

Characteristics and Outcome of Long-Stay Patients in a Paediatric Intensive Care Unit in Cape Town, South Africa

By

Tracey Lee Nupen (MBChB; FCPaeds SA)

NPNTRA001

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Supervisor(s):

Morrow, B. M. (PhD) and Argent, A. C. (MD; FCPaeds SA; FRCPCH)

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1) Abstract

Objectives: To describe a rational basis for the definition of a long-stay patient (LSP) in a South African paediatric intensive care unit (PICU); to review the characteristics and outcomes of the patients who comply with the LSP definition; to assess the proportion of resources allocated to the LSP cohort; and to determine if the results of this study could be used as a predictive tool for future admissions.

Methods: A retrospective descriptive study of routine data collected over one calendar year (2009) from a 20-bedded multidisciplinary PICU was conducted. The definition of a LSP in this setting was established using various models. The characteristics and outcomes of the long- and short- stay groups were compared using nonparametric Mann-Whitney U and Chi² tests, with significant results entered into a stepwise multiple regression model. The proportion of ICU days consumed by LSP was calculated. Human Research Ethics Committee approval was obtained (Ref/Rec 105/2011).

Results: 1126 children were admitted to the PICU during the study period (median age 8 months (IQR 2 – 32 months); 60.9% male), occupying 5936 PICU bed days. LSP were defined as having a PICU stay of >19 days (>95th percentile of the median and visual “tail” of the distribution curve). 54 (4.8%) LSPs utilised 1807 (30.4%) bed days with an associated mortality of 29.6%. Mortality and standardised mortality ratio (actual/mean predicted mortality) in LSP and SSP respectively was 29.6% and 12% ($p = 0.002$) and 2.4 versus 0.7 ($p = 0.002$) respectively. Median duration of ICU stay for LSP and SSP was 29.5 days versus 2 days ($p < 0.0001$). On univariate analysis, LSPs were younger (4 months (2 – 17 months) versus 9 months (2 – 34 months) for SSPs; $p = 0.03$) and a smaller proportion of LSPs were male compared to SSP (48% versus 61.6%, $p = 0.049$).

The final multiple regression model only identified female gender as being independently associated with the outcome of long-stay making it impossible to develop a predictive model for long PICU stay based on this dataset. There were no differences in the recorded descriptive characteristics between LSPs who died compared to those who survived.

Conclusion: Long-stay patients represent a small percentage of PICU admissions, yet have a significantly increased mortality and consume a disproportionate amount of resources compared with short-stay patients. No predictive model could be established for the early recognition of potential long-stay patients in order to effectively plan PICU bed allocation. Further investigations are needed to assess the quality of life of survivors of long PICU stay. Identification of LSP may be useful in clinical practice.

2) Acknowledgements

I am deeply grateful to both of my supervisors for their advice and guidance throughout this project. Sincere thanks to Associate Professor Brenda Morrow for her patience, gentle encouragement and for sharing her contagious passion for research. Thanks also to insightful Professor Andrew Argent for generously giving his time and sharing his vast experience. You are champions of Child Health research in South Africa.

I would like to thank my friends and family for their love and support, especially my sister Lisa, and my husband, Duncan.

I am indebted to my colleagues at Red Cross War Memorial Children's Hospital for diligently capturing data and maintaining the database in a demanding clinical setting. I would also like to acknowledge the unsung heroes of the paediatric intensive care unit – the Nursing staff, physiotherapists, occupational therapists and social workers, in particular Carla Brown – who all show commitment above and beyond their duty to patients.

Finally, I would like to extend my gratitude to the patients, and their families, who inspired this research to deepen our knowledge and understanding. My sincerest hope is that this work will make a meaningful contribution to good practice in paediatric critical care medicine in South Africa.

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4) List of Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
BiPAP	Biphasic Positive Airway Pressure
CPAP	Continuous Positive Airway Pressure
F	Female
HIV	Human Immunodeficiency Virus
HREC	Human Research Ethics Committee
ICP	Intra-cranial Pressure
ICU	Intensive Care Unit
IQR	Interquartile range
kg	kilograms
LOS	Length of Stay
LSP	Long-Stay patient
M	Male
mm Hg	Millimeters of Mercury
MVA	Motor Vehicle Accident
PICU	Paediatric Intensive Care Unit
PI M	Paediatric Index of Mortality
PRISM	Paediatric Risk of Mortality
SBP	Systolic Blood Pressure
SSP	Short-stay Patient
RCWMCH	Red Cross War Memorial Children's Hospital
UCT	University of Cape Town
UK	United Kingdom
USA	United States of America
US \$	United States Dollar

5) CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW

5.1 Background

The costs of care in paediatric intensive care units (PICUs) can range from about US\$70 to > US\$1000 per day depending on the sophistication and complexity of the services offered.(1) Time spent in the PICU should be productive and cost efficient for both the healthcare providers and the patient, while ensuring quality of care for all patients in the healthcare system is not jeopardised.(2)

Long-stay patients (LSP) in the PICU represent a small percentage of the PICU population, but may consume a disproportionate amount of healthcare resources and have higher mortality rates than short-stay patients (2-6). The perceived vulnerability of LSP to morbidity and mortality raises questions about appropriate allocation of relatively scarce resources to these patients.

The uncertain outcomes of the LSP can make management decisions difficult (7) and the limited data for LSPs in different settings compounds these complexities, especially as the individual LSP forms part of a broad case mix with variable diagnosis-specific outcomes e.g. the expected outcome for a child with Guillain-Barré syndrome who is a LSP will differ from a child with Duchenne muscular dystrophy who may also be a ventilated LSP.

While it is accepted that length of stay (LOS) may be reflection of severity of illness and PICU quality and performance, there is no uniform definition of what constitutes a long-stay. A particular length of stay may be designated as a threshold to identify the long-stay patient, but this threshold varies widely in the literature (2, 3, 5, 8-10). Defining this relatively small patient group may help answer important questions, e.g. who will benefit from long term stays? Does a

LSP carry a poor prognosis? What percentage of resources is consumed by this group? What are the ethical questions around this group? (3). In addition, the characteristics of LSP from PICU data and parameters vary worldwide as they are influenced by patient demographics, comorbidities, type of illness and severity of illness, factors cumulatively referred to as the case mix (11)

Early identification of patients at risk of becoming LSPs using admission characteristics would be helpful in establishing specific management strategies designed to shorten LOS and improve quality of care (4, 12, 13). Knowledge of characteristics predicting LSPs would be beneficial, particularly if any factors could be modified. Predictors may assist in clinical decision making and be useful to clinicians responsible for counselling the families of critically ill patients. The benefits of actively integrating palliative care delivery into the PICU irrespective of outcome are being more widely recognised (14)

The Paediatric Index of Mortality 2 (PIM2) score (15) is the model used in the PICU of Red Cross War Memorial Children's Hospital (RCWMCH) to calculate expected mortality of groups of patients (16). It enables us to track and compare the outcomes of groups in the PICU, compare outcomes with other units and track and compare outcomes over periods of time in a standardised fashion. This model estimates mortality risk from data readily available at the time of PICU admission.

Intensive care is now offered to children with complex and chronic conditions who may not have been admitted in the past (17). Some critically ill children, who previously would have died, now survive because of improvements in intensive care. These changes have arisen as a result of changed attitudes to disability, a better understanding of critical illness, specialised PICU training, centralisation of PICU care services, advances in paediatric cardiac surgery, improved perioperative care and new treatment modalities (17-19).

The advances in PICU care have resulted in increased survival of critically ill patients, a number of whom require long term PICU stay. These new issues, especially where they concern patients requiring palliative care or patients with chronic (frequently undiagnosed) metabolic or mitochondrial diseases, set a major challenge not only to staffing needs and costs, but also to the whole intensive care system, structure and function (18).

Exploring the characteristics and outcomes of LSPs allows us the opportunity to explore the concern that the ability of intensive care medicine to support life has progressed at a faster rate than knowledge and guidelines of who will benefit most from PICU therapy, as well as guidelines for limitation or withdrawal of life sustaining treatment (3).

5.2 Objectives

The objectives of the literature review were to investigate the different definitions of the paediatric intensive care long-stay patient (LSP), to describe the characteristics and outcomes of this cohort and to evaluate its relative resource consumption. A subsidiary objective was to identify potential predictors of poor outcome in the LSP. Literature from countries of low to middle income was of particular interest.

5.3 Literature Search Strategy

The literature search was conducted using the Pubmed search engine with the following search strings:

- (Long-stay OR prolonged stay) AND paediatric intensive care unit
- Length of stay AND paediatric intensive care unit
- Characteristics AND (long-stay OR prolonged stay) AND paediatric intensive care unit
- Outcomes and (long-stay OR prolonged stay) AND paediatric intensive care unit
- Predictors and (long-stay OR prolonged stay) AND paediatric intensive care unit

- (Developing world OR third world OR South Africa) AND paediatric intensive care unit

Articles were included if they studied subjects under 18 years of age, with any study design, in the English language. Adult studies were excluded. Exclusively neonatal intensive care unit studies were excluded as neonates are a unique cohort with unique problems often related to prematurity. Our PICU drainage population has access to multiple neonatal intensive care units (NICUs) so they do not form a large part of our PICU population.

Reference lists of articles were reviewed to broaden the search strategy.

Search Results

The search strategy yielded 45 papers, of which 40 full text articles were reviewed and 32 were included in the literature review. A further 9 articles were identified and included from the reference lists of these papers.

The majority of articles reviewed were published over the last decade. The oldest article included in the review was published in 1987, but much of the content remains relevant.

5.4 Summary of data

A summary of the literature studying LSP is presented in Table 1.

5.5 Definitions of LSP

Length of stay (LOS) is a marker of severity of illness, resource utilization and performance of the PICU. LOS may also be affected by factors that are unique to individual patients and cannot be modified. There may be utility in identifying LSPs early so appropriate interventions could be taken in order to optimise their care. (2)

The threshold for prolonged length of stay varies widely between > 7days (8); >12 days (2); >13 days (3) ; >27 days (6, 7, 17) and > 29 days (9) (Table 1).

Weissman reviewed the adult critical care literature to explore methods of evaluating LOS patterns (8). He then retrospectively reviewed 4499 ICU patients admitted over a six-year period and confirmed his hypothesis that using the mean to determine LOS was not appropriate because distribution patterns were often markedly skewed by patients with extended stays. Therefore other descriptors were needed. In addition, objective methods were needed to identify outliers with longer stays. Methods included using histograms of frequency distributions to visually identify outliers and conventional outlier analysis of labelled patients staying greater than two standard deviations from the mean duration of stay. Other methods involved designating a specific length of stay e.g. 7 or 10 or days, or a specific percentage of patients as the outlier threshold. Each method designated a different number of patients as LSPs. Weissman highlights the importance of using objective statistical methods to examine the characteristics of a data set so that appropriate analyses can be selected when planning costly healthcare services (8).

Table 1: Summary of literature: definition of PICU LSP, setting, outcome and resource allocation.

STUDY	DEFINITION OF LSP	STUDY SETTING	POPULATION SIZE		OUTCOME Mortality Rate (%)		RESOURCE ALLOCATION (% Bed Days)
			TOTAL (n)	LSP n (%)	OVERALL	LSP	
POLLACK et al (1987) (3)	>13 days (in keeping with adult studies)	<ul style="list-style-type: none"> Single centre 16 Beds Retrospective Descriptive Study 	647	46 (7.1%)	7.3%	17.4%	50.1%
JEENA et al (1999) (24)	> 19 days Choice of LSP definition not specified	<ul style="list-style-type: none"> Single Centre 12 Beds – 6 neonatal – 6 paediatric Retrospective Descriptive Study 	1561	293 (18.8%)	35.4%	84.7%*	30.6%
MARCIN et al (2001) (2)	> 12 days (> 95 th percentile)	<ul style="list-style-type: none"> 32 PICUs – 16 stratified, random selection – 16 volunteer units Non concurrent cohort study 	11 165	504 (4.5%)	4.4%	15.3%	36.1 %
VAN DER HEIDE et al (2004) (9)	>29 days Choice of LSP definition not specified	<ul style="list-style-type: none"> Single Centre 7 Beds Retrospective case control 	2 172	19 (1.9%)	7.5%	36.8% (case) ^β	Not assessed
NAGHIB et al (2010) (6)	> 27 days (3 x median length of stay)	<ul style="list-style-type: none"> Single centre 34 Beds Retrospective descriptive study 	2607	116 (4.1%)	4.6%	22%	63%
NAMACHIVAYAM et al (2012) (5)	>27 days (ANZPICR † criteria)	<ul style="list-style-type: none"> Partly retrospective descriptive Partly prospective 19 Beds 	27 536	269 (1%)	5.4%	44.25%	18.5%

* 45.7% of LSP survivors had died or were severely mentally disabled

^β Mortality in control group was 26.4%

† Australian and New Zealand Paediatric Intensive Care Registry

5.6 Characteristics of LSPs

It is difficult to compare the characteristics and outcome of long-stay patients described in the literature owing to the different methods used to analyse length of stay data.

The largest study (2), showed that baseline characteristics including younger age, prior ICU admission, emergency admission, patient never been discharged from hospital, gastrostomy in situ, tracheostomy and total parenteral nutrition dependency, were significantly different ($p < 0.001$) in LSPs compared to short-stay patients (SSPs). This highlights that younger children with co-morbid disease and chronic assistive devices may have an increased risk of long PICU stay.

Capturing specific comorbid factors as PICU admission characteristics would be a useful practice in order to make comparisons amongst studies that have focused on LSP in subgroups of interest such as those with chronic care devices (tracheostomy, gastrostomy and total parenteral nutrition), patients requiring prolonged mechanical ventilation and LSP post cardiac surgery (2, 20, 21). A Greek prospective observational study collected data on 300 patients to study short-term and long term mortality following paediatric intensive care. They found that comorbidity was the major determinant of long term mortality (22).

Prolonged length of stay in PICU after congenital heart disease surgery has been associated with poor outcome and places a considerable burden on financial resources and influences operation list scheduling. (23). Brown *et al* (2003) conducted a retrospective review of pre, intra and post-operative factors collected from 355 paediatric patients who had cardiopulmonary bypass. After multiple analysis, factors were deemed significant if associated with LOS with $p < 0.02$. LSP was defined as a PICU stay > 13 days ($> 95^{\text{th}}$ centile). These LSP had a threefold greater mortality rate and occupied 30% of the bed days in the cardiac intensive care unit. Significant pre-operative

factors included mechanical ventilation, resuscitation, comorbid medical condition, weight < 10kg and neonatal age group (20).

The diagnoses and patient profiles of long stay patients differ widely amongst studies due to the varied case mix. Studies from India and South Africa describe LSP diagnoses related mainly to infection (10, 24) while studies from developed countries list congenital heart disease, neurological disease and metabolic disorders as the more common diagnoses in their LSPs (6). HIV infected children without access to antiretroviral therapy were studied in a single centre PICU in South Africa by Rabie et al (2007) and were found to have a significantly longer duration of stay than the non-HIV infected group ($p=0.0001$) (25). Poor outcome was also significantly associated with HIV infection to the point where the benefits of admitting HIV infected children to the PICU was debated (26). Antiretroviral medication is currently readily available in South Africa and this is reflected in improved PICU outcome of HIV infected patients on antiretroviral therapy with South African PICU case fatality rates in ventilated HIV infected children with respiratory tract infections dropping from as high as 100% in 2003 down to 30% in 2012 (27).

A case control study by Van der Heide *et al* (2004) did not identify significant differences in baseline characteristics nor mortality rate when comparing long-stay patients to a diagnosis-matched control group. This study was a small (cases=19, controls=15) single centre study (9).

5.7 Outcomes of LSPs

Mortality alone is a poor measure of outcome and more meaningful outcome data such as functional outcomes and quality of life data should be collected on LSP survivors (7).

Conlon et al (2009) reported that although long-stay in their unit was associated with significantly higher mortality, the long term quality of life scores for the majority of surviving

LSP were normal (7). However, only 70 of the 125 questionnaires posted to parents were completed which indicates 44% of their LSP survivors were not included in the study.

Research done over a 20 year period in a Melbourne PICU reported that only 27% of their LSPs had favourable long term functional and favourable quality of life outcome (normal, functionally normal or mild disability). Two-thirds of children who spent >28 days in their PICU had an unfavourable outcome (moderate disability, severe disability or death). Long term functional outcome was evaluated by a modified Glasgow outcome scale and quality of life was assessed using the Health Utilities Index Mark. At the time of follow up 116 of their 233 LSP (49.8%) had died (5)

There must be awareness that if PICU mortality rates have been traded for a higher prevalence of morbidity then there are potential ramifications for provision and delivery of healthcare to this vulnerable population (28). PICU survivors with significant handicap place a large burden on social and healthcare services

5.8 Predictive Tools

The term “risk adjustment” describes the process of adjusting for risk factors when comparing outcomes after intensive care. Identifying suitable risk adjustment tools is only a first step. It is then important that they be applied effectively to monitor outcome and improve the quality of paediatric intensive care (29). It would be useful to know if mortality prediction tools could also be used to predict length of stay.

Mortality prediction models that use patient characteristics to predict the risk of death in the PICU have been developed. Brady et al recruited 22 of the 26 PICU s in the United Kingdom in a study that compared the PIM, PIM2, PRISM and PRISM III mortality prediction tools (30). All published tools were found to have poor calibration, but provided good discriminatory power indicating high probability of concordance between outcomes and predictions of death.

These scoring systems do not prognosticate reliably and are not accurate enough to be used as a screening tool for individual admissions (16). The challenge is that mortality prediction models need to be validated before they can be applied in an environment that is substantially different from the environment in which they were developed (31).

PIM and PRISM scores differ in the amount of information required to calculate the risk of death, the duration of the observation period and the time point used to define when observation should commence. The PIM model requires fewer parameters making it easier to collect data on large numbers of intensive care patients.

The PIM2 model was found to be most accurate in a study by Anthony Slater *et al* (29), which recruited ten PICUs across Australia and New Zealand and reviewed data on 26 966 patients. The PIM2 scoring system was developed from data collected between 1997 and 1999 from 13 PICU s in Australia, New Zealand and the United Kingdom

The Paediatric Index of Mortality 2 (PIM2) score is the model used in the PICU of Red Cross War Memorial Children's Hospital (RCWMCH) to estimate the predicted mortality of groups of patients and has proven to be an appropriate tool in this setting as it is comparable to the score derivation units (16).

5.9 Resource Consumption

Despite the variation in the duration of stay that defines a LSP in the literature, it remains clear that the LSP group has remained relatively small over the last three decades (2, 3, 5, 6, 9). The LSP group comprised 7.1% of the total population in the oldest study (3) reviewed and 1% of the most recent study reviewed (5) .

The percentage of bed days the LSPs occupy has been used as a measure of resource allocation. The LSP groups consistently consumed a significant and disproportionately large percentage of

bed days. The two largest studies reviewed were by Marcin *et al* 2001 (11 165 admissions) and Namachivayam *et al* 2012 (27 536 admissions). The former study found that the LSP group (4.5%) consumed 36.1% of the bed days and the latter study reported that the LSP group (1%) consumed 18.5% of the total bed days. A longitudinal retrospective, multicentre study in Brazil described how 76 admissions (1% of the total admissions) who required prolonged mechanical ventilation (>21 days) potentially prevented the admission of 830 acute and unstable PICU admissions (21).

Prolonged length of stay in PICU after congenital heart disease surgery has been associated with poor outcome, places a considerable burden on financial resources and may influence operation list scheduling (23).

5.10 Summary

A variety of statistical methods may be used to define a long-stay patient. A uniform and rational definition of what constitutes a long stay patient should be established to compare and analyse data on this group of outliers. This may be site- specific.

Significant predisposing characteristics of LSPs noted in the larger studies include younger age, comorbid medical conditions and dependence on assistive devices. Data collected on characteristics of LSPs varies broadly in the literature as many studies focus on subgroups of long stay patients such as post-operative cardiac patients or patients on prolonged ventilation, but LSP in studies from the developing world are consistently described as having a heavier burden of infectious diseases.

Although numerous mortality risk scores have been developed to capture a multitude of admission characteristics, they remain population specific, and may not have external validity (31). These scoring systems are neither accurate enough to be used to make decisions about individual patients nor do they predict prolonged length of stay.

Death versus survival is a poor measurement of outcome and objectively scoring the quality of life after a PICU stay may be a more valuable indicator, but there is paucity of this data from African countries.

The overwhelming majority of the literature supports the perceived vulnerability of long-stay patients to increased mortality risk and to a disproportionate consumption of resources (2-6).

5.11 Future Research

An important aspect of follow up of the surviving long-stay patient is an objective quality of life score. Meaningful outcome data can be collected using quality of life scores which take physical, emotional, social, school and psychosocial sub scores into account.

There are some LSP who are discharged from the PICU and deemed inappropriate for readmission. The mortality rate in this group has not been widely published and this data is often not included in PICU mortality statistics when the death of the long-stay patient occurs in the general ward. This could indicate we are underestimating the morbidity and mortality of LSPs.

There may be utility in identifying who is likely to become a LSP early in the PICU admission in order to care for them more economically in other locations, to engage the support of other healthcare team members earlier in the process, and to help disclose the additional risks of infection and higher mortality rates to their families (12).

6) CHAPTER 2: Publication-ready Manuscript

6.1 Title Page

Characteristics and Outcome of Long-Stay Patients in a Paediatric Intensive Care Unit in Cape Town, South Africa

Tracey L. Nupen,¹FCPaed (SA); Andrew C. Argent,^{1,2}MD, FCPaed (SA) and Brenda M. Morrow,¹(PhD)

¹ Department of Paediatrics and Child Health, Faculty of Health Sciences, University of Cape Town, South Africa

² Paediatric Intensive Care Unit, Red Cross War Memorial Children's Hospital, Cape Town, South Africa

Corresponding author: T. L. Nupen (traceynupen@yahoo.co.uk)

All analyses were performed at the Paediatric Intensive Care Unit, Red Cross War Memorial Children's Hospital, Cape Town, South Africa.

Keywords: Pediatric Intensive Care Unit, outcomes, long-stay patients, length of stay

6.2 Abstract

Objectives: To determine the local definition of a paediatric intensive care unit (PICU) long-stay patient (LSP); to describe the characteristics, outcomes and resource consumption of LSPs; and to identify predictive factors for long PICU stay.

Design: This was a retrospective descriptive study of routinely collected data.

Setting: A 20-bedded multidisciplinary PICU in a tertiary paediatric hospital in Cape Town, South Africa.

Patients: All children admitted to the PICU during the 2009 calendar year were included.

Interventions: None

Measurements and main results: After defining LSP statistically as those with a PICU stay >19 days, the characteristics and outcomes of long- and short-stay groups were compared using nonparametric tests. Variables significantly associated with LSP on univariate analysis were entered into a stepwise multiple regression model.

1126 children (median age 8 months; 60.9% male) were admitted to the PICU, occupying 5936 bed-days. 54 (4.8%) LSPs utilised 1807 (30.4%) bed-days. Mortality and standardised mortality ratio (actual/mean predicted mortality) in LSPs and SSPs respectively was 29.6% versus 12% ($p=0.002$) and 2.4 versus 0.7 ($p=0.002$) respectively. Median duration stay for LSP and SSP was 29.5 days versus 2 days ($p<0.0001$). LSPs were significantly younger (4 months (2–17 months) versus 9 months (2–34 months) for SSPs; $p=0.03$) and a smaller proportion of LSPs were male (48% versus 61.6% for SSPs, $p=0.049$). On multivariate analysis only female gender was independently associated with long PICU stay, precluding the development of a predictive model.

Conclusion: LSPs represent a small percentage of PICU admissions, yet have a higher mortality and consume a disproportionate amount of PICU resources. No predictive model could be established for the early recognition of potential long-stay patients in order to effectively plan PICU bed allocation. Further investigations are needed to assess the quality of life of survivors of long PICU stay.

6.3 Introduction

Paediatric intensive care (PICU) is a costly, specialised and limited resource that should be used as effectively and efficiently as possible. PICU costs can range from about US\$70 to > US\$1000 per patient day depending on the sophistication and complexity of PICU services offered (1). In the context of poorer countries where access to intensive care is limited, it is particularly important to ensure resources are used rationally, whilst upholding the ethical principle of distributive justice (32). Rational PICU use includes careful monitoring of patient outcomes related to resource utilization and the use of appropriate admission criteria in order to contain financial, staffing and social costs (12).

Whereas patients were admitted to the PICU largely for the management of acute emergencies, intensive care is now offered to children with complex and chronic conditions who may not have been admitted in the past (17). Advances in PICU care have resulted in increased survival of critically ill patients, a number of whom require long term PICU stay. These children require a different spectrum of resource allocation in terms of involvement of the extended multi-disciplinary team (e.g. psychologists, social workers, rehabilitation therapists, school teachers) to improve their experience of the PICU, as well as optimising their functional outcome. This constitutes a challenge, not only to staffing needs and costs, but also to the whole intensive care system, structure and function (18).

It has been suggested that patients who have a long duration of stay in the PICU use a disproportionate amount of resources in different settings (2, 3, 5, 12, 33). Together with the perceived vulnerability of long-stay patients (LSPs) to increased mortality and morbidity, there is a concern about appropriate resource allocation to this group. There is a paucity of outcome data for LSPs patients, especially from Africa. Existing outcome data describes a wide spectrum of patients who have outcomes ranging from excellent to poor (3, 5, 10, 34). On an individual level it is clear that the expected outcome for a child with Guillaine Barré Syndrome will differ

from a child with end-stage Duchenne muscular dystrophy, although both may be LSP in the PICU.

While it is accepted that length of stay (LOS) may be a reflection of severity of illness and PICU quality and performance, there is no uniform definition of what constitutes a PICU long-stay. Previous studies defined LSP as having a PICU LOS of anywhere beyond seven days to more than 30 days (2, 3, 8, 9), with various methods being used to identify these thresholds.

It is useful to describe the characteristics, impact and outcomes of long-stay patients in order to plan their care more economically, to ensure optimal involvement of the multi-disciplinary team, to optimise outcome, to enable appropriate counselling of family members and to develop guidelines for the limitation or withdrawal of medical care (12). The existing literature on LSP in PICU is mostly from developed countries which have population and burden of disease profiles that may differ from developing countries. This study, therefore, aims to determine an appropriate threshold for defining long PICU stay in a South African PICU; to describe the characteristics and outcomes of these long stay patients; and to determine any predictive factors associated with long PICU stay.

6.4 Materials and Method

Study Design

The setting was the 22-bedded multidisciplinary PICU of Red Cross War Memorial Children's Hospital, situated in Cape Town, South Africa. This PICU admits approximately 1400 children under 14 years of age per annum, of which about 500 are emergency admissions, mostly for the management of infectious diseases, with the vast majority requiring invasive mechanical ventilation. Extra-corporeal membrane circulation (ECMO) was not available at the time of this study. The overall mortality rate is approximately 12%. PICU beds are in great demand and there is pressure to maintain rapid patient turnover. Long-term invasive and non-invasive ventilation is available for stable patients, not requiring PICU level care, in other wards in the hospital.

This was a retrospective descriptive study of all children admitted to the PICU over one calendar year from 1 January to 31 December 2009. Clinical data were extracted from a pre-existing PICU database.

Permission to conduct this study was obtained from the institutional Human Research Ethics Committee (HREC REF: 105/2011) and the need for informed consent was waived owing to the retrospective nature of the study.

Analysis

The definition of PICU LOS constituting a long-stay patient in our setting was modelled using techniques described by Weissman (1997) (8):

1. For normally distributed data - two standard deviations above the mean.
2. Five times the median length of stay.
3. Beyond the 75th and 95% percentile of the median.
4. A graph of the frequency distribution of length of stay vs. number of admissions was created to visually examine the data. A specific LOS was identified from visual

examination of the start of the “tail” of the distribution curve (if not normally distributed).

The best-fit model for our data was then chosen to distinguish between long- and short-stay patients (SSP).

The Shapiro-Wilk test was used to test for normality. Data were not normally distributed and are therefore presented throughout this paper as median (interquartile range, IQR) for continuous data and proportions for categorical data. The characteristics and outcomes of the long-stay group were compared to the short-stay group using Mann-Whitney U and Chi² tests (Yates corrected where cell values were <10).

Variables found to be significantly associated with the binary outcome of interest (LSP) on univariate analysis were entered into a forward stepwise logistic regression model to evaluate which characteristics were associated with prolonged length of stay and to create a predictive algorithm.

The proportion of ICU days consumed by the long-stay patients was calculated to determine resource allocation.

Statistical analyses were conducted using Statistica (StatSoft Inc 2011; Tulsa USA) and a significance level of $p < 0.05$ was chosen.

6.5 Results

1126 children (median (IQR) age 8 (2 – 32) months; 60.9% male), occupying 5936 bed days, were admitted to the PICU over the study period. Baseline patient data are presented in Table 1.

Defining the long-stay patient

The data were not normally distributed, therefore it was not considered appropriate to use two standard deviations above the mean to identify LSP (8).

The model using $> 75^{\text{th}}$ centile for length of stay corresponded to six days; 253 (22.5%) patients fulfilled this criterion, with a median length of stay of 11 (8 – 17) days and a 14% mortality rate.

When using five times the median duration of stay (>15 days); 76 (6.7%) of patients fulfilled the definition with a median (IQR) LOS of 25.5 (18.5 – 35.5) days and 30% mortality.

Modelling LSP using $>95^{\text{th}}$ percentile was found to be equivalent to the visual examination of the start of the “tail” of the distribution curve (Figure 1); with 54 (4.8%) of patients spending ≥ 20 days in PICU, with a median (IQR) duration of stay of 29.5 (25 – 40) days and a 29.6% mortality rate.

We therefore chose to define LSP as those having a duration of stay >19 days according to two best-fit models.

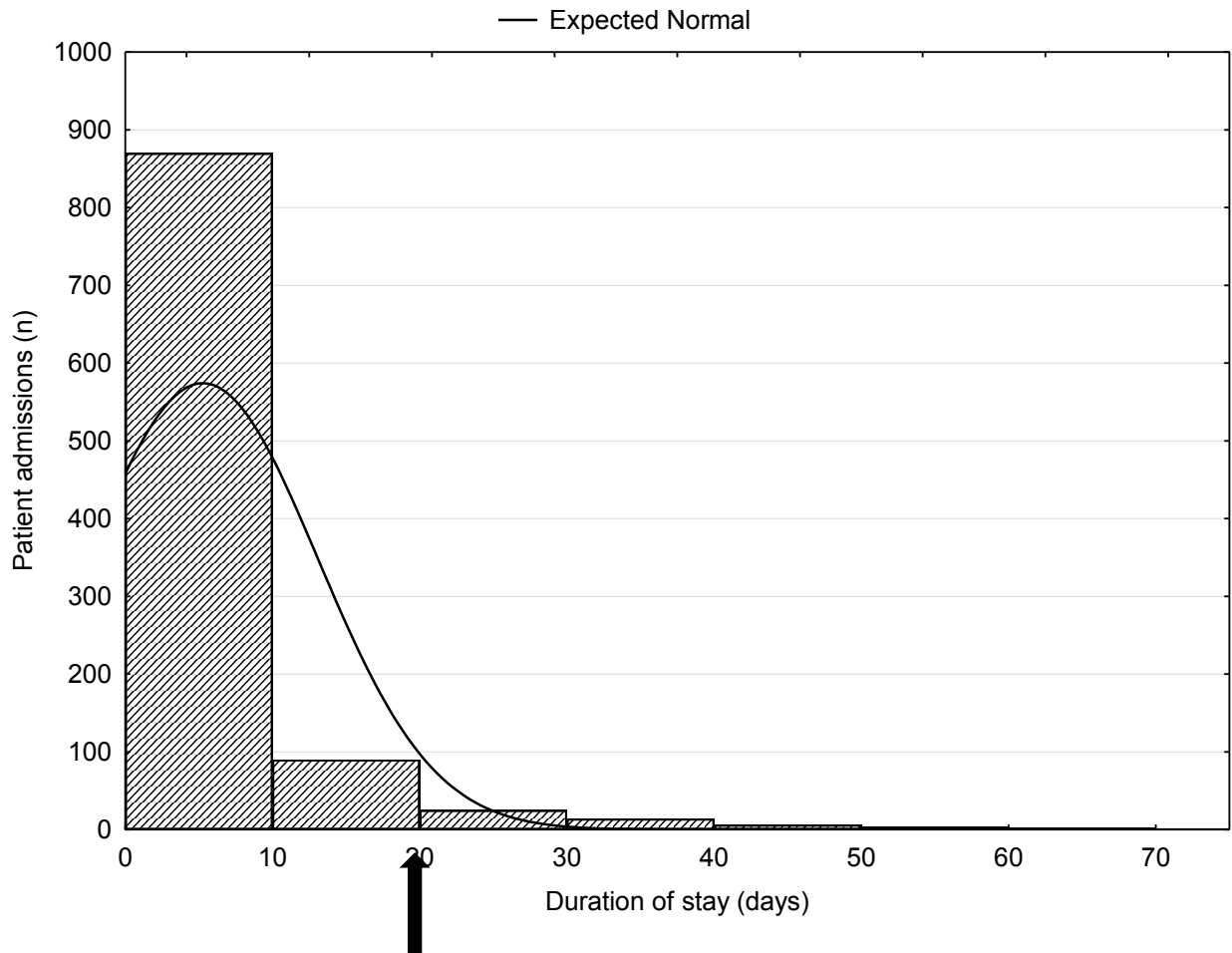


Figure 1: The Length of Stay Distribution Curve. The arrow reflects the start of the visual tail and 95th percentile.

LSP Characteristics and outcomes

In comparison to SSP, LSP were significantly younger, a greater proportion was female, and admitted for emergency care. The main reason for admission of LSP was for the management of paediatric illness, which included sepsis, pneumonia and congenital heart disease, whereas SSP were more commonly admitted for post- operative care, trauma related injury and poisoning (Tables 1 and 2).

Long-stay patients had a significantly higher mortality and standardised mortality rate (actual / mean predicted mortality using PIM2 score) compared to short-stay patients (Table 1).

There were no significant differences between long-stay patients who died and those who survived (Table 3).

In the final multiple regression model, only female gender was independently associated with the outcome of long-stay making it impossible to develop a predictive model for LSP (Table 4).

Table 1: Admission characteristics and outcomes of all patients admitted to Paediatric Intensive Care Unit during the study period, and comparison between long and short-stayers.

	All n = 1126	Long-stayers N=54	Short-stayers N=1072	p
Gender M:F	686 : 440 (60.9% male)	26:28 (48% male)	660:412(61.6% male)	0.049
Age (months)	8 (2 – 32)	4 (2 – 17)	9.0 (2.0 – 34.0)	0.03
Weight (kg)	7 (3.6 – 13.2)	4.75 (3.1 – 10.2)	7.15 (3.6 – 13.6)	0.04
Risk of mortality using PIM2 score	0.0723 (0.0259 – 0.1923)	0.096 (0.0487 – 0.1490)	0.0712 (0.0255 – 0.1938)	0.4
Emergency admissions	832 (73.9)	46 (85.2)	786 (73.3)	0.05
Reason for admission				
Paediatric illness	676 (60)	41 (75.9)	635 (58.3)	0.02
Poisoning	15 (1.3)	0	15 (1.4)	0.8
Non-accidental injury	4 (0.4)	1 (1.9)	3 (0.3)	0.5
Post cardiac surgery	188 (16.7)	9 (16.7)	179 (16.7)	0.9
Post thoracic surgery	16 (1.4)	0	16 (1.5)	0.8
Post abdominal surgery	74 (6.6)	1 (1.9)	73 (6.7)	0.2
Post cranial surgery	50 (4.4)	1 (1.9)	49 (4.6)	0.5
Post spinal surgery	151.3)	0	15 (1.4)	0.8
Post airway surgery	16(1.4)	0	16 (1.5)	0.8
Post surgery - other	15 (1.3)	0	15 (1.4)	0.8
MVA	26 (2.3)	0	26 (2.4)	0.5
Other accident	31 (2.8)	1 (1.9)	30 (2.8)	0.99
HIV Test not done	544(48.3)	22(40.7)	522(48.6)	0.3
HIV positive, not symptomatic of AIDS	78(6.9)	1 (1.9)	77 (7.2)	0.2
HIV negative	409(36.3)	22 (40.7)	387(36.1)	0.5
HIV positive and mildly symptomatic	95(8.4)	7 (13.0)	88 (8.2)	0.3
Mortality	145(12.9)	16 (29.6)	129 (12.0)	0.0002
Risk adjusted mortality (actual/mean predicted)	0.77	2.4	0.7	0.002
Duration PICU stay (days)	3.0 (1 – 6)	29.5 (25 – 40)	2 (1 – 5)	<0.0001

Continuous data are presented as median (interquartile range) and categorical data as n (%) unless otherwise indicated.

PICU=Paediatric Intensive Care Unit

HIV=Human Immunodeficiency Virus

M:F=Male to Female ratio

AIDS=Acquired Immunodeficiency Syndrome

PIM2=Paediatric Index of Mortality Score Version 2

MVA=Motor Vehicle Accident

Table 2: “Paediatric illness” primary admission diagnoses of long- and short-stayers.

Primary diagnoses	Long-stayers n=41	Short-stayers N=1072	p
Sepsis (including meningococcal)	2(4.9)	54(5.0)	0.75
Pneumonia/pneumonitis	13(31.7)	195(18.2)	0.03
Cardiomyopathy/endo-/myo-/peri-carditis	3(7.3)	24(2.2)	0.1
Congenital heart disease without surgery	13(31.7)	58(5.4)	<0.0001
Necrotising enterocolitis	1(2.4)	19(1.8)	0.8
Trachea-oesophageal fistula or oesophageal atresia	3(7.3)	2(0.2)	<0.0001
Burns related	1(2.4)	7(0.7)	0.7
Non-HIV immunodeficiency	1(2.4)	4(0.4)	0.5
Chronic Lung Disease	1(2.4)	1(0.1)	0.1
Other Shock	1(2.4)	2(0.2)	0.2
Congenital diaphragmatic hernia	1(2.4)	5(0.5)	0.5
Rheumatic heart disease	0(0)	5(0.5)	0.5
Gastroschisis	0(0)	4(0.4)	0.3
Central Nervous System	0(0)	62(5.8)	0.2
Guillain-Barré syndrome	0(0)	2(0.2)	0.1
Gastroenteritis	0(0)	61(5.7)	0.2
Upper airway Obstruction	0(0)	17(1.6)	0.9
Bronchiolitis	0(0)	11(1.0)	0.9
Apnoea	0(0)	11(1.0)	0.9
Asthma	0(0)	5(0.45)	0.5
Gastrointestinal Tract	0(0)	21(2.0)	0.7
Tuberculosis	0(0)	3(0.3)	0.2
Renal failure	0(0)	5(0.5)	0.5
Kwashiorkor	0(0)	2(0.2)	0.1
Inhaled Foreign Body	0(0)	2(0.2)	0.1

Data are n (%)

Table 3: Differences between long-stay patients who died and those who survived.

	Alive n=38	Died n=16	p
Gender M:F	18:20	8:8	0.9
Age (months) median (IQR)	4.5 (2.0 – 17.0)	3.5 (2.0 – 15.0)	0.9
Weight (kg)	4.8 (3.1 – 10.2)	4.9 (3.3 – 10.0)	0.9
Risk of mortality	0.0994 (0.0558 – 0.1412)	0.0904 (0.0227 – 0.2542)	0.8
Emergency admissions	34	12	0.3
Reason for admission			
Paediatric illness	30	11	0.7
Poisoning	0	0	-
Non-accidental injury	1	0	0.7
Post cardiac surgery	5	4	0.5
Post thoracic surgery	0	0	-
Post abdominal surgery	0	1	0.7
Post cranial surgery	1	0	0.7
Post spinal surgery	0	0	-
Post airway surgery	0	0	-
Post surgery - other	0	0	-
MVA	0	0	-
Other accident	1	0	0.7
HIV status			
Test not done	17	5	0.5
HIV positive, not symptomatic of AIDS	1	0	0.7
HIV negative	14	8	0.6
HIV positive and mildly symptomatic	4	3	0.8
Duration ICU stay before discharge or death (days)	27 (25 – 36)	38.5 (26.5 – 45.0)	0.08

Table 4: Final multivariate logistic regression model (adjusting for all variables shown) for the binary outcome of long stay.

	Adjusted Odds ratio	95% confidence interval	p
Female gender	1.7	1.001 – 3.03	0.047
Age	0.99	0.98 – 1.01	0.2
Weight	1.01	0.96 – 1.05	0.8
Paediatric illness as reason for admission	1.5	0.71 – 3.33	0.3
Emergency admission	1.46	0.60 – 3.55	0.4

Resource utilisation

The LSP, who constituted 4.8% of the PICU population, were calculated to have utilised 30.4% (1807) of the total bed days throughout the study period (Figure 2).

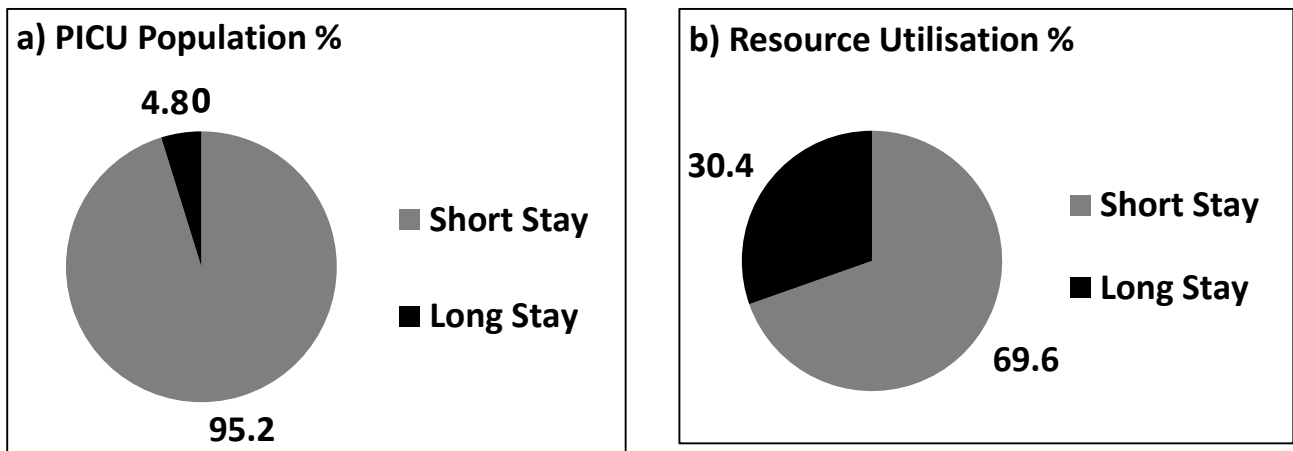


Figure 2: Illustration of the proportion of long- stay patients in a) the PICU Population and b) their resource consumption (in terms of bed utilisation) relative to short-stay patients.

6.6 Discussion

This study contributes data from a South African setting in keeping with over two decades of international research. Our findings support other reports that LSPs represent a small but consistent proportion of the PICU population, which utilises substantial PICU resources yet have a worse outcome compared to other PICU patients (2, 3, 5, 12).

Although LSPs are increasingly acknowledged as an integral part of PICU planning and care, they have historically been a difficult group to prospectively identify and investigate (2), mainly due to the lack of a uniform definition of what constitutes a LSP. A particular length of stay may be designated as a threshold to identify the long-stay patient, but this threshold varies widely in the literature (2, 3, 5, 8-10). We have established a rational basis for our long stay definition and found significant differences between our short and long stay populations.

Similar to previous studies (2, 20), we found the best match for defining LSPs as being >95th percentile of the median length of stay, which corresponded to the start of the tail of the frequency distribution curve. This duration of >19 days is the same as that reported by Jeena et al, in another South African PICU over a decade ago(24), but lower than that reported by other studies using different methods (5-7, 9, 20) .

It is important to standardise institutional definitions of LSP in order to engage in ongoing audits and practice improvement initiatives; to plan the care of LSP more economically, including counselling of families about additional risks and complications of an extended PICU stay and to motivate for the involvement of the extended multi-disciplinary team to provide holistic care to the child whilst in PICU and to ensure the prompt recognition of medical futility. It would also be useful to have a uniform, global, definition of a LSP patient for appropriate data comparison amongst PICUs. The definition delineated in this study could provide a rational comparison for further studies conducted in similar contexts across the world.

On univariate analysis in our study, LSPs were found to be younger; a greater proportion were female, and were admitted for emergency reasons compared to short- stay patients, similar to previous reports (2). Although lower admission weight was associated with long PICU stay, this was not adjusted for patient age or height and cannot therefore be interpreted as malnutrition, wasting or stunting. Capturing characteristics related to nutrition in future studies would be helpful as it could reflect the health of our population and be a potentially modifiable factor.

Previous studies from South Africa (24) and India (10) described most admission diagnoses in LSP were of infective origin while studies from developed countries list congenital heart disease, neurological disease and metabolic disorders as the more common diagnoses in LSP (6). Our PICU admission diagnoses and patient profile differed widely due to the varied case mix in our multidisciplinary setting. It was notable, however, that LSPs were diagnosed more frequently with pneumonia, congenital heart disease without surgery, and trachea-oesophageal fistula or oesophageal atresia than the short-stay group. The high incidence of pneumonia is expected in the South African context of a large burden of infectious diseases (35). We did not record comorbid conditions other than HIV, as this is the most prevalent comorbidity in our population group. In future studies it would be useful to capture all comorbid diseases and chronic care devices as it has been suggested they these may predispose to long PICU stay (2, 3). We did not review all the individual cases to assess whether there were additional co-morbid factors and that is a weakness of the study. In any prospective study we would collect that data as other authors have shown that these may be relevant.

Diagnosis-specific mortality rates may guide critical care pathways (2) and admission policies. There is the perception that certain conditions, like Guillain-Barre syndrome, will result in a prolonged LOS, but carry an excellent outcome, whilst other diagnoses such as extensive

burns or cardiomyopathy may also result in a prolonged LOS, but with a much poorer prognosis. This requires further research to inform admission policies in individual units.

Mortality prediction models that use patient characteristics to predict the risk of death in the PICU have been developed. The challenge is that mortality prediction models need to be validated before they can be applied in an environment that is substantially different from the environment in which they were developed (31). The PIM2 model was previously found to be most accurate for the prediction of mortality (29) and is the score we used in this study. Discrimination and calibration for PIM 2 scores proved comparable to the score derivation units in a retrospective audit of case records and prospectively collected data from our PICU in 2006 (16). We found that although the admission PIM2 score was an excellent predictor of overall mortality ($p < 0.0001$), it was not a predictive factor for long PICU stay in this study.

Length of stay (LOS) is a marker of severity of illness, resource utilization and performance of a PICU. International studies have consistently reflected the small PICU LSP group (1% -7.5% of total PICU population) consume a disproportionately large amount of the available resources (18%-50%) (2, 3, 5, 6, 9). Our data support these findings, with LSPs constituting <5% of the PICU population, yet were calculated to have utilised 30.4% of the total bed days throughout the study period, and had an almost threefold risk of a fatal outcome compared to the short-stay group. The significant increase in mortality rate in LSPs is a consistent finding in the literature with LSP mortality rates ranging from twofold to almost tenfold higher than SSPs (2, 3, 5, 6, 9). The fact that the standardised mortality ratio was also significantly higher than short-stay patients demonstrated that outcome was far worse in LSP than was predicted on admission.

We were unable to identify any clinically relevant predictive factors associated with long PICU stay on admission data. It is suggested that in future prospective studies, patients be

reassessed after two or more weeks of PICU stay to attempt to identify factors predictive of outcome at that point.. Once a patient has been recognised as a LSP, it would be appropriate to discuss the ongoing care plan as a multidisciplinary team, including family counselling as appropriate (6, 36). Ongoing assessment of the LSP would ensure medical futility criteria were timeously reviewed. It is unethical to prolong suffering and to use valuable resources on a child who is too ill to benefit from PICU care (3).

An Australian study concluded that more than two-thirds of children who spent >28 days in their PICU had an unfavourable outcome (moderate disability, severe disability or death), with almost half the LSPs having died at six- months follow up post PICU discharge (5). A Canadian prospective observational study found longer PICU stays to be independently associated with both worse quality of life scores and worse functional outcome at one month follow up (37). PICU length of stay is a treatment-related exposure that has been highlighted as a predictor of post-critical illness psychiatric morbidity such as posttraumatic stress disorder and depression (38). In this study outcome was measured by comparing PICU survival and non-survival. Owing to the retrospective nature of this study, we were unable to measure the quality of life or morbidity of survivors of long PICU stay, and this constitutes a limitation of this study. We did not collect data related to previous PICU admissions, and how this influenced subsequent outcome, and this is recommended for future studies.

This study has not addressed the nature of care in the PICU required by LSPs. In many cases the nursing, therapeutic input and psychosocial needs of these children and their families may differ profoundly to those of the acutely ill short-stay patients. Parents too are at higher risk of adverse effects of their children's admission. A prospective study in Boston focussed on LSPs and their families and highlighted the frequency of conflicts and the issues underlying those conflicts (36).

Long term functional outcome and quality of life measures may be more useful in the context of improved PICU survival, and it is recommended that these outcomes be used in future, prospective studies of LSP (5). There is much scope for future research on the quality of life of PICU survivors from our unit, especially in the South African context where there is a low ratio of health professionals to patients, the social welfare disability grant offered to a patient with a moderate to severe disability is currently \$120 per month and there is poor infrastructure and inaccessible transport in much of the country (39). Identifying whether high PICU mortality has been traded for a higher prevalence of morbidity has potential ramifications for provision and delivery of healthcare to this vulnerable population (28).

The poor outcome of LSP reported here and in previous studies raises concerns around inappropriate resource consumption in the PICU. We recognise that in the South African setting, equitable distribution of healthcare services must be an ethical consideration when budgeting and planning for healthcare resource allocation (32).

6.7 Conclusions

It is important to standardise institutional definitions of LSPs. Our PICU defined LSPs as patients with a length of stay (LOS) >19 days based on the two best fit models: >95th centile of duration of stay and the visual “tail” of the LOS distribution curve. The definition delineated in this study could provide a rational basis for comparison between similar PICUs across the world.

Long-stay patients represent a small percentage of PICU admissions yet have a significantly increased mortality rate (greater than expected at the time of admission) and consume a disproportionate amount of resources compared with short-stay patients. This pattern from a South African setting is in keeping with international trends.

We were unable to establish a predictive model for the early recognition of potential long-stay patients in order to effectively plan PICU bed allocation.

Further investigations are needed to assess the quality of life of survivors of long PICU stay, particularly in low and middle income countries.

6.8 Acknowledgements

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8) APPENDICES

APPENDIX 1: THE PROTOCOL

Introduction

Paediatric intensive care is a costly, specialised and limited resource that should be used as effectively and efficiently as possible.

In the context of poorer countries where access to intensive care is limited, it is particularly important to ensure resources are used rationally.

Rational use includes appropriate admission criteria to the paediatric intensive care unit (PICU) and carefully monitoring outcomes of resource utilization. Patients who are too well or too sick to benefit from intensive care should not be admitted.

It is clear that patients who have a long duration of stay in the PICU may use a disproportionate amount of the resources.(1-4, 8, 9, 12)

The perceived vulnerability of patients with a PICU long stay to increased mortality and morbidity raises concern about resource allocation. There is a paucity of outcome data for long stay PICU patients, but those that exist describe a wide spectrum of patients who have outcomes that range from excellent to poor.(2, 4, 7, 10)

It may be useful to describe this unique group of long-stay patients in order to identify potential long-stayers early in their PICU admission so that their care can be planned more economically, the multi-disciplinary team can be involved early and so that additional risks can be discussed with their families.(9). By doing this it may be possible to optimise outcome and prevent complications of extended PICU stay.

We aim to develop a rational basis for what constitutes a long stay patient (LSP) in the PICU. A particular length of stay is designated as a threshold to identify the long stay patient and this threshold varies in the literature from >7 days (5) to >12 days (1)to >13 days(2)to >30days(6).These different thresholds have been chosen subjectively or by using statistical methods.

The literature on long-stay patients in PICU is mostly from developed countries which have population and burden of disease profiles that may differ from developing countries. This study would contribute data from an African PICU setting, with its associated resource limitations and high burden of disease, including diseases of poverty and HIV- related infection (11).

The PICU at Red Cross War Memorial Childrens Hospital (RCWMCH) in Cape Town, South Africa serves the medical and surgical department for both emergency and elective admissions. PICU beds are in great demand and there is pressure to maintain rapid patient turnover.

Determining the patients who would qualify as long stay patients in the RCWMCH PICU and exploring the characteristics and outcomes of these long stay patients will hopefully enable us to provide more equitable intensive care.(2)

Objectives

- 1) To use existing data from the RCWMCH PICU 2009 database to describe a rational basis for the definition of a long-stay patient in our unit.
- 2) To review the characteristics and outcomes of the patients who comply with the long-stay patient definition, and to compare these to those defined as “short-stay” patients.
- 3) To assess the proportion of PICU days consumed by the long-stay patients (resource allocation) compared to short-stay patients.

Subsidiary Objective

To determine if the results of this study could be used as a predictive tool for future admissions

Method

Study Design

The study is a retrospective descriptive study of data collected over one calendar year from a pre-existing database in the Red Cross War Memorial Childrens Hospital PICU in Cape Town, South Africa.

The Red Cross War Memorial Childrens Hospital PICU database is a pre-existing database (approved by the UCT HREC, 039/2011) which captures objective, measurable patient and outcome data which can be expressed on an Excel Spreadsheet.

The distribution of length of stay will be reviewed with published data in the literature (5, 12) and the definition of a long-stay patient in this setting will be established.

The characteristics and outcomes of the long-stay group will be compared to the short-stay group.

The proportion of ICU days consumed by the long-stay patients will be calculated to determine resource allocation.

Setting

The setting is the 20-bedded multidisciplinary PICU of Red Cross War Memorial Children’s Hospital, situated in Cape Town, South Africa. This PICU admits approximately 1400 patients aged from birth to about 14 years per annum (with the majority under two years of age), of which about 500 are emergency admissions, mostly for infectious diseases. The mortality rate is approximately 10%.

The majority of patients come from the Metro West region of the Western Cape. There are patients from other parts of the Western Cape and other provinces, particularly the resource limited Eastern Cape, who require admission due to lack of access to specialist care and intensive care in those regions. Most patients come from impoverished backgrounds with a high burden of diseases of poverty and comorbid conditions, including HIV.

This PICU is unique in terms of the very high patient turnover and large annual admission numbers, with a high burden of diseases in poverty. In this context, where bed availability is at a premium, it is essential to consider resource allocation pragmatically.

There is a 10-bedded tracheostomy unit which acts as a step down unit for patients requiring long term ventilatory support and the unit supports and educates patients who are suitable candidates for home ventilation.

Participants

All PICU admissions from the 1st January 2009 until the 31st December 2009 will be included in the study. Each admission is allocated a unique admission number on the data base.

There are no exclusion criteria.

Measurements

Duration of stay will be measured in completed days in the PICU from the date and time of admission.

The characteristics of the long-stay patients will be captured on a standardised data capture sheet {Appendix 3} which is completed on admission and updated at discharge. Characteristics include age, gender, weight, category of admission, diagnoses, HIV status, blood pressure, ventilation status, pupillary reaction, history of preceding cardiac arrest and a Paediatric Index of Mortality Score (PIM2).

The PIM2 score estimates mortality risk from the data available at PICU admission. Literature supports the PIM2 score a suitable mortality prediction model to use for monitoring quality of paediatric intensive care.(13, 14, 15)

Outcome is measured as death or survival.

The utilization of PICU resources by the long-stay patients will be expressed as the proportion of PICU beds occupied by the long-stay patients over the given time frame and as bed-day cost.

Analysis

A graph of the frequency distribution of the length of stay will be created to visually examine the data. The mean \pm standard deviation, median and range of length of stay will be reported. The Shapiro-Wilk test will be used to test for normality. The central tendency will then be determined. Distribution patterns of length of stay are often markedly skewed by patients with a prolonged PICU stay (12). This skewness makes traditional parameters such as mean and standard deviation less useful when describing length of stay.

Long-stay patients will be identified by showing the relationship between patient volume (admissions) and length of stay (days) using graphs and descriptive statistics.

The following definitions of long PICU stay will be modelled:

1. Two standard deviations above the mean. This would only be appropriate if data were normally distributed.

2. Beyond the 75th and 95% percentile of the median.
3. A multiple of the median e.g. five times the median duration of stay.
4. A specific duration taken from visual examination of the start of the “tail” of the distribution curve (if not normally distributed)

The characteristics and outcomes collected on the data capture sheet (appendix 1) between the short-stay and long stay groups will be compared using Mann-Whitney U tests (assuming nonparametric data) and Chi-square tests for categorical variables. Variables found to be significantly different on univariate analysis will be entered into a forward stepwise logistic regression model to evaluate which characteristics are associated with prolonged length of stay and to create a predictive algorithm.(2)

Ethics

This study is essentially a retrospective audit and carries no risk to the subjects. Approval will be obtained from the Faculty of Health Sciences Research Ethics Committee.

Anonymity

The standard data collected from each patient on the PICU database is given an anonymous admission number so each patient’s data set is anonymous during analysis. No information which could lead to the identification of individual patients will be made available in any output arising from this study.

There will be a confidential review of the unprocessed data and, where required, patient folders. This confidential review will only be done by the primary investigator and the study supervisors, Professor Argent and Ass. Professor Morrow.

Risk and informed consent

This study requires no direct patient interaction and will have no effect on intervention, therapy or outcomes of the cohort so we request that the requirement for informed consent is waived.

Relevance

Conclusions from this study may be used to support further discussion around PICU admission and discharge policies and to contribute to the small body of literature on this topic from the developing world.

This study will conform to the requirements of the Declaration of Helsinki (last updated 2008)

Logistics

Academic support has been provided to the primary investigator by the University Of Cape Town (UCT) School of Public Health and Family Medicine through the Mmed research methods workshop for registrars.

The UCT Statistics Department will be approached for support with the analysis of the data.

If the study proposal is approved then it will be submitted to the postgraduate office for approval by the Professional Masters Committee Chair and the Board of the Faculty of Health Sciences.

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APPENDIX 2: HREC APPROVAL LETTER AND PROOF OF EXTENSION UNTIL 2015

UNIVERSITY OF CAPE TOWN



Faculty of Health Sciences
Human Research Ethics Committee
Room E52-24 Grootte Schuur Hospital Old Main Building
Observatory 7925
Telephone [021] 406 5626 • Facsimile [021] 406 6411
e-mail: shuretta.thomas@uct.ac.za

13 June 2012

HREC REF: 105/2011

Dr T Nupen
c/o A/Prof B Morrow
Paediatrics
Red Cross War Memorial Children's Hospital

Dear Dr Nupen

PROJECT TITLE: CHARACTERISTICS AND OUTCOME OF LONG-STAY PATIENTS IN A PAEDIATRIC INTENSIVE CARE UNIT IN CAPE TOWN, SOUTH AFRICA

Thank you for your letter to the Faculty of Health Sciences Human Research Ethics Committee, received 22nd May 2012.

The HREC is granting extension of the above-mentioned study for a further year **until 30th June 2013.**


We acknowledge that Dr Tracy-Lee Nupen will now take over as Principal Investigator for the above-mentioned study.

Please submit a further progress report if the research continues beyond the expiry date (FHS016). Please submit a brief summary of findings if you complete the study within the approval period so that we can close our file (FHS010).

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

Please quote the HREC REF in all your correspondence.

Yours sincerely

 **PROFESSOR M BLOCKMAN**
CHAIRPERSON, HSF HUMAN ETHICS

S Thomas



FHS016: Annual Progress Report / Renewal

HREC office use only (FWA00001637; IRB00001938)			
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 June 2015
<input type="checkbox"/> Not approved	See attached comments		
Signature Chairperson of the HREC		Date Signed	21/10/2014

Comments to PI from the HREC	RESEARCH ETHICS COMMITTEE 2014 -10- 27 HEALTH SCIENCES FACULTY UNIVERSITY OF CAPE TOWN

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)	20 October 2014		
HREC REF-Number	105/2011	Current Ethics Approval was granted until	June 2014
Protocol title	Characteristics and Outcome of Long-Stay Patients in a Paediatric Intensive Care Unit in Cape Town, South Africa		
Protocol number (if applicable)	SCAH DRC 565/11		
Are there any sub-studies linked to this study?	<input type="checkbox"/> Yes <input type="checkbox"/> No		
If yes, could you please provide the HREC Ref's for all sub-studies? Note: A separate FHS016 must be submitted for each sub-study.			
Principal Investigator	Tracey Lee Nupen		
Department / Office Internal Mail Address	Department of Paediatrics, Red Cross Hospital, Registrars Office, 5 th floor ICH Building c/o Nicole Le Chat		

1.1 Does this protocol receive US Federal funding?		No
1.2 If the study receives US Federal Funding, does the annual report require full committee approval?		
1.3 Has sponsorship of this study changed? If yes, please attach a revised summary of the budget.		

APPENDIX 3: DATABASE DATA COLLECTION FORM

- PICU Admission Number
- Date of Birth
- Age (months)
- Weight (kg)
- Gender
- Date and time of admission
- Date of discharge or death
- Primary diagnosis
- Other diagnoses
- Outcome (death versus survival)
- Category of admission (elective versus emergency, medical versus surgical, accidental versus non-accidental injury, poisoning)
- HIV status
- Blood Pressure
- Mechanical ventilation within the first hour of ICU admission
- Pupillary Reaction to bright light
- Cardiac Arrest Preceding ICU admission
- PIM2 Score (see Appendix 4)

APPENDIX 4: Paediatric Index of Mortality 2 (PIM2) with General Instructions

PIM2 is calculated from the information collected at the time of PICU admission. Observations are recorded at the time of first face-to-face contact between the PICU doctor and the patient. The first value of each variable measured within the time period of first contact to 1 hour after PICU arrival is used. The first contact may be in your ICU, your emergency department, a ward in your own hospital or another hospital(e.g. on a retrieval). If information is missing record zero, except for systolic blood pressure which should be recorded as 120 mm Hg. Include all children admitted to your ICU.

1. Systolic Blood Pressure, mmHg
2. Pupillary reaction to bright light (>3mm and both fixed=1, other or unknown=0)
3. PaO₂ (unknown=0), FiO₂ at the time of PaO₂ if oxygen via ETT or headbox (unknown=0)
4. Base Excess in arterial or capillary blood, mmol/l (unknown=0)
5. Mechanical Ventilation at any time during the first hour in ICU (no=0, yes=1)
6. Elective admission to ICU (no=0, yes=1)
7. Recovery from surgery or a procedure is the main reason for ICU admission (no=0, yes=1)
8. Admitted following cardiac bypass (no=0, yes=1)
9. High Risk Diagnosis. Record the number in brackets. If in doubt, record 0.
 - [0] None
 - [1] Cardiac arrest preceding ICU admission
 - [2] Severe combined immune deficiency
 - [3] Leukemia or lymphoma after first induction
 - [4] Spontaneous cerebral haemorrhage
 - [5] Cardiomyopathy or myocarditis
 - [6] Hypoplastic left heart syndrome
 - [7] HIV infection
 - [8] Liver failure is the main reason for ICU admission
 - [9] Neuro-degenerative disorder
10. Low risk diagnosis. Record the number in the brackets. If in doubt record 0.

[0] None

[1] Asthma is the main reason for ICU admission

[2] Bronchiolitis is the main reason for ICU admission

[3] Croup is the main reason for ICU admission

[4] Obstructive sleep apnoea is the main reason for ICU admission

[5] Diabetic keto-acidosis is the main reason for ICU admission

Coding Rules

1. Record systolic blood pressure as 0 if the patient is in cardiac arrest, record 30 if the patient is shocked and the blood pressure is so low that it cannot be measured.
2. Pupillary reactions to bright light are used as an index of brain function. Do not record an abnormal finding if this is due to drugs, toxins or local eye injury.
3. Mechanical ventilation includes mask or nasal CPAP or BiPAP or negative pressure ventilation
4. Elective admission. Include admission after elective surgery or admission for an elective procedure, or elective monitoring, or review of home ventilation. An ICU admission or operation is considered elective if it could be postponed for more than 6 hours without adverse effect.
5. Recovery from surgery or a procedure includes a radiology procedure or a cardiac catheter. Do not include patients admitted from the operating theatre where recovery from surgery is not the main reason for ICU admission (e.g. a patient with a head injury who is admitted from theatre after insertion of an intracranial monitor; in this patient the main reason for ICU is the head injury).
6. Cardiac bypass. These patients must also be coded as recovery from surgery.
7. Cardiac arrest preceding ICU admission includes both in-hospital and out-of-hospital arrests. Requires either documented absent pulse or the requirement for external cardiac compression. Do not include past history of cardiac arrest.
8. Cerebral haemorrhage must be spontaneous (e.g. from an aneurysm or arterio-venous malformation). Do not include traumatic cerebral haemorrhage or an intracranial haemorrhage that is not intracerebral (e.g. subdural).
9. Hypoplastic left heart syndrome. Any age, but include only cases where a Norwood procedure or equivalent is or was required in the neonatal period to sustain life.
10. Liver failure acute or chronic must be the main reason for ICU admission. Include patients admitted for recovery following liver transplantation for acute or chronic liver failure.
11. Neuro-degenerative disorder. Requires a history of progressive loss of milestones or a diagnosis where this will inevitably occur.
12. Bronchiolitis. Include children who present either with respiratory distress or central apnoea where the clinical diagnosis is bronchiolitis.

13. Obstructive sleep apnoea. Include patients admitted following adenoidectomy and/or tonsillectomy in who obstructive sleep apnoea is the main reason for ICU admission (and code as recovery from surgery).

APPENDIX 5: INSTRUCTIONS TO AUTHORS OF CHOSEN JOURNAL

http://journals.lww.com/pccmjournal/Documents/PCC_Inst_for_Authors.pdf



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Conflicts of Interest and Source of Funding: "Author A" has received honoraria from "Company I." "Author B" is currently receiving a grant (#12345) from "Organization Y," and is on the speaker's bureau for "Organization X" – the CME organizers for Company I. For the remaining authors none were declared.

Human and Animal Subjects. All studies of human subjects must contain a statement within the Materials and Methods section indicating approval of the study by the Institutional Review Board (or institutional review body) that subjects have signed written informed consent, or that the Institutional Review Board

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Title Page. The title page should contain 1) the title; 2) first name, middle initial, and last

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Text Material. The text should be organized into the following sections: Introduction, Materials and Methods, Results, Discussion, and Conclusions followed by Acknowledgments, References, Figure Legends, and Tables. Secretarial and editorial assistance are not acknowledged. Results may be presented in the text, in the figures, or in the tables. The Discussion section should interpret the results without unnecessary repetition. References to related studies should be included in the text section.

In addition, the following should be observed:

- The full term for which an abbreviation stands should be used at its first occurrence in the text unless it is a standard unit of measure. The abbreviation should appear in parentheses after the full term. Abbreviations should not be in the title, figure legends or table titles.
- For standard American units, do not use values that are more significant than your analysis is capable of accurately measuring (e.g., PaO₂ 84 torr [11.2 kPa], not 83.7 torr).

- Hemodynamic measurements for pressure (e.g., MAP) should appear in mm Hg and gas tension measurements (e.g., Po₂) should appear in torr with SI units in parentheses. The units of vascular resistance are dyne.sec/cm⁵.
- Please provide *r*² values for parametric data.

References. All references should be cited in sequential order in the text and typed on a separate sheet of paper. References should be identified in text, tables, and legends by full-size Arabic numerals on the line and in parentheses. Do not use wordprocessing footnote, endnote, or paragraph numbering functions to make a list of references. Titles of journals should be set in italics and abbreviated according to the style used in *Index Medicus*. If journal titles are not listed in *Index Medicus* they should be spelled out. Unpublished data or personal communications should be noted parenthetically within the text but not in the References section. Inclusive page numbers (e.g., p. 1–10) should be used for all references. Listed below are samples of standard references; however, a complete listing of references can be found on the International Committee of Medical Journal Editors web site, www.icmje.org.

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Standard Book with Authors: Civetta JM, Taylor RW, Kirby RR. *Critical Care*. Third Edition. Philadelphia, Lippincott, Williams & Wilkins, 1996

Standard Book with Editors: Norman IJ, Refern SJ (Eds): *Mental health care for elderly people*. New York, Churchill Livingstone, 1996

Standard Chapter in a Book: Phillips SJ, Whisnant JP: Hypertension and stroke. In: Laragh JH, Brenner BM (Eds). *Hypertension: Pathophysiology, diagnosis and management*. Second Edition. New York, Raven Press, 1995, pp 465–478

Standard Web Site/Electronic Format: Marion DW, Domeier R, Dunham CM, et al: Practice management guidelines for identifying cervical spine injuries following trauma. Available online at: <http://www.east.org>. Accessed July 1, 2000

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Tables and Figures. The number of figures and tables should be appropriate for the length of the manuscript; do not use superfluous illustrations. Tables expanding more than

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Figures.

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Correspondence can also be sent to:
Patrick M. Kochanek, MD, MCCM
Editor, *Pediatric Critical Care Medicine*
Society of Critical Care Medicine
500 Midway Drive
Mt. Prospect, IL 60056