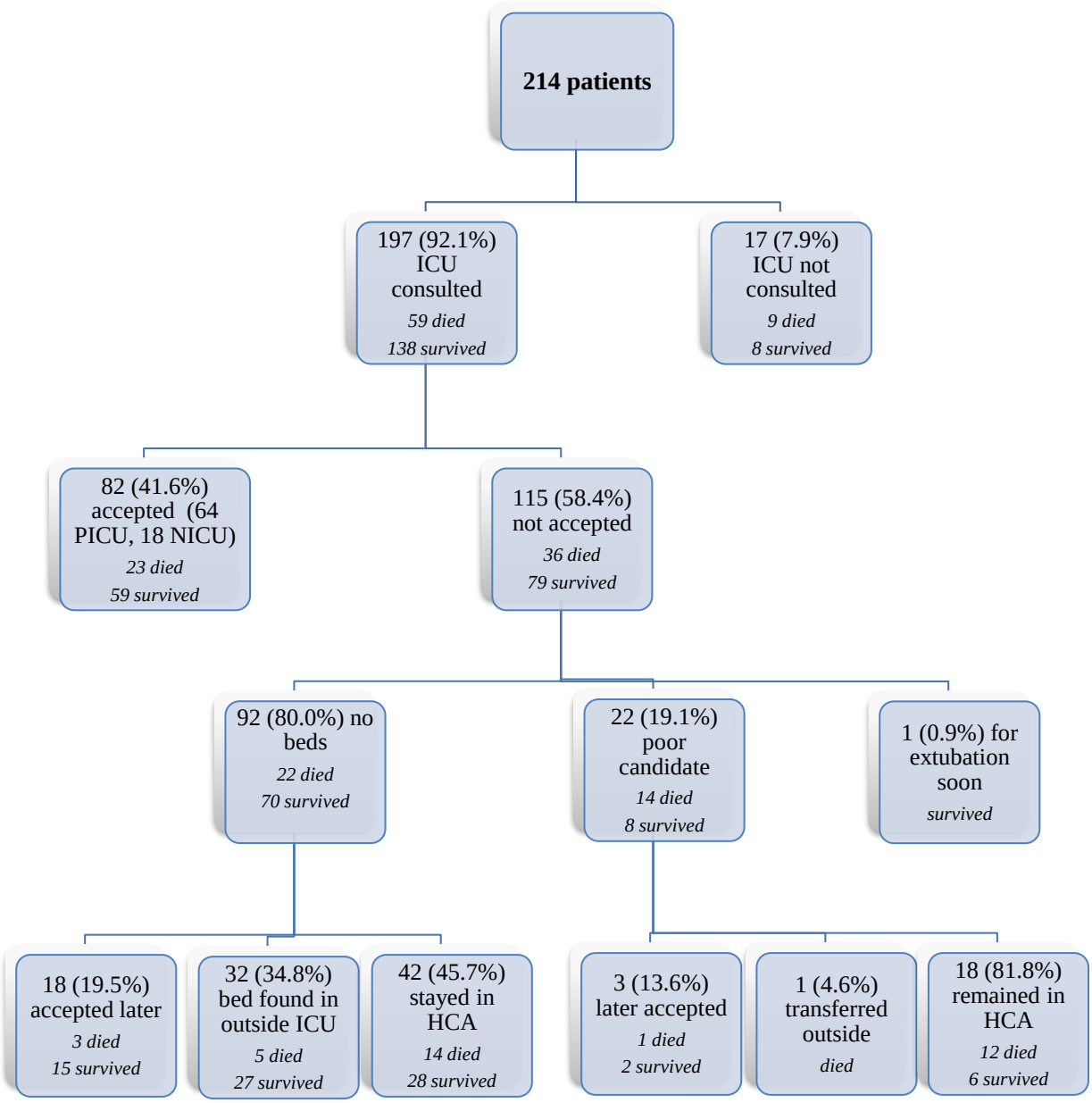


Figure 3.2 ICU acceptance and mortality outcomes of patients ventilated in HCA

Of the 115 patients not accepted to an internal ICU on the day of consult, 22 (19.1%) were deemed poor candidates for ICU and remained in the HCA with 14 (63.6%) of these 22 patients dying. Twenty-one (18.2%) of the 115 patients were accepted later to an internal ICU. (Three of these patients had initially been deemed to be poor candidates however their clinical conditions improved in HCA and they were reassessed and later accepted by the ICU teams.) Thirty-three (28.7%) of the 115 patients were accepted to an outside ICU, with 5 of these patients dying. (One of these patients had been deemed a poor candidate by CHBAH internal ICU however an outside ICU did accept this patient. Ultimately this patient died in HCA before the transfer occurred.) Therefore, out of the 115 patients not accepted to an internal ICU, 61 (53.0%) remained in HCA with 26 (42.6%) of these patients dying. A further 17 patients who were never referred to an ICU remained in HCA, with 10 of these patients dying.

Once an internal ICU was consulted and a case accepted, the median time to transfer was 7.17 hours (*IQR*: 4.00 - 12.80 hours) with a range of 1.00 to 29.00 hours for those cases accepted on the day of consult. The patient taking 29 hours to be transferred to ICU had been accepted into the ICU during day nursing staff hours but not enough nursing staff was available at night to accept the patient and thus the patient was transferred the following day. When time to transfer was analysed including the patients accepted later to an internal ICU the median time to transfer was 9.50 hours (*IQR*: 4.80 - 18.50 hours) with a range of 1.00 to 72.00 hours. The patient taking 72 hours to be transferred was initially not accepted into the ICU due to lack of beds and was accepted at a later stage when a bed was available. When comparing the time taken to transfer patients to either ICU, there was no significant difference between PICU and NICU ($p = 0.42$). The median length of stay in the HCA was 3 days (*IQR*: 2 -5 days) with a range of 1 to 21 days. Median length of ventilation in the

HCA was 2 days (*IQR*:1;3 days) with a range of 1 to 10 days. Median length of stay in hospital was 13 days (range 1;210 days).

3.3 Comparison between good and poor ICU candidates

An analysis was carried out to determine whether characteristics differed between the 148 patients assessed as good candidates for ICU admission not withstanding bed status and the 20 refused ICU due to being a poor candidate. In this analysis, patients where ICU was not consulted were excluded, as well as patients where ICU had no beds and did not clarify whether or not the patient was an ICU candidate. This analysis is depicted in Table 3.6.

Table 3.6 Characteristics of patients deemed good candidates for ICU compared to patients who were deemed poor candidates

	Good candidate (*n*=146)	**Poor candidate (*n*=22)**	***p*-value**
Age in months *Mdn* (*IQR*)	2.55 (1.00 - 6.47)	14.25 (3.03 – 42.56)	.01
Weight for Age Z -score, *Mdn* (*IQR*)	-1.56 (-3.41;-0.54)	-2.05 (-2.91;-1.42)	.95
Height for Age Z-score, *Mdn (IQR)*	-1.50 (-3.69;-0.34) *(n=103)*	-2.09 (-2.60;-1.59) *(n=13)*	.70
Weight for Height Z-score, *Mdn (IQR)*	-0.63 (-2.48;0.78) *(n=96)*	-1.71 (-2.73;-0.73) *(n=13)*	.32
HIV, *n* (%)			
Positive	15 (10.3)	2 9.1)	.86
Negative	131 (89.7)	20 (90.9)	
Diagnosis, *n* (%)			
Respiratory	99 (67.8)	3 (13.6)	0.02
Cardiac	6 (4.1)	2 (9.1)	.28
Renal	5 (3.4)	1 (4.5)	.52
Neurology	7 (4.8)	6 (27.3)	.04
Endocrine	1 (0.7)	0 (0.0)	.73
Infectious	19 (13.0)	6 (27.3)	.02
Neonatal	3 (2.1)	2 (9.1)	.84
Other	6 (4.1)	2 (9.1)	.34
Weighted diagnosis according to PIM score, *n* (%)			
Very high risk	3 (2.1)	6 (27.3)	<.001
High risk	22 (15.1)	10 (45.4)	.32
Low risk	121 (82.8)	6 (27.3)	<.001
Mechanical ventilation, *n* (%)			
Respiratory	128 (87.7)	8 (36.4)	<.001
Cardiac	11 (7.5)	10 (45.4)	<.001
Neurological	5 (3.4)	4 (18.2)	.06
Post-surgery/ intervention	2 (1.4)	0 (0.0)	.72
Need for inotropes, *n* (%)			
Yes	39 (26.7)	14 (63.6)	<.001
No	107 (73.3)	8 (36.4)	<.001
PIM score, *Mdn (IQR)*	-5.16 (-5.75;-4.16) *(n=116)*	-2.09 (-5.25;0.42) *(n =12)*	.02
Probability of mortality (%), *Mdn (IQR)*	0.57 (0.32;1.54) *(n =116)*	10.91 (.52;39.63) *(n=12)*	.02

3.4 Mortality and Mortality Scores

Of the 214 patients, 68 (31.8%) died. Twenty-one (30.8%) of the 68 deaths occurred in PICU, six (8.8%) in NICU and five (7.3%) in an outside ICU. The remaining 36 (52.9%) deaths occurred in HCA. In 9 of these cases, ICU was not even consulted. Of the patients that went to ICU, 23.7% died. Of those that went to an internal ICU 26.2% died with 26.3% occurring in PICU and 26.1% occurring in NICU. Of those who went to an external ICU 15.6% died. Of the patients that remained in HCA 45.6% died. The majority of deaths occurred in the infant group. Twenty-eight (41.2%) occurred in the infant group. Twenty (29.4%) deaths occurred in the neonatal age group, 12 (17.6%) in the age group 1-5 years, and 8 (11.8%) deaths above 5 years. Although the majority of deaths occurred in the infant group, when analysing number of deaths per each age group of ventilated patients, patients aged 1-5 years had the highest percentage mortality rate (48.0% of 1-5-year-old group), with neonates having the next highest mortality rate at 38.5% of the neonatal group.

Majority of diagnoses in patients that died was lower respiratory tract infection (36.8%) with sepsis being the next most common diagnosis (20.6%). Table 3.7 outlines the diagnoses of all the patients that died.

Table 3.7 Diagnoses of patients that died

Diagnosis	**Cases (*n*, %)**
Respiratory	**25 (36.8)**
Lower respiratory tract infection	25 (36.8)
Cardiac	**8 (11.8)**
Congenital heart disease (hypoplastic left heart, complex congenital heart disease, tricuspid atresia, partial anomalous pulmonary venous drainage)	4 (5.9)
Dilated cardiomyopathy/Myocarditis	4 (5.9)
Renal	**2 (2.9)**
Nephrotic syndrome	2 (2.9)
Hepatic	**1 (1.5)**
Fulminant liver failure	1 (1.5)
Neurology	**3 (4.4)**
Status epilepticus	2 (2.9)
Encephalopathy (Shigella)	1 (1.5)
Infectious	**20 (29.4)**
Sepsis	14 (20.6)
Acute gastroenteritis	1 (1.5)
Meningitis	5 (7.4)
	3 (4.4)
Neonatal	2 (2.9)
Necrotising enterocolitis	1 (1.5)
Jaundice	
Other	**6 (8.8)**
Poisoning (unknown)	1 (1.5)
Malignancy (3 acute lymphoblastic leukaemia, retinoblastoma, brain tumour - no histology)	5 (7.4)

Currently no standardised mortality score is used to assess these patients for admission to ICU. PIM scores could be calculated for 114 of the 148 patients who were deemed to be good ICU candidates and for eight of the 20 patients who were deemed to be poor ICU candidates. The analysis showed that PIM scores were lower in good candidates, *Mdn* = -5.19 (*IQR:*-5.78;4.18) while PIM scores in poor candidates were calculated at *Mdn* = -2.52 (*IQR:*-4.67;-0.74), $p<0.001$. Probability of mortality scores were thus higher in poor candidates, *Mdn* = 7.98% (*IQR:*1.09;92.70) whilst probability of mortality scores were much

lower in good candidates at *Mdn* = 0.55% (*IQR:*0.31;1.54), p<0.001. However, the PIM score should not be used to determine whether a patient should be admitted to ICU or not but should rather be used once a patient is admitted to an ICU to predict risk of mortality.

Sufficient data was available to perform PIM scores on 111 of the 146 patients who survived and 32 of the 68 patients that died. PIM scores were higher in patients who ultimately died, *Mdn* = -3.90 (*IQR:*-5.50;-1.11) than in patients who survived, *Mdn* = -5.10 (*IQR:*-5.79;-4.23), *p* = 0.01. Probability of mortality scores were higher in patients who ultimately died, *Mdn* = 2.02% (*IQR:*0.41;24.7%) than in patients who survived, *Mdn* = 0.61% (*IQR*:0.31;1.44%), *p* = 0.09. Factors contributing to increased risk of mortality included need for inotropic support and high-risk diagnoses, both of which contribute to a worse PIM score. A standard mortality ratio (SMR) was calculated for those cases where enough data was available to calculate a PIM score. The SMR was 2.23, indicating that more deaths occurred overall in both ICU and HCA than was expected as predicted by the PIM score.

In patients who were assessed as poor candidates, PIM scores between those that died and those that survived were analysed. This analysis was limited by small numbers of where PIM scores could be calculated. PIM scores in those that died were higher, *M* = -2.70 (*SD* ± 2.33) whereas the PIM in those that survived was *Mdn* = -2.52 (*IQR*:-4.25;0.24), p=0.76. Probability of mortality in patients that died were much higher, *M* = 16.89% (*SD* ± 19.11%) while the probability of mortality in those that survived was *Mdn* = 7.98% *(IQR:*2.71;51.95), p=0.68.

Conversely, in patients who died, PIM scores between those that were deemed poor candidates and those that were deemed good candidates were analysed. This analysis was limited by small numbers of where PIM scores could be calculated. PIM scores in poor candidates were lower, *M* = -2.70 (*SD* ± 2.33) while PIM scores in good candidates were *Mdn* = -4.16 (*IQR:*-5.58;-1.61), p= 0.34. Probability of mortality scores were much higher in poor candidates, *M* = 16.89% (*SD* ± 19.11%) while probability of mortality in good candidates was *Mdn* = 1.54% (*IQR:* 0.37%;16.72%), p = 0.35.

We analysed PIM scores and probability of mortality scores in those patients that died in ICU compared to those that died in HCA. We excluded patients where ICU was never consulted as the attending practitioner assessed these patients as poor candidates. See table 3.8 for this comparison. The SMR for those patients who died in ICU was 1.32 while the SMR for patients who died in HCA was 3.27. These SMR's show that in both ICU and HCA more patients died than was expected as predicted by the PIM score. However, the SMR was much worse in HCA, indicating that mortality was much more than expected as predicted by the PIM score.

Table 3.8 PIM scores in patients who died in HCA versus patients who died in ICU

	Patients who died in ICU (n=20)	**Patients who died in HCA (n=8)**	***p*-value**
PIM score, *Mdn (IQR*)	-5.06 (-5.58;-2.42)	-2.04 (-4.68;-0.81).	.12
Probability of mortality scores %, *Mdn (IQR*)	0.63 (0.37% ;8.20%)	*14.46* (1.09;31.04)	.20

When comparing patients who were deemed to be good candidates and were ventilated in HCA versus patients who were ventilated in an ICU, whether internal or external, the odds ratio of mortality was 1.80 (95% confidence interval of 1.39 to 6.03) indicating that mortality was increased in patients who were ventilated in a HCA versus patients who were ventilated in an ICU.

CHAPTER 4

4.0 DISCUSSION

Chris Hani Baragwanath Academic Hospital is in the unique position of being able to ventilate patients for a period of time in a high care area before the patient is transferred to an ICU. In this study, 214 patients that were ventilated in the HCA in a 9-month period were assessed. Of these 214 patients, 197 were referred to an ICU with 41.6% being accepted to an internal ICU on the day of consult. Of the 115 patients initially not accepted to an ICU, 80% who were denied access to ICU care were due to there being no beds. Ultimately 69% of patients were accepted to either an internal or outside ICU. Of the 135 patients who were accepted to an ICU, 23.7% died. Of the 79 patients that remained ventilated in HCA, 45.6% died. However, 33 patients who remained in HCA were deemed poor candidates and 66.6% of these died. Fourty-six of the patients who remained in HCA were assessed as good candidates but no ICU beds were available and 30.4% of these patients died. Nevertheless, the odds of mortality of patients who were assessed as good candidates and remained ventilated in HCA versus patients who were ventilated in an ICU was 1.8 (95% confidence interval of 1.39 to 6.03). Additionally, the SMR of patients ventilated in ICU was 1.32 versus 3.27 in HCA. This indicated that in both areas, more patients died as was expected as predicted by the PIM score, however the SMR was significantly worse in HCA.

The 214 patients admitted to the HCA for mechanical ventilation during the period of this study constituted 4.5% of all patients admitted to the paediatric service. A study in the Cape Town Metro district stated that 6.9% of paediatric admissions to hospitals required ICU [24].

These figures include paediatric patients requiring ICU for reasons other than ventilation. In another study at King Edward VIII Hospital in Durban, South Africa 7% of the general paediatric hospital population was admitted to ICU [10].

When analysing patient demographics it was found that the 8.9% of the patients in our study were HIV positive. This is higher than the national prevalence of 2.4% in children up to the age of 14 years [16]. However, it is unsurprising that the prevalence of HIV infection in the patients in our study is high as paediatric patients with HIV infection, especially those not yet on treatment, are more susceptible to infection that may require hospital admission. Therefore, it is expected that in a population of hospitalised paediatric patients the HIV prevalence will be higher than in the general population.

The median age of the patients in our study was 2.35 months with the majority of patients, 116 (54.2%) being infants between 28 days and 1 year, with the next major age group represented being neonates at 24.3%. Of the neonates, 26.9% were premature. Fewer numbers of patients were seen in the older age groups. Studies from both developed and developing countries vary in their age distribution of patients admitted to the PICU. A study in Nigeria, a developing country, differed in that the majority of admissions were older than 1 year with 32.1% being between 1-8 years. A lower percentage (21.9%) of patients admitted were neonates and 19.9% were between 1 month and 1 year [25]. Broad variations in average age of admissions in developing countries were found. Lower averages of age at admission were found in studies in France, Canada and the United States at 3 months, 12 months and 31 months respectively [26, 27]. However, studies in Greece, Israel and New Zealand showed that the average age of admission were higher at 4.5 years, 4.9 years and 7.8 years

respectively [28-30]. With regards to neonatal admissions in a NICU, a study in the United States showed that 57% of the neonates were premature [31].

Analysis of anthropometry was separated into neonates (including premature neonates) and children older than 28 days. Analysis for children older than 28 days showed that the majority of patients fell within the normal range of Z-scores for WFA, HFA and WFH. However, 48.8% of patients were underweight, 28.4% of these patients were severely underweight, 29.6% were severely stunted and 15.7% were severely wasted. The median weight for HIV-negative patients was 4.03kg (*IQR*:2.95;6.5) and the median weight for HIV-negative patients was 4.12kg (*IQR*:2.98;7.08), p = 0.43. Recent surveys on nutrition in children under five years in South Africa that showed that 9% of children are underweight, 24% are stunted and 5% are wasted [17]. Our findings were poorer than national statistics. However, similar findings were reported in an ICU in Brazil where 50% of ICU patients were malnourished and 50% of these malnourished patents were severely malnourished [18]. Many factors may be affecting these figures. Firstly, patients admitted were ill patients who may have had acute loss of weight. Secondly, patients needing ICU may have had underlying comorbidities or chronic illness. Thirdly, patients with malnutrition are at increased risk of infection and thus more likely to be admitted to hospital or need mechanical ventilation [18]. Lastly, with the high prevalence of ex-premature infants, where the exact gestational age below 37 weeks was unknown, the weights may have been adjusted incorrectly by a few weeks and may have affected the data.

The most common diagnosis at presentation was acute lower respiratory tract infections. This finding is similar to those in previous studies done in both developing and developed

countries where the most common diagnoses in ICU patients is a respiratory cause [27, 32, 33]. Statistics from the World Health Organisation also show that lower respiratory tract infections are the leading cause of mortality worldwide in children older than one month [34]. Furthermore, the majority of patients required ventilation for either type 1 or 2 respiratory failure, further correlating with other studies on indications for ventilation in ICU patients [35-37]. The second most common diagnoses in the high care patients in this study was sepsis. Sepsis has also been found to be a common indication for ICU admission in developing countries [37, 38].

The analysis of patients who were assessed to be good ICU candidates versus those who were assessed to be poor candidates was limited by small numbers. This was due to the ICUs often not clarifying whether a patient was not accepted to the ICU due to being a poor candidate or due to a lack of resources (beds or staff). In only 22 cases did the ICU specify that they were poor candidates. When PICU was consulted the patients were, for the most part, personally assessed with a decision on candidacy made at the bedside. This occurred to a lesser degree for patients referred to NICU.

There was no significant difference in terms of WFA ($p=0.48$), HFA ($p=0.92$), or WFH ($p=0.11$) when comparing patients seen as good or as poor candidates for ICU admission. This demonstrates that malnutrition is not being used as an exclusionary factor for ICU admission. This is in line with another study in Brazil that has shown that although malnutrition may result in increased length of mechanical ventilation and ICU stay, it has not been shown to be a risk factor for increased mortality and should not be used as a reason for ICU refusal [18].

There was no significant difference between HIV-positive and HIV-negative patients ($p=0.44$) with regards to being accepted into an ICU. This demonstrates that a patient's HIV status is not being used as an exclusionary factor for ICU. Studies have shown that with the advent of HAART, HIV-positive patients on treatment have improved short- and long-term outcomes, though not matched yet with HIV-negative counterparts [21]. HIV positive patients do however have longer durations of stay in ICU and therefore place a heavier burden on PICU facilities than do HIV-negative patients. This however should not be used as a reason to deny them intensive care[2, 19, 21, 39].

Patients with respiratory diagnoses were more likely to be accepted to ICU ($p<0.001$) whereas patients with sepsis and neurological illness were seen as poor candidates for ICU admission ($p=0.08$ and $p=0.02$ respectively). Out of the patients accepted to ICU, only 5.4% were patients with neurological conditions and only 11.5% of patients had sepsis. Patients already needing inotropic support in HCA were considered poorer candidates for ICU ($p<0.001$). Only 25.7% of patients who were accepted into ICU required inotropes, while 75% of patients who were not accepted into ICU required inotropes. Need for inotropes does negatively contribute toward a PIM score and thus may denote worse prognosis. However, whether inotropic requirements should be used as an exclusionary criterion for ICU has not been studied on its own.

Patients with low risk diagnoses (e.g. asthma, bronchiolitis, croup, diabetic ketoacidosis) as defined by the PIM score, were considered better candidates and more likely to be accepted to an ICU ($p<0.001$). Patients with very high-risk diagnoses (e.g. cardiac arrest, leukaemia, lymphoma, liver failure,) were deemed to be poor candidates ($p<0.001$). The analysis for

patients with high risk diagnoses (e.g. spontaneous cerebral haemorrhage, myocarditis, cardiomyopathy, neurodegenerative disorders, NEC) was not statistically significant. This result shows that patients with low risk diagnoses and better prognoses are being accepted to ICU, whereas very high-risk patients where prognosis is uncertain are not getting the benefit of ICU care. This falls in line with CHBAH PICU current guidelines that do not consider patients to be good candidates if they have severe disease with poor hope of recovery (Appendix D). However, guidelines for ICU admissions in developed countries with more resources have more vague criteria which include a broad range of patients with few exclusionary criteria [40, 41]. This is in line with ethical principles, as in resource-rich countries, decisions regarding fair distribution of resources occurs less frequently and the principle of justice plays a less significant role. Guidelines like these that are drawn up in resource rich settings are difficult to apply to resource limited settings. In developing countries criteria are stricter, excluding patients with poor prognoses [42]. At Red Cross War Memorial Children's Hospital in Cape Town exclusionary criteria have been established for patients who would not be considered for admission into ICU. These criteria include patients where care is futile, where patients have an underlying lethal condition or where poor outcome is predicted [2, 42].

Of the 214 patients ventilated in HCA, 197 were referred to CHBAH ICUs. Only 41.6% cases were accepted to an internal ICU on the day of consult. The majority of the patients were denied admission due to no beds being available and 19.1% were assessed as poor candidates by the ICU team. Sixty-nine percent of patients were ultimately accepted into an ICU (either internal or outside) with the remainder staying in the HCA. PICU had a higher acceptance rate than NICU (67.2% vs. 33.3%). The poorer acceptance rate to NICU may be in part due to their main drainage area being the neonatal unit's labour ward with a birth rate

of approximately 60-100 babies a day. In addition, there is pressure on the NICU to accept neonates with surgical diagnoses from draining hospitals that do not have surgical capabilities. In contrast, the main draining points for PICU are the HCA itself as well as paediatric surgical wards, with a proportion also accepted form outside draining hospitals.

The median time from consult to ICU transfer was 9.50 hours (*IQR*: 4.80 - 18.50 hours; range: 1.0-72.0) when analysing both patients transferred on day of consult and those accepted later. There was no significant difference between PICU and NICU. A study at Red Cross War Memorial Children's Hospital in Cape Town South Africa in 2014/2015 showed that patients took a mean of 5.00 hours (2.50-12.90) to get to the PICU after presenting to the emergency department. Although patients often had a long and complicated pathway to get to the PICU they felt that this delay was unacceptably long [37]. Delays from HCA to an ICU at CHBAH are even longer and reasons may include beds being prepared (discharging patient out of bed and cleaning), waiting for transport within the hospital (various outlying buildings), and preparing to transport. Future studies into contributing factors and improving on these should be performed.

Of the 214 patients, 68 (31.8%) died with 36 (52.9%) of these 68 deaths occurring in HCA. Of the 135 patients that went to an ICU, 32 (23.7%) died, while of the 79 patients that remained in HCA 36 (45.6%) died. Similar mortality rates were found in patients admitted to an internal ICU and those needing transfer to an outside ICU. This is corroborated by previous studies where mortality between these patient groups is similar [36]. Patients who are referred from outside or are referred away to an ICU tend to have a longer duration of ICU stay with increased need for intensive care therapies but do not have an increased risk

of mortality [36]. The overall mortality rate of 23.7% in an ICU whether internal or outside is much higher than those found in developed countries. Studies from the 1990's and early 2000's report rates of 2-6%, 4.0%, 7.1%, and 7.5% for the United States, New Zealand, Netherlands and the United Kingdom respectively [29, 43-45]. However figures from developing countries are much more variable with reported mortality rates of 8.8%, 11.0%, 14.0%, 35.0% and 36,1% for Egypt, Red Cross War Memorial Children's Hospital in Cape Town in South Africa, Pakistan, King Edward VIII Hospital in Durban in South Africa and Nigeria respectively [2, 10, 25, 46, 47].

Although the most deaths (28) occurred in the infant group, the highest percentage of deaths per age group occurred in the 1-5year old group (48.0% of total 1-5 year olds). The 1-5year group having the highest mortality is in keeping with South African mortality estimates where the under-5 mortality rate is the greatest at 42/1000, with infant mortality rate at 34/1000 and neonatal mortality rate is at 11/1000 [48]. Studies from various countries differed in terms of in which group mortality was greatest [28, 30, 38, 45, 49].

High mortality rates of 45.6% were found for those patients that remained in HCA. Unsurprisingly, poorer mortality rates were found for those patients assessed as poor candidates were found when compared with patient who were assessed as good candidates (65.0% vs. 23.0%). Some of these patients were assessed as poor candidates by the attending paediatrician and not referred to ICU. Some were assessed as poor candidates by the neonatologist or paediatric intensivist upon referral. Analysis of PIM and probability of mortality scores showed that patients who died did have higher probability of mortality scores than those that survived (2.1% vs. 0.6%). Probability of mortality scores were also

higher for patients that were assessed as poor candidates than those that were assessed as good candidates for ICU (7.9% vs. 0.6%). Probability scores for patients who died in ICU were much lower than those for patients who died in HCA (0.6% vs. 16.6%). The mortality rate in HCA was higher than ICU (45.6% vs. 23.7%). Mortality rates for PICU and NICU were similar (26.3% and 26.1% respectively). The SMR for those patients who died in ICU was 1.32 while the SMR for patients who died in HCA was 3.27. Few studies report on paediatric PIM scores and SMR's however, in those that can be found, SMR's vary greatly. A study in the United Kingdom [12] reports SMR's between 0.57 and 0.87 whilst a study in Turkey [14] reports SMRs between 3.68 and 4.00.This study's SMR's show that in both ICU and HCA more patients died than was expected as predicted by the PIM score. The likely reasons for the PIM score under predicting mortality could be due to the high burden of illness severity being managed in an under-resourced environment (both physical and human) resulting in differences in quality of care.

Although the probability of mortality scores in HCA were high, the mortality rate was still more than expected. The high SMR in HCA demonstrates that patients who have a lower risk of mortality are still dying in this area, evidence that managing these patients outside an ICU increases their risk of mortality. Morbidity and mortality is increased when patients are ventilated and managed outside of an ICU [2].

CHAPTER 5

5.0 LIMITATIONS

The retrospective design of the study is a significant limitation to this study. In many cases, patient's records could not be retrieved and information from the existing database had to be relied on.

In terms of anthropometry, lengths were not recorded for all patients. There were also significant outliers in weight measurements and measurement of length was, in general, done poorly by health practitioners.

Many of the neonatal patients were born premature. Where gestational age was available, weights were corrected for gestational age. However, as weight could not always be corrected due to lack of data, the anthropometrical analysis may have been skewed.

As many files for patients could not be found, PIM scores could not be calculated in all patients.

When the ICU's were consulted, in many of the cases if no bed was available the ICU did not distinguish whether if there was a bed available, the patient would be a good candidate or not. Thus, when comparisons were made between patients who were deemed good candidates and those who were poor candidates, these patients had to be excluded from the analysis.

Time when an ICU was consulted was recorded. The time that the ICU actually accepted the patient was not always recorded. Therefore, time to transfer of patient to ICU was calculated form time of consult not time of acceptance. Factors delaying transfer were not recorded for each individual patient.

CHAPTER 6

6.0 CONCLUSIONS

A small percentage of paediatric patients (4.5%) admitted to the general paediatric wards may require mechanical ventilation. At Chris Hani Baragwanath Academic Hospital, this ventilation may, for a period, occur in a HCA outside of an ICU setting. The study's analysis of these patients showed higher than expected percentages of patients who were HIV infected, severely underweight, severely stunted and severely wasted when compared to national statistics. Such patients may be at higher risk of severe illness requiring ventilation, resulting in these findings.

When evaluating ICU candidacy, there was no statistically significant difference in HIV status or nutritional status in patients who were assessed as good candidates for ICU, in keeping with other studies showing that these should not be used as exclusionary criteria for ICU admission [2, 18, 19, 21, 39]. Patients with respiratory diagnoses or with low risk diagnoses, as defined by the PIM score [11], were found to be better ICU candidates whilst patients with very high-risk diagnoses or inotropic requirements were found to be poorer ICU candidates. This is in keeping with stricter ICU admission guidelines enforced in resource-poor settings [2, 40-42].

Less than half of the cases (41.6%) were accepted to an internal ICU on the day of consult with the majority (80%) of patients being denied admission due to no ICU beds being available. Ultimately, 69% of patients were accepted into either an internal or outside ICU. Significant delays in transferring patients to ICU occurred with multiple contributing factors including preparation of beds and staffing issues.

Mortality rates for patients who were admitted to an ICU (internal or outside) were higher than rates found in developed countries but within the range found in developing countries [2, 10, 29, 43-45]. The SMR in both HCA and ICU were high, indicating more patients died than was expected. The SMR's were higher than those found in studies in developed countries but similar to those in developing countries[12, 14]. Our findings demonstrated that patients who are ventilated outside of an ICU have an increased risk of mortality (odds ratio 1.8) and would benefit from intensive care treatment in an ICU. However, in our low-income environment limited ICU facilities prevent children from receiving the care they need [50, 51]. Ideally increased beds and availability of ICU services is required however if this is not achievable in the short-term future, measures should be put in place in the interim to make efficient, equitable and practical use of the resources available [2, 37, 49, 50, 52, 53].

CHAPTER 7

7.0 RECOMMENDATIONS

This study highlights the need for increased ICU services to improve morbidity and mortality of paediatric patients requiring ventilation during hospital admission. However in our low-income environment limited bed space in ICU, lack of infrastructure, high cost of trained healthcare workers and limited resources has limited the development of our ICUs, preventing children receiving the care they need [50, 51]. Increasing ICU capacity may not be immediately feasible and thus emphasis needs to be placed on the optimal use of resources available [10, 50, 54]. This may include having stricter criteria for ICU admissions.

Measures to use ICU optimally will include having clear ICU admission criteria, clear to both the intensivists using the protocols and the health practitioners in HCA and other hospital areas that consult ICU for their patients; effective, practical and equitable use of scarce resources; optimising costs, effective transport systems both to the hospital and to ICU; use of intensivists and other well trained health professionals; use of intermediate facilities such as the HCA for patients with increase monitoring needs (though not ventilation) with more intensive training of nursing and medical staff in charge of their care [2, 10, 15, 37, 49, 50, 52, 53, 55].

In a low-income, resource-limited developing country where infectious diseases predominate and under five mortality is high the question arises whether focus should be

placed on improving intensive care which caters for a small number of patients or whether there should instead be a shift to improving primary health care [15, 49]. Much of our healthcare burden is due to our country's large disparities in wealth and education and measures to address our health care challenges should also include addressing underlying issues in the social sector [15]. An ideal health system would identify sick children early on to administer prompt effective treatment. This may reduce the need for intensive care [37, 53]. This reasoning would require a greater emphasis on primary health care, strengthening not only intensive care treatment but health care at all levels [50].

APPENDICES

Appendix A: Paediatric High Care Database

VENTILATED PATIENTS WARD 36 HCA

Confidential

Demographic Information

Study ID	_____
Date of Birth	_____
Gender	○ Male ○ Female
Weight for age - Z scores	○ < -3 ○ -3 --> -2 ○ -2 --> +2 ○ +2 --> +3 ○ > +3
	_____
Height for age	○ < -3 ○ -3 --> -2 ○ -2 --> +2 ○ +2 --> +3 ○ > +3
Weight for height	○ < -3 ○ -3 --> -2 ○ -2 --> +2 ○ +2 --> +3 ○ > +3
HIV Status	○ Newly diagnosed positive ○ Positive on HAART ○ Negative ○ Exposed but uninfected
Unit in Charge	○ 1 ○ 2 ○ 3 ○ 4 ○ Haem/Onc
Area Admitted From	○ 31 --> 36A ○ General paeds wards (17, 18, 19, 33) ○ Short stay ward (39) ○ Specialist ward (43, 44, cardiac) ○ Medical casualty ○ Surgical casualty ○ Another hospital
Date of Admission	_____
Time of Admission	_____

Clinical Details

Study ID _____

Diagnosis

- ○ Bacterial/Viral Pneumonia
- ○ Bronchiolitis
- ○ PCP
- ○ Pulmonary Tuberculosis
- ○ Chemical pneumonitis
- ○ Apnoeas
- ○ Upper Airway Obstruction
- ○ Acute gastroenteritis
- ○ Haemolytic Uraemic Syndrome
- ○ Necrotising enterocolitis
- ○ Volvulus/malrotation
- ○ Congenital heart disease
- ○ Cardiomyopathy
- ○ Myocarditis
- ○ Cardiac failure
- ○ Anaemia
- ○ Neonatal Sepsis
- ○ Sepsis
- ○ Cellulitis
- ○ Disseminated Intravascular Coagulation
- ○ Meningitis
- ○ Acute Flaccid Paralysis
- ○ Encephalopathy
- ○ Status Epilepticus
- ○ Congenital Nephrotic Syndrome
- ○ Acute kidney injury
- ○ Organophosphate poisoning
- ○ Other Toxin Ingestion
- ○ Leukaemia
- ○ Lymphoma
- ○ Retinoblastoma
- ○ Neonatal jaundice
- ○ Near-drowning

_____

Indication for Ventilation

- ○ Type 1 Respiratory Failure
- ○ Type 2 Respiratory Failure
- ○ Apnoeas
- ○ Work of breathing
- ○ Stridor
- ○ Cardiac Support (shock)
- ○ Cardiac failure
- ○ Cardiorespiratory arrest
- ○ Severe metabolic acidosis
- ○ Decreased level of consciousness
- ○ Status Epilepticus
- ○ Pre-/post surgery or intervention

Date of Intubation _____

Time of Intubation _____

Need for Inotropic Support

- ○ Yes
- ○ No

Was ICU consulted?

- ○ Yes
- ○ No

Which ICU?

- ○ NICU
- ○ MICU

If ICU not consulted why not?
- ○ Not a candidate
- ○ Patient died

Date ICU consulted _____

Time ICU Consulted _____

Accepted to ICU?
- ○ Yes
- ○ No

If yes, time accepted to ICU _____

If yes date transferred to ICU _____

If yes time transferred to ICU _____

If no, why not accepted?
- ○ Not a candidate
- ○ Candidate but no beds

If no, bed found in outside ICU?
- ○ Yes
- ○ No

If accepted to outside ICU date transferred _____

If accepted to outside ICU time transferred _____

If no ICU beds found what happened
- ○ Ventilated in HCA until improved
- ○ Withdrew care in HCA
- ○ Died in HCA

Overall outcome of patient
- ○ Accepted to ICU and recovery
- ○ Accepted to ICU and died
- ○ Not accepted to ICU and recovered in HCA
- ○ Not accepted to ICU and died in HCA
- ○ Not accepted to ICU and withdrew treatment in HCA and recovered
- ○ Not accepted to ICU and withdrew treatment in HCA and died
- ○ Accepted to outside ICU and recovered
- ○ Accepted to outside ICU and died
- ○ Unknown

PIMS score

Study ID	_____
Pupils fixed to light	○ Yes ○ No
Elective admission	○ Yes ○ No
Ventilated in first hour	○ Yes ○ No
Absolute value of base excess	_____
SBP on admission	_____
SBP2/1000	_____
100 * FiO2/PaO2	_____
Recovery post procedure?	○ Yes ○ No
Very high risk diagnosis?	○ Yes ○ No
High risk diagnosis	○ Yes ○ No
Low risk diagnosis	○ Yes ○ No
Score	_____
Comment	_____

Appendix B: PIM Score, Probavility of mortality score and Standard Mortality rate

PIM SCORE

PIM = (3.8233 * Pupils) – (0.5378 * Elective) + (0.9763 * MechVent) + (0.0671 * (absolute Base Excess)) – (0.0431*SBP) + (0.1716*(SBP*SBP/1000)) + (0.4214 * (100*FiO2/PaO2)) –(1.2246*Recov_CardBypPr) – (0.8762*Recov_CardNonBypPr) – (1.5164*Recov_NonCardPr) +(1.6225* VHR diag) + (1.0725*HRdiag) – (2.1766*LRdiag) – 1.7928

PROBABILITY OF MORTALITY SCORE

= exp(PIM score)/(1+exp(PIM score))

STANDARD MORTALITY RATE

= number of 'observed deaths' / by the number of 'expected deaths' (as calculated by PIM score)

Appendix C: Human Research Ethics Committee Clearance Certificate

R14/49 Dr Shannon Kim Cawood

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M150821

NAME: (Principal Investigator)	Dr Shannon Kim Cawood
DEPARTMENT:	Paediatrics Rahima Moosa Mother and Child Hospital
PROJECT TITLE:	Description of Patients and their Outcomes after Receiving Mechanical Ventilation in Paeditrics High Care Area in a Low Resource Setting
DATE CONSIDERED:	28/08/2015
DECISION:	Approved unconditionally
CONDITIONS:	Title Change (09/12/2015)
SUPERVISOR:	Dr Charl Verwey
APPROVED BY:	Professor P Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	09/12/2015

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix D: Medical Advisory Committee Permission to Conduct Research



GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

MEDICAL ADVISORY COMMITTEE
CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PERMISSION TO CONDUCT RESEARCH

Date: 23 July 2015

TITLE OF PROJECT: Number, clinical features and outcomes of patients receiving mechanical ventilation in a paediatric high care area at Chris Hani Baragwanath Academic Hospital

UNIVERSITY: Witwatersrand

Principal Investigator: S Cawood

Department: Paediatrics

Supervisor (If relevant):

Permission Head Department (where research conducted): Yes

Date of start of proposed study: July 2015
Date of completion of data collection: Dec 2017

The Medical Advisory Committee recommends that the said research be conducted at Chris Hani Baragwanath Hospital. The CEO /management of Chris Hani Baragwanath Hospital is accordingly informed and the study is subject to:-

- Permission having been granted by the Human Research Ethics Committee of the University of the Witwatersrand.
- the Hospital will not incur extra costs as a result of the research being conducted on its patients within the hospital
- the MAC will be informed of any serious adverse events as soon as they occur
- permission is granted for the duration of the Ethics Committee approval.

.....
Recommended
(On behalf of the MAC)
Date: 23 July 2015

.....
Approved/Not Approved
Hospital Management
Date: 24/07/15

Appendix E: Paediatric ICU admission guidelines

Paediatric ICU admission guidelines

(October 2012)

1. Patient Selection Principle

a. Prospective candidates for admission to the PICU should be likely to derive demonstrable benefit from PICU treatment modalities; such patients would have:

i. A severe disease process, with severe physiological derangement, which is actually or potentially life-threatening.

ii. There is a reasonable likelihood of the disease process being reversible.

iii. There is a reasonable potential for the patient to return to an independent, functional existence for a reasonable period of time.

b. PICU resources are limited, and there are frequently more requests for PICU admission than can be accommodated; in such cases the principles in 2(a) will be applied to select the patients who will potentially derive the most benefit from available resources.

c. Optimal PICU care frequently requires the use of invasive modalities of monitoring and therapy, which all have an attributable risk and cause patient discomfort; the expected benefits of PICU care in the individual patient must outweigh the risks.

d. Admission to PICU should not be considered where that care is:

i. Unnecessary : patient's disease process is of too low a severity to require PICU treatment modalities: the patient could be expected to recover adequately with modalities of care that are available in the general wards.

ii. Unsuccessful : patient's disease process is so severe or advanced that the chances of recovery to a functional state, even with the application of optimal PICU care, are unacceptably poor.

iii. Unsafe : risks of treatment outweighs the expected benefit

iv. Unkind : unacceptable quality of life for the patient is likely to result from admission

v. Unwise : resources are diverted from patients who are potentially more likely to benefit

2. Specific Issues

a. Patient with endstage organ failure are not considered good PICU candidates.

b. Patients with advanced neoplastic disease are not considered good PICU candidates

c. Patients deemed to be neurologically devastated from any cause are not considered good PICU candidates

d. HIV positivity per se is NOT an exclusion criterion for PICU admission.

i. HIV status, stage and associated illnesses (such as PJP) are, however, considered in assessing overall disease severity and potential for recovery.

e. Patients with severe malnutrition (kwashiorkor or marasmus) are not considered to be good PICU candidates.

f. Patients with genetic syndromes and malformations with unfavourable natural histories are not considered good PICU candidates.

g. Patients who have undergone surgery for palliation may be considered for short-term admission (<48 hours) to PICU.

h. Patients with congenital cardiac lesions not amenable to surgical correction or with the Eisenmenger syndrome are not considered good PICU candidates. Cardiac patients remain candidates for admission to PICU but will be subject to the triage principles outlined above.

REFERENCES

1. Frey, B., *Overtreatment in threshold and developed countries.* Arch Dis Child, 2008. **93**(3): p. 260-3.
2. Argent, A.C., et al., *Pediatric intensive care in South Africa: an account of making optimum use of limited resources at the Red Cross War Memorial Children's Hospital**. Pediatr Crit Care Med, 2014. **15**(1): p. 7-14.
3. Gupta, P., et al., *Association of center volume with outcomes in critically ill children with acute asthma.* Ann Allergy Asthma Immunol, 2014. **113**(1): p. 42-7.
4. Tilford, J.M., et al., *Volume-outcome relationships in pediatric intensive care units.* Pediatrics, 2000. **106**(2 Pt 1): p. 289-94.
5. Bhagwanjee, S. and J. Scribante, *National audit of critical care resources in South Africa - unit and bed distribution.* S Afr Med J, 2007. **97**(12 Pt 3): p. 1311-4.
6. Odetola, F.O., et al., *Do outcomes vary according to the source of admission to the pediatric intensive care unit?* Pediatr Crit Care Med, 2008. **9**(1): p. 20-5.
7. World Health Organisation. *Bridging the Gap in South Africa*. 2010 31/05/2015 [cited 2015 18 February]; Available from: http://www.who.int/bulletin/volumes/88/11/10-021110/en/.
8. Kapiriri, L. and D.K. Martin, *A strategy to improve priority setting in developing countries.* Health Care Anal, 2007. **15**(3): p. 159-67.
9. Kapiriri, L. and D.K. Martin, *Priority setting in developing countries health care institutions: the case of a Ugandan hospital.* BMC Health Serv Res, 2006. **6**: p. 127.

10. Jeena, P.M., A.G. Wesley, and H.M. Coovadia, *Admission patterns and outcomes in a paediatric intensive care unit in South Africa over a 25-year period (1971-1995).* Intensive Care Med, 1999. **25**(1): p. 88-94.

11. Straney, L., et al., *Paediatric index of mortality 3: an updated model for predicting mortality in pediatric intensive care**. Pediatr Crit Care Med, 2013. **14**(7): p. 673-81.

12. Tibby, S.M., et al., *A comparison of three scoring systems for mortality risk among retrieved intensive care patients.* Arch Dis Child, 2002. **87**(5): p. 421-5.

13. Wells, M., et al., *Poor discriminatory performance of the Pediatric Risk of Mortality (PRISM) score in a South African intensive care unit.* Crit Care Med, 1996. **24**(9): p. 1507-13.

14. Ozer, E.A., et al., *The Comparison of PRISM and PIM scoring systems for mortality risk in infantile intensive care.* J Trop Pediatr, 2004. **50**(6): p. 334-8.

15. Mayosi, B.M. and S.R. Benatar, *Health and health care in South Africa--20 years after Mandela.* N Engl J Med, 2014. **371**(14): p. 1344-53.

16. *South African National HIV Prevalence, Incidence and Behaviour Survey, 2012*. 2014 01 April 2014 [cited 2015 07/07/2015]; Available from: http://www.hsrc.ac.za/uploads/pageContent/4565/SABSSM%20IV%20LEO%20final.pdf.

17. *The State of the World's Children 2015: Executive Summary*. 2015 02 June 2015 [cited 2015 07/07/2015]; Available from: http://www.unicef.org/publications/files/SOWC_2015_Summary_and_Tables.pdf.

18. de Souza Menezes, F., H.P. Leite, and P.C. Koch Nogueira, *Malnutrition as an independent predictor of clinical outcome in critically ill children.* Nutrition, 2012. **28**(3): p. 267-70.

19. Argent, A.C., *Managing HIV in the PICU--the experience at the Red Cross War Memorial Children's Hospital in Cape Town.* Indian J Pediatr, 2008. **75**(6): p. 615-20.

20. Jeena, P.M., et al., *Challenges in the provision of ICU services to HIV infected children in resource poor settings: a South African case study.* J Med Ethics, 2005. **31**(4): p. 226-30.

21. Cowburn, C., et al., *Short-term mortality and implementation of antiretroviral treatment for critically ill HIV-infected children in a developing country.* Arch Dis Child, 2007. **92**(3): p. 234-41.

22. Chris Hani Baragwanath Hospital. *Chris Hani Baragwanath Hospital, The Biggest Hospital in South Africa*. Unknown 31/05/2015 [cited 2015 18/02/2015]; Available from: http://www.chrishanibaragwanathhospital.co.za/.

23. Harris, P.A., et al., *Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support.* J Biomed Inform, 2009. **42**(2): p. 377-81.

24. Westwood, A., M. Levin, and J. Hageman, *Paediatric admissions to hospitals in the Cape Town Metro District: A survey*. 2012. Vol. 6. 2012.

25. Embu, H.Y., et al., *Paediatric admissions and outcome in a general intensive care unit.* Afr J Paediatr Surg, 2011. **8**(1): p. 57-61.

26. Davis, A.L., et al., *Comparisons of French and U.S.A. pediatric intensive care units.* Resuscitation, 1989. **17**(2): p. 143-52.

27. Krmpotic, K. and A.T. Lobos, *Clinical profile of children requiring early unplanned admission to the PICU.* Hosp Pediatr, 2013. **3**(3): p. 212-8.

28. Lanetzki, C.S., et al., *The epidemiological profile of Pediatric Intensive Care Center at Hospital Israelita Albert Einstein.* Einstein (Sao Paulo), 2012. **10**(1): p. 16-21.

29. McHugh, G.J. and P.R. Hicks, *Paediatric admissions to the general intensive care unit at palmerston north hospital.* Crit Care Resusc, 1999. **1**(3): p. 234-8.

30. Volakli, E., et al., *Demographic profile and outcome analysis of pediatric intensive care patients.* Hippokratia, 2011. **15**(4): p. 316-22.

31. Harrison, W. and D. Goodman, *Epidemiologic Trends in Neonatal Intensive Care, 2007-2012.* JAMA Pediatr, 2015. **169**(9): p. 855-62.

32. Mickell, J.J. and T.L. Furgiuele, *Acute mechanical ventilation: an index of the absolute need for pediatric intensive care unit beds.* Crit Care Med, 1988. **16**(5): p. 504-9.

33. van Lelyveld, S.F., et al., *Short- and long-term outcome of HIV-infected patients admitted to the intensive care unit.* Eur J Clin Microbiol Infect Dis, 2011. **30**(9): p. 1085-93.

34. Bryce, J., et al., *WHO estimates of the causes of death in children.* The Lancet. **365**(9465): p. 1147-1152.

35. El Halal, M.G., et al., *Admission source and mortality in a pediatric intensive care unit.* Indian J Crit Care Med, 2012. **16**(2): p. 81-6.

36. Gregory, C.J., et al., *Comparison of critically ill and injured children transferred from referring hospitals versus in-house admissions.* Pediatrics, 2008. **121**(4): p. e906-11.

37. Hodkinson, P., et al., *Pathways to Care for Critically Ill or Injured Children: A Cohort Study from First Presentation to Healthcare Services through to Admission to Intensive Care or Death.* PLoS One, 2016. **11**(1): p. e0145473.

38. Kapil, D. and A. Bagga, *The profile and outcome of patients admitted to a pediatric intensive care unit.* Indian J Pediatr, 1993. **60**(1): p. 5-10.

39. Rabie, H., et al., *Children with human immunodeficiency virus infection admitted to a paediatric intensive care unit in South Africa.* J Trop Pediatr, 2007. **53**(4): p. 270-3.

40. *Guidelines for intensive care unit admission, discharge, and triage. Task Force of the American College of Critical Care Medicine, Society of Critical Care Medicine.* Crit Care Med, 1999. **27**(3): p. 633-8.

41. Siddiqui, N.U., et al., *Mortality patterns among critically ill children in a Pediatric Intensive Care Unit of a developing country.* Indian J Crit Care Med, 2015. **19**(3): p. 147-50.

42. Turner, E.L., et al., *A Review of Pediatric Critical Care in Resource-Limited Settings: A Look at Past, Present, and Future Directions.* Front Pediatr, 2016. **4**: p. 5.

43. Gemke, R.J. and G.J. Bonsel, *Comparative assessment of pediatric intensive care: a national multicenter study. Pediatric Intensive Care Assessment of Outcome (PICASSO) Study Group.* Crit Care Med, 1995. **23**(2): p. 238-45.

44. Pollack, M.M., et al., *Pediatric intensive care outcomes: development of new morbidities during pediatric critical care.* Pediatr Crit Care Med, 2014. **15**(9): p. 821-7.

45. Prince, N.J., et al., *Weight-for-age distribution and case-mix adjusted outcomes of 14,307 paediatric intensive care admissions.* Intensive Care Med, 2014. **40**(8): p. 1132-9.

46. Bekhit Oel, S., A.A. Algameel, and H.H. Eldash, *Application of pediatric index of mortality version 2: score in pediatric intensive care unit in an African developing country.* Pan Afr Med J, 2014. **17**: p. 185.

47. Haque, A., et al., *Clinical profiles and outcomes of children admitted to the pediatric intensive care unit from the emergency department.* J Coll Physicians Surg Pak, 2015. **25**(4): p. 301-3.

48. You D, H.L., Ejdemyr S, Beise J, *Levels & Trends in Child Mortality, Report 2015, Estimates Developed by the UN Inter-agency Group for Child Mortality Estimation*, L. N, Editor. 2015, United Nations Inter-agency Group for Child Mortality Estimation: New York, USA.

49. Piva, J.P., et al., *The burden of paediatric intensive care: a South American perspective.* Paediatr Respir Rev, 2005. **6**(3): p. 160-5.

50. Ballot, D.E., et al., *Selection of paediatric patients for intensive care.* S Afr Med J, 1995. **85**(11 Suppl): p. 1221-3, 1226.

51. Murthy, S., A. Leligdowicz, and N.K. Adhikari, *Intensive care unit capacity in low-income countries: a systematic review.* PLoS One, 2015. **10**(1): p. e0116949.

52. Sinuff, T., et al., *Rationing critical care beds: a systematic review.* Crit Care Med, 2004. **32**(7): p. 1588-97.

53. Wightman, A., et al., *Who should get the last PICU bed?* Pediatrics, 2014. **133**(5): p. 907-12.

54. Safar, P. and A. Grenvik, *Critical care medicine. Organizing and staffing intensive care units.* Chest, 1971. **59**(5): p. 535-47.

55. Biarent, D., et al., *[The future of pediatric intensive care].* Rev Med Brux, 2006. **27 Spec No**: p. Sp39-43.