THE DEVELOPMENTAL STATUS OF PAEDIATRIC INTENSIVE CARE UNIT SURVIVORS AT AN ACADEMIC HOSPITAL IN GAUTENG

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DECLARATION

I, Andrea Maria Lentzakis, declare that this Dissertation is my own, unaided work. It is being submitted for the degree of Master of Science in Physiotherapy at the University of Witwatersrand, Johannesburg. It has not been submitted before for any degree at any other University.

Andrea Lentzakis

_____ day of _____20_____ in _____

ABSTRACT

Background: Limited research has been done on the effects of the PICU on the development of infants once discharged. Children are exposed to many risk factors; these include chromosomal abnormalities, genetic or congenital disorders, central nervous system disturbances, severe attachment disorders, respiratory distress, brain haemorrhage, chronic infection and severed nutritional deprivation (Bayley, 2006; Grantham- McGregor, et al, 2007; Moura et al, 2010). Children can only be deemed as healthy once they are able to fulfil their activities of daily living.

Study design: This study was a cross-sectional descriptive study.

Aim: To identify if paediatric intensive care unit survivors aged one month to three and half years, with medical conditions, are at risk of developmental delay.

Objectives: The objectives of this study were to describe the motor, cognitive and language development outcome of PICU survivors aged one month to three and a half years and to describe the developmental findings of these children once discharged from PICU using the Bayley-III. To investigate the prevalence of developmental delay in children once discharged from PICU and to describe what facets of their development are predominantly affected. Also to determine if there is an association between demographic and clinical information of PICU survivors. Lastly to compare the developmental outcome of PICU survivors to their healthy peers.

Methods: Forty-two participants were recruited once discharged from the PICU at Charlotte Maxeke Johannesburg Academic Hospital. Children that were included were those that has been previously admitted to the intensive care unit at CMJAH, aged one month to three and a half years old corrected age, admitted with a medical condition and those that has been between one month and six months post discharge from the PICU. Children with any pre-existing neurological problem such

as CP, Down's syndrome, HIE and hydrocephalus were excluded from the study. They were assessed using the Bayley Scales of Infant and Toddler Development-III. Data of 42 healthy participants who had no history of PICU was used for comparison. This control group were healthy neonates from CMJAH in South Africa who were discharged home with their mothers.

Results: The data of 24 males and 18 females were analysed. The mean corrected age of the participants at the time of the Bayley-III assessment was 8.84 months the mean age of the control group was 10.58 months. The mean length of ICU stay was 12.85 days and the mean time on ventilation was 8.61 days. The mean cognitive composite score for the PICU group was 104.17 and for the control group was 94.17. The mean language composite score for the PICU group was 108.02 and for the control group was 103.93. The mean motor composite score for the PICU group was 104.26 and for the control group was 95.45. There was a statistical significant association between neonatal complications and the composite scores of the Bayley III ($p=0.013$ for cognitive, $p=0.012$ for language and $p=0.003$ for motor). It was also found that that there was a statistical significant association ($p = 0.023$) between the age of the participants and the motor scores.

Conclusion: From the results of this study it is evident that both groups mean scores were within one standard deviation of the norm (above 85) and that the PICU group scored higher than the control group. This could be explained from the fact that the mean age of the PICU group was less than the control group. However there were some children in the PICU group that scored lower than 85 on the Bayley-III. A score of less than 85 is deemed at risk and less than 70 is deemed delayed. Thus from the results of this study, it is clear that children discharged from the PICU should be followed up to determine if there is developmental delay. Further research is required.

Keywords: developmental outcome, Bayley-III, paediatric intensive care unit, medical conditions.

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List of abbreviations:

ADL:	Activity of daily living
AGE:	Acute gastroenteritis
ART:	Antiretroviral therapy
Bayley-III:	Bayley Scales of infant and toddler development, third edition
BPD:	Bronchopulmonary dysplasia
BW:	Birth Weight
CMJAH:	Charlotte Maxeke Johannesburg Academic Hospital
CNS:	Central Nervous System
CP:	Cerebral Palsy
CW:	Current weight
ELBW:	Extremely low birth weight
HAP:	Hospital-acquired pneumonia
HFOV:	High Frequency Oscillatory Ventilation
HIE:	Hypoxic Ischaemic Encephalopathy
HIV:	Human Immunodeficiency Virus
HRQoL:	Health related quality of life
ICU:	Intensive care unit
ID:	Intellectual disability
IPPV:	Intermittent positive pressure ventilation
LBW:	Low birth weight
LOS:	Length of stay
LRTI:	Lower respiratory tract infection
MR:	Mental retardation
NCPAP:	Nasal Continuous Positive Airway Pressure
NVD:	Normal vaginal delivery
PICU:	Paediatric Intensive care unit
RDS:	Respiratory Distress Syndrome
ROP:	Retinopathy of prematurity
TB:	Tuberculosis

VLBW:	Very low birth weight

Definition of terms:

Developmental surveillance

This is a process where skilled professionals perform a thorough analysis of young infants to determine their developmental status. It is defined as a “flexible, continuous process whereby knowledgeable professionals perform skilled observations of children during the provision of healthcare”. It includes attending to the parents concerns, obtaining relevant developmental history, and making accurate and informative observations of children (Paediatrics, 2001).

Developmental screening

This is a brief assessment designed to identify children who may need a more thorough assessment (Paediatrics, 2001).

Developmental delay

According to First and Palfrey (1994), developmental delay exists when a child does not reach the developmental milestones at the expected age. Paediatrics (2006) described it as a condition in which a child is not developing and/or achieving skills according to the expected time frame.

IPPV

Intermittent positive pressure ventilation is where a mechanical ventilator uses a controlled pressure of gas to assist in ventilation or the expansion of lungs (Handelsman, 1991). This provides increased tidal volumes for patients with a variety of pulmonary conditions.

Low birth weight

Babies defined as having low birth weight are those born less than 2500g, according to the World Health Organisation (Siza, 2008).

Prematurity

Infants born less than the gestational age of 37 weeks are considered to be premature (WHO, 2018).

CHAPTER 1: Introduction

1.1. Background

Developmental delay is defined as, “the failure to acquire age appropriate functionality, it may involve one or more streams of development.” (Aly, Taj and Ibrahim, 2010).

A child is expected to achieve specific milestones by a certain age otherwise they may be classified as having developmental delay. Screening children helps to identify children at risk of developmental delay and thus appropriate measures can be taken to prevent further complications (First and Palfrey, 1994).

The Bayley Scales of Infant and Toddler Development, third edition (Bayley III) is a valid and reliable tool for assessing children with developmental delay. It assesses children from the age of one month to 42 months old. It helps pave the way for an intervention plan. It consists of cognitive, language and motor scales (Bayley, 2006).

In one of the Lancet series articles, an estimate of more than 200 million children under five years old do not reach their developmental potential due to poverty, poor health, nutrition and deficient care (Grantham-McGregor et al, 2007). Many studies report that birth to five years is a critical time for development in children. The development of language, cognition, emotion, social, behaviour and physical skills happens at this period (Ozkan et al, 2012; Pem, D, 2012 and Moura et al, 2010). These articles look at the environmental and biological factors that influence development.

In the cohort study by Moura, et al (2010), they found that factors such as the child’s sex, economic class, mother’s schooling, birth spacing, gestational diabetes, preterm birth, low birth weight (LBW), 5 minute Apgar score, hospital admission at 12 months and the stimulation the child received at home to

contribute to developmental delay. An Apgar score of less than seven was three times more likely to lead to developmental delay at 24 months.

In the study by Ozkan, M, et al (2012), the development of 692 children, aged three months to five years, was analysed by using the Denver-II and collecting demographic data. Out of the 692 children, 193 came out with abnormal results on the Denver-II. The factors contributing to this were an illiterate mother and gestational age of 32-36 weeks. The most predictive suspect factors were a father with a low-level of education, a birth weight of less than 1500g, maternal age of less than 20 years old, low household income and gestational age at 27 to 31 weeks.

Children with the above risk factors as well as traumatic brain injury, pneumonia, lower respiratory tract infection and sepsis are commonly seen in the paediatric intensive care unit (PICU) at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH). The PICU has fifteen beds and admits neonates and paediatric patients with both medical and surgical conditions up to the age of fourteen years. At CMJAH there are average 230 admissions to the PICU per year according to the unit statistics.

The article by Mopeli, Ballot and White (2016) investigated the conditions in children admitted to CMJAH. The study was conducted over a 19-month period, during this time 883 admissions were documented. Eighty-four out of the 131 (64.1%) had LRTIs. Furthermore a study conducted by Jardine and Ballot (2015) on the use of nasal CPAP at CMJAH reported that the ICU is shared between neonates, paediatrics and paediatric surgery patients.

There are 150 000 to 250 000 admissions to paediatric intensive care units (PICUs) every year in the United States (Board, 2005). A large number of children are admitted to ICUs worldwide and an adequate follow-up plan may help to reduce the incidence of developmental delay in these children (Board, 2005).

Functional health is defined as, " an individual's ability to perform normal daily activities, to fulfil usual roles and to maintain health and well-being." (Knoester, Grootenhuis and Bos, 2007). A child's normal role and purpose in life is to explore and to play. Should such a child be unable to fulfil this role due to being unwell post discharge from ICU then they should not be deemed as healthy (Knoester, Grootenhuis and Bos, 2007).

A study done on the developmental outcome of very low birth weight infants, who had previously been in the neonatal unit at CMJAH, by Ballot et al. (2012) showed that factors such as resuscitation at birth, prolonged hospitalisation and duration of supplemental oxygen were risk factors for poor functional outcome. These are all factors that children in the PICU are exposed to and could also have an impact on their neurodevelopmental outcomes. Human immunodeficiency virus (HIV) is also seen in children particularly in sub-Saharan Africa and because of this developmental delay is a common problem among these children (Potterton et al, 2009).

Taylor, Butt and Ciardulli (2003) further stated that the outcome of PICU survivors is largely unknown and further research is required (Browne, 2011). Research on outcomes of PICU survivors is scarce and long-term follow-up investigation is required (Knoester, Bronner and Bos, 2008; Angus and Carlet, 2003).

Some studies have been done investigating the impact of ICU on children specifically in the Netherlands and Australia. In a study done by Knoester, Grootenhuis and Bos (2007) reviewing 27 studies they found that "physical sequelae" and neurological abnormalities were present in PICU survivors.

Cunha et al (2012) conducted a study that included 1495 children and he found that the change in Health related quality of life (HRQoL) was dependent on the patients' diagnosis because cardiorespiratory and musculoskeletal conditions seemed to improve and trauma and sepsis worsened over time. It was noted that the key factor for prediction of change in HRQoL, functional and developmental outcome is the pre-admission status (whether or not the

child was disabled before being admitted to the PICU). A similar study on HRQoL was done by Knoester et al (2007) where they found that it improved over time but a HRQoL assessment should be incorporated as standard follow-up procedure once discharged from PICU.

Another study conducted by Ambuehl et al (2007) in Switzerland at a tertiary PICU assessed the quality of life using the health state classification system. It has four domains, physical function, role function, social-emotional function and health problem. Six hundred and sixty-one patients were included in the study and the general outcome of these participants was good. It was found that patients with cardiovascular disease and head injuries had a poorer outcome compared to patients with respiratory, general medical and neurological conditions. The outcome was that every fifth child needs special care in the form of Physiotherapy, Speech Therapy, rehabilitation or a special school (Ambuehl et al 2007).

A prospective observational study by Ebrahim et al (2013) looked at the adaptive behaviour and functional outcomes and HRQoL of children urgently admitted to the ICU. Functional outcome was investigated using the paediatric cerebral performance category and the paediatric overall performance category. HRQoL was investigated using the Paediatric quality of life inventory and the Visual Analogue Scale. Ninety-one patients were enrolled in this study. It was found that acute severity of illness on ICU admission is associated with disease morbidity (Ebrahim et al, 2013). Bone, Feinglass & Goodman (2014) performed a retrospective analysis of a multicentre PICU database. Twenty-four PICU databases were evaluated. The findings of this study were that this population of children admitted to ICUs could benefit from follow-up after discharge from ICU. Three risk factors were identified in this study; unscheduled admission, invasive mechanical ventilation and PICU length of stay of more than two and half days (Bone et al, 2014).

It is evident from the studies by Cunha et al (2012), Bone et al (2014), Ambuehl et al (2007) and Ebrahim et al (2013) that children admitted and

discharged from PICUs require further follow-up to be able to optimise any HRQoL problems later on in life.

When considering the above information, those studies were done in Australia, America and Switzerland, it is evident that limited research has been done in a sub-Saharan setting where malnutrition, poverty and critical illnesses such as HIV, malaria and TB are prevalent in this context.

In researching into the implications ICU has on development we will be able to better treat and intervene while these children are still in the ICU and provide appropriate services once they are discharged.

1.2. Problem Statement

Insufficient research has been done into the neurodevelopmental implications PICU has on children. We need to know if these children should be followed up post discharge and what services may be required, particularly in a sub-Saharan context. Currently, children admitted and those that survive PICU are not routinely followed up and particularly no developmental follow-up is provided. Only surgical patients are followed-up but not developmentally.

A holistic multidisciplinary approach is needed to follow-up these children at CMJAH.

1.3. Research Question

Are PICU survivors aged one month to three and a half years old at risk of having developmental delay?

1.4. Aim

To identify if PICU survivors aged one month to three and a half years old are at risk of having developmental delay.

1.5. Objectives

- To describe the motor, cognitive and language developmental findings of children (aged one month to three and a half years old) once discharged from the PICU using the Bayley – III.

- To investigate the prevalence of developmental delay in children once discharged from the PICU.

- To describe what facets of developmental (motor, cognitive and language) are predominantly affected according to the Bayley-III.

- To determine whether there is an association between the demographic and clinical information of PICU survivors in relation to their developmental outcome.

- To compare the developmental outcome of PICU survivors with their healthy peers.

1. 6. Significance of the study

The results of this study will help one to better understand the developmental outcome of children once discharged from PICU. Once this study is concluded, it will be clearer as to whether PICU survivors should be followed up post discharge. This information will enable health professionals to implement an adequate follow-up plan to ensure that developmental delay is minimised.

CHAPTER 2: Literature Review

This literature review covers articles related to the PICU environment, types of conditions admitted to the PICU, care and interventions implemented in the PICU, prevalent pathologies seen in the PICU, CMJAH PICU, developmental assessment tools, complications of ICU on paediatric development and outcome, risk factors associated with child development, developmental delay, HIV and its effect on child development and lastly ending off with an overview of the Bayley Scales of Infant and Toddler Development, third edition (Bayley-III).

The articles span from 1992 to more recent research done and published in 2018. Key words used included 'developmental delay', 'Bayley Scales of Infant and Toddler Development, third edition, 'paediatric ICU risk factors' and 'paediatric screening tools'. The search engines used include 'Pubmed', 'Google scholar', 'ClinicalKey', 'Elsevier' and 'ScienceDirect'.

2.1. Infant Development

2.1.1. Development of the Infant Brain

According to de Graaf-Peters and Hadders-Algra (2006), the central nervous system (CNS) is forever changing and developing. This continuous development of the CNS has major implications for the developmental outcome of the child. A child's first few years are vital, as important development occurs (Grantham- McGregor, et al, 2007). The brain is developing rapidly through neurogenesis, axonal and dendritic growth, synaptogenesis, cell death, synaptic pruning, myelination and gliogenesis. Each stage is important for the one preceding it and following it. Each stage is an important building block for the next phase and any disturbances to the processes could have long-term effects on the developing brain (GranthamMcGregor, et al, 2007).

Neuronal plasticity allows the CNS to learn new skills, remember information and reorganise processes even after injury has occurred (Johnston, 2009). It is a prominent feature of the CNS and it allows one the ability to adapt to changes in the environment and learn and store new information, it is the basis of learning for humans (Johnston, 2004).

Considering the above concept of neural plasticity, children are more likely to recover from injuries to the brain than adults and early intervention facilitates this process (Johnston, 2009; Grantham-McGregor et al, 2007).

The CNS starts developing in the fifth week postmenstrual age (PMA). This development continues for two decades before it has reached its full potential (de Graaf-Peters and Hadders-Algra, 2006). The sprouting of the axons and dendrites continues till the child is five years old. This information shows that depending on the age of disruption to the CNS, the child can present with a variety of neurodevelopmental delays (de Graaf-Peters and Hadders-Algra, 2006). Although the child can sustain negative effects from the environment, due to the prolonged time the axons continue to sprout, positive changes are possible. A child between the ages of one month and three and a half years of age is able to recover and respond positively to environmental stimuli (Johnston, 2009).

2.1.2. Developmental theories

A child's overall development needs to be considered as a whole and not one aspect in isolation. A child who is able to move, is able to explore and learn to feed their minds. Movement feeds cognitive and perceptual development (Campbell, 2012).

A child's development leads to one end goal, function. Campbell (2012) describes function as having a definite end or purpose and it should be

meaningful and goal directed. The international classification of function (ICF) gives therapists the ability to look at the patient as a whole and to find their functional limitations so as to help the patient perform their activities of daily living (ADL) (Campbell, 2012).

Children's function and ADLs are different to that of a teenager or adult. Infant's function is described as play. Some examples of 'play' as a function include going up and down the stairs, putting things in and out of containers or simply bashing a toy on the table. Although they may seem meaningless they are an important factor of the developmental process and growth of the child. There are many theories on motor development in children, neural-maturationist theory, cognitive theories (Behavioural and Piagetian) and the dynamical systems theory (Campbell, 2012).

Arnold Gesell developed the neural-maturationist theory. Gesell believed that a child's motor development was as a result of the maturation of the central nervous system (CNS) and that stages of development followed a set pattern. Development followed alternating periods of flexor and extensor development based on CNS maturation (Harbourne and Dusing, 2017).

The cognitive behavioural theory was based on B.F. Skinner who emphasized the force of the environment. It was thought that the environment shaped both motor and cognitive development and that Pavlovian and operant responses to environmental stimuli drove the stages of development (Harbourne and Dusing, 2017).

The Piagetian theory is based on the work of Jean Piaget. This theory looks at the interaction of cognitive-neural structures and the opportunities from the environment. Stages of development represent alternating phases of equilibrium and disequilibrium. First actions were considered to be entirely

reflexive with voluntary actions developing later (Harbourne and Dusing, 2017).

The dynamic systems theory is the most widely accepted current view on childhood development. Esther Thelen and colleagues proposed this theory. This framework delves into the interaction of the child, the environment and the motor task. This theory is called dynamic as it is ever changing. The constraints (the child, the environment and the task) do not stay the same. Analysing a child's motor development, according to the dynamic systems theory should not be looked at in isolation. Thelen (1995) stated that what is different from the assumption of Piaget and others is that growing humans need to be accepted as true dynamic systems. This theory was unique in that, unlike others, it does not isolate one factor as being key in driving development but believes that multiple cooperative systems drive development (Harbourne and Dusing, 2017).

In an article by Malina (2004) he stated "All children, except some with severe disabilities have the potential to develop and learn a variety of fundamental movement patterns and more specialised motor skills." This aids the way children experience different dimensions of their environments. Malina (2004) describes motor development as the process through which a child acquires movement patterns and skills. The environment the child is exposed to directly influences their motor performance. There are several factors that should be considered when looking at motor development;

1. Neuromuscular maturation
2. Physical growth and behavioural characteristics of the child
3. Tempo of physical growth, biological maturation and behavioural development
4. Residual effects of prior movement experiences

These four factors interact with the environment to influence the motor development of the child. When assessing the motor development of a child this should be taken into consideration.

The International Classification of Functioning, Disability and Health for children and youth (ICF-CY) was derived from the International Classification of Functioning Disability and Health (ICF) (WHO, 2001). The ICF is used to record the characteristics of the patient and its' environmental influences. It is a universal tool understood by everyone (WHO, 2007).

The ICY-CY incorporates body structure and function, activity and participation factors. It uses these domains alongside environmental and personal factors. It is then possible to holistically describe the impact of disability on individual functioning and on life experiences (FitzGerald, et al, 2018). The ICF-CY directly corresponds with the Dynamic Systems theory by Thelen.

2.1.3. Normal developmental milestones

Children are expected to reach certain milestones at different stages of their lives. Monitoring these milestones is important for fields like physiotherapy amongst others, as it allows the physiotherapist the chance and opportunity to identify any delay in performance and thus intervene and implement treatment strategies (Campbell, 2012).

A seminal paper by the World Health Organisation tracked developmental milestones of over one thousand healthy breastfed infants around the world. They reinforced the idea that typical development occurs over a range of time and that individual differences often exist in timing and order of achieving milestones in healthy children (WHO Growth Reference Study group, 2006). These "Windows of Achievement" importantly allow for some variation in development, which is in keeping with Thelen's Dynamic Systems Theory.

Motor development is the attainment of muscle power and coordination along with cerebral networks that relate motor actions of the limbs to sensory (vision and proprioception) perception (Aly, Taj & Ibrahim, 2010). Children progress through these milestones in a sequential process (Aly, Taj & Ibrahim, 2010).

Cognitive development is the measure of a child's ability to solve problems through intuitions, perception and verbal and nonverbal reasoning. This is the child's ability to learn and understand. A child's cognitive ability is the basis of their imagination and thus their environment and surroundings play a huge part in the cognitive ability (Aly, Taj & Ibrahim, 2010).

Language development involves the articulation, receptive, expressive language skills and non-verbal symbols. At 0-6 months a child can understand spoken language, at 2-3 months they are able to express without using words, at about one year they begin to speak either using syllables or single words and by 2-3 years a child is able to construct full sentences.

Social development is the child's ability to form relationships and personal development involves self-help skills and the development of skills required in ADLs such as dressing, toileting and feeding themselves (Aly, Taj & Ibrahim, 2010). It is vital to be aware and monitor to milestones so as to intervene and make an early diagnosis should a child not achieve them within the expected range.

2.2. Factors affecting development

2.2.1. Socioeconomic factors

The socioeconomic background of a child and mother is a factor that has been shown to impact on child development. In a 2007 series in The Lancet it was estimated that more than 200 million children younger than five years of age from low and middle-income countries were not achieving their full developmental potential (Grantham-McGregor et al, 2007; Pem, 2015). The reasons for this were discovered to be poverty, poor health, nutritional deficiencies, deficit in care and inadequate learning opportunities. The number of children affected will increase with economic recession. Most of these children live in South Asia and Sub-Saharan Africa (Pem, 2015). Some

factors associated with poverty are childhood and prenatal stress, which can result in lack of stimulation and can affect the child's brain development (Walker et al., 2011; Engle et al, 2011).

Maternal factors such as malnutrition, environmental factors and depression can affect the development of the child. According to Walker at al (2011) there is maternal under nutrition (body-mass index<18.5kg/m^2) in 10-19% of women in low-income and middle-income countries with the rates being higher in sub-Saharan Africa and south Asia. A mother's body-mass index during pregnancy can predict the birth weight of her unborn child. The lower the body-mass index of the mother the lower the child's birth weight and the greater risk they have of being born underweight which is a factor that could affect their development. During pregnancy the child is at risk to environmental toxins (prenatally) and after birth (postnatal) through food, water and their home environment (dust or soil). A study done in Poland showed that prenatal exposure to low concentrations of lead could result in poor mental development in children (Walker at al., 2011; Engle et al, 2011).

Maternal depression is a factor that can affect the development of the child in many ways. In Bangladesh, maternal depression was associated with infant stunting (Walker et al, 2011); this could possibly be due to unresponsive parenting. Many factors can result in maternal depression; poverty, high stress, lack of empowerment and poor social support. There is a clear link between maternal depression and child development (Walker et al., 2011 & Engle et al., 2011).

In a study done by Moura et al (2010), which was based in Brazil, it was found that a mother's schooling background was associated with the child having developmental delay.

The intrinsic factors of the child can also affect their development. A child exposed to infectious diseases will most likely have an impact on their development. Studies in Brazil showed that the number of diarrhoea episodes before the age of two years impacted the child's development. This also

affects their nutritional status and thus may also results in stunting (Walker et al., 2011). Malaria can also results in developmental impact. Younger children under the age of five years are at a higher risk of getting malaria. Malaria has been associated with a poorer cognitive function at school level (Walker et al., 2011). HIV is a known risk factor for infant development and will be discussed in more detail.

Estimates suggest that 300 million children younger than five years are exposed to violence (Walker et al., 2011). This is not a problem isolated to low-income and middle-income countries but relates to all income countries. Exposure to violence can result in deficits in emotional, behavioural and social domains of development.

2.2.2. Health conditions

2.2.2.1. Acute Illness

Globally infectious diseases are the leading cause of morbidity and mortality in young children (Seibt et al, 2018).

Acute lower respiratory infections account for an estimated 1.3 million deaths each year in children under five years of age (43% of these being in Africa) (Annamalay et al, 2016). Respiratory viruses are the most common cause of infections in children. Rhinovirus (RV) is the most cause of respiratory infections in children and is the main cause of pneumonia and bronchiolitis (Annamalay et al, 2016). In a study done in New Zealand, it was discovered that the leading causes of hospitalisations in children under two years of age were lower respiratory tract, enteric and skin and soft tissue infection (Seibt et al, 2018).

Apart from acute respiratory tract infections, gastroenteritis, helminth infection, meningitis and otitis media all have the potential to impact negatively on development. Limited studies on the long-term impact of these conditions on the development of children in developing countries have been done (Walker et al, 2007).

Sepsis is defined as an infection with a systematic inflammatory response to infection that is associated with more than a disturbance of the systems. It is seen in abnormal body temperatures, elevated heart rates, tachypnoea, hyperventilation and altered white blood cell count (Martí- Carvajal et al, 2007). Sepsis is a major healthcare problem in PICUs worldwide. Sepsis is an infection-initiated clinical syndrome that can progress to shock, multiple organ dysfunction syndrome and death (Farris et al, 2013). A study conducted in Shanghai investigated the records of four PICUs at four different hospitals. It was found that children who have a low Glasgow severity score or who are younger have a higher mortality rate (Er Ke Za Zhi, 2012).

Farris et al (2013) did a further analysis on the RESOLVE (Researching severe Sepsis and Organ dysfunction in children: a global perspective) trial. They investigated the 28-day functional outcomes of a large cohort of paediatric subjects who survived an episode of severe sepsis; they also examined the risk factors of poor functional outcome. Thirty-four percent of the survivors had a decline in their functional status at 28 days and 18% were determined to have a poor functional outcome. Factors associated with increased risk of poor outcome were; central nervous system and intra-abdominal infection sources compared to lung infection, a history of recent trauma, cardiopulmonary resuscitation prior to enrolment and a baseline Paediatric Risk of Mortality III (PRISM) score of 20-29.

In an attempt to prevent functional decline it is recommend that adequate follow-up is needed. Further interventions such as physical and occupational services initiated early in ICU may assist this (Farris et al, 2013).

Acute diarrhoea is defined by the World Health Organisation (WHO) as the passage of three or more loose or liquid stools per day for three or more days and for less than 14 days. The American Academy of Paediatrics (AAP)

define acute gastroenteritis as the diarrheal disease of rapid onset with or without symptoms and signs of nausea, vomiting, fever and/or abdominal pain (Florez et al, 2016). Acute gastroenteritis is a common disease seen in young children and usually results in high morbidity and mortality (Florez et al, 2016).

2.2.2.2. Chronic Illness

Numerous chronic childhood conditions have been shown to impact negatively on early child development. These include chronic respiratory, neurological, cardiac and musculoskeletal conditions.

HIV has been well described as a risk factor for infant and child development (Potterton et al, 2009; Potterton et al, 2016; Springer et al, 2018). South Africa has the largest population of people living with human Immunodeficiency virus (HIV) in the world (Department of Health, South Africa, 2010; UNAIDS, 2011). In 2008, there were approximately 1 million children in sub-Saharan Africa infected with HIV, this accounts for more than 90% of HIV-infected children in the world (Baillieu & Potterton, 2008). HIV is neurotrophic and crosses the immature blood brain barrier to cause early infection of the developing CNS. This can result in HIV encephalopathy, which can have devastating effects on the long-term development of the child (Hilburn et al, 2011).

Neurological complications and developmental delay are seen in HIV positive children (particularly those children who are infected perinatally) (Potterton et al, 2009).

HIV exposed but uninfected infants face biological and environmental risk factors. In South Africa, the antenatal HIV prevalence is one of the highest in the world (Springer et al, 2017). Springer et al (2017) conducted a prospective cohort study, which looked at the risk for infectious morbidity in HIV-exp uninfected and HIV unexposed uninfected infants. Fifty-eight HIV-exp uninfected and thirty-eight HIV unexposed uninfected infants were evaluated

at 11 – 14 months of age. They were each assessed using the BSID-III. The results yielded were not different between the two groups however there is still a need to follow-up these children (Springer et al, 2017). Potterton et al (2016) conducted a study at an urban paediatric HIV clinic in Johannesburg, South Africa. Sixty-eight medically stable children between the ages of three and five years were assessed with the Griffiths Scales of Mental Development. These children had received combination Antiretroviral treatment at eight months. Despite the treatment received, children infected with HIV are still at risk for developmental delay (Potterton et al, 2016).

From the above literature it is important to not children who are HIV-exp and to follow them up to ensure appropriate referral if necessary.

Asthma is a common chronic childhood condition worldwide. Although a chronic condition it presents with acute exacerbations, which may require hospitalisation. Most children with asthma do not require admission to the PICU but in some severe cases they may need to be admitted, intubated and ventilated (Hon et al, 2010). By being exposed to ventilation these children are at risk for increased number of days in the PICU and thus more reliant on oxygen and at risk of possible developmental delay.

2.2.2.3. Prematurity and low birth weight

A child born prematurely has a gestational age of less than 37 weeks (Kahn-D'Angelo et al, 2012; Eras et al, 2013). Preterm is divided into three groups; low birth weight (LBW) is from 1501 to 2500 grams, very low birth weight (VLBW) is 1000 to 1500 grams and extreme low birth weight (ELBW) is less than 1000 grams (Kahn-D'Angelo, 2012). Early preterm is when a child is born at a gestational age of less than 30 weeks. A child born moderately preterm is born between 32 and 35 weeks gestational age (Kerstjens et al, 2012). Late Preterm is considered when a child's gestational age is between 34 and 36 weeks. These infants are at a greater risk for short and long-term morbidity. There has been an increase in preterm births over the past two decades (Eras et al, 2013). This increase is due to the increase in multiple

births due to assisted reproductive medicine (Eras et al, 2013). This study by Eras et al (2013) found that multiples are at greater risk for long-term problems such as cerebral palsy (CP), cognitive impairment, language delay and learning disabilities. Preterm births are caused by multiple factors (genetic, social and environmental factors) (Kahn-D'Angelo et al, 2012). In the updated World Health Organisation Preterm fact sheet updated in 2017, it was reported that 60% of preterm births occur in Africa and South Asia (WHO, 2017). It has been proven that complications of prematurity do have an impact on development. The shorter the length of gestation, the greater the risk of postnatal complications. The severity of complications increases with a decrease in gestational age (Blencowe et al., 2013; Katz et al., 2013).

They are at risk of respiratory distress syndrome (RDS), apnoea, feeding difficulties, hypoglycaemia, brain injuries, bronchoplumonary dysplasia (BPD), retinopathy of prematurity (ROP) amongst others. Late preterm infants are prone to increased ICU admissions and increased ICU stay. Evidence has shown the preterm infants are at a greater risk of developmental delay compared to term infants (Ballantyne et al, 2016; KahnD'Angelo, 2012; De Jesus et al, 2012; Tyson et al, 2008).

Nasal Continuous Positive Airway Pressure (NCPAP) has become an accepted treatment for hyaline membrane disease (HMD). HMD widely affects premature babies. Incidence of HMD is related to the degree of prematurity on the lungs; therefore incidence of HMD increases with a decrease in gestational age (Jardine and Ballot, 2015). NCPAP is not only used in HMD but also in apnoea of prematurity, respiratory distress due to other aetiologies, upper airway obstructions and an alternative to endotracheal intubation or to wean off ventilation (Jardine and Ballot, 2015).

Children born moderately preterm (32-35 gestational age) are at an increased risk of neonatal morbidities and developmental delay. Neonatal morbidities include asphyxia, respiratory insufficiency, septicaemia, hypoglycaemia, hyperbilirubinemia, apnoea, hypothermia and feeding problems. Some of these morbidities warrant admission to the NICU. It is,

however, unclear whether these morbidities are associated with developmental delay (Kerstjens et al, 2012). Kerstjens et al (2012) conducted a study and asked parents to complete the Ages and Stages questionnaire. Patient history was obtained from medical records. Only hypoglycaemia and asphyxia were shown to be associated with developmental delay.

2.3. Developmental delay

Developmental delay is measured according to the child's milestones. If a child is delayed in one or more areas, it is commonly known as 'global developmental delay' (Aly, Taj & Ibrahim, 2010).

As discussed earlier there are many risk factors that can affect a child's development and result in developmental delay. As Walker et al (2007) has shown that the many risk factors can have a detrimental effect on the future of the child as well as the country. Lack of cognitive stimulation and stunting amongst others prevent millions of children from reaching their developmental potential and results in cognitive deficits as well as decreased social emotional functioning in school and adult life. This is vital for the country to be able to emerge out of poverty (Walker et al, 2007; Grantham-McGregor et al, 2007).

The study by Grantham-McGregor (2007) showed that early interventions to prevent developmental delay could help prevent the loss of potential in these children and in turn help the country.

A study done by Ballot et al (2017) investigated 74 term neonates who were born between July 2013 and October 2013 and discharged home within 48 hours of birth. The Bayley-III was administered to these children at least once. The results of this study showed that no child had a composite score of below 70 for any of the subscales for the Bayley-III. Thus it shows that the Bayley-III can be used to assess developmental outcome in inner city Southern African children.

Developmental assessment will be covered in section 2.5.

An article published in Paediatrics 2006 discussed an algorithm for developmental surveillance and screening. They acknowledged the importance of early identification of developmental disorders and the effect on well being of children and their families. This algorithm is used to help health professionals with a plan for screening and monitoring development. It is recommended that developmental surveillance be done at every visit at 9 months, 18 months and 30 months. It involves identifying children who are at risk of developmental delay, getting parents views on their child's development, documenting the developmental history, observing the child and keeping accurate and detailed records (Paediatrics, 2006). This algorithm is considered the golden standard.

The algorithm according to Paediatrics (2006) is as follows:

1. Paediatric patient at preventive care visit (developmental concerns should be atopic discussed at each visit in the first 5 years of life).
2. Perform surveillance (eliciting and attending to parents' concerns, maintaining a developmental history, making accurate and informed observations of the child, identifying presence of risk and protective factors, documenting the process and findings).
3. Need to determine if there is a risk.
4. What age the child is at the current visit (9-, 18-, 30-months).
5. Administer the screening tool.
6. Results of the screening tool.
7. Make appropriate referrals if necessary.
8. Developmental and medical evaluations.
9. Is developmental delay identified?
10. If developmental delay is identified, initiate chronic condition management.

Early intervention therapies for children at risk for developmental delay can be crucial for the developmental outcome of these children. As discussed in Peadiatrics (2006) it is vital to identify these children at risk for developmental delay and to make correct referral for chronic condition management. This management can be Physiotherapy, Speech Therapy or Occupational

Therapy. A non-randomised controlled study done by Strehlau et al (2018) investigated the need for neurodevelopmental assessment in HIV-exp uninfected and early treated HIV-infected children. The conclusion of this study was that early child development should form part of the management of these children. It is very important to refer children early on to minimise the risk of developmental delay.

2.4. Paediatric Intensive Care

CMJAH is a tertiary teaching and referral centre that provides healthcare services to people in the Gauteng province and surrounding provinces in South Africa. It has a 220-bed paediatric service which caters for medical and surgical patients. There are fifteen beds in the PICU (Mopeli et al, 2016). According to Mopeli et al (2016) there are four neonatologists and one paediatric pulmonologist. Mopeli et al (2016) conducted a retrospective review in the PICU at CMJAH. They reviewed records from January 2013 to July 2014. The study indicated that the PICU admitted less than 900 children in 19 months. The mortality rate was 24,4% of the medical conditions admitted. The most frequent cause for admission was LRTI (this is indicative of high rates of Pneumonia in South Africa). Thirty-four percent of the children were HIV-exp, 12,2% were HIV PCR-positive (Mopeli et al, 2016).

Children with chronic and complex diseases are admitted to the PICU (Namachivayam et al, 2010). There has been a great amount of development around PICUs worldwide (Knoester et al, 2008; Namachivayam, et al 2010; Cunha et al, 2012). The need to reduce mortality rates has increased. The PICU is a very hostile environment for children and their parents. Loud noises of the alarms and monitors, the bright lights and the stress associated with these factors can all play a role in the outcome of the survivors (Yoel and Jacob, 2002). Children with medical, surgical and trauma are admitted to the PICUs for close monitoring and further investigation and intervention.

Ebrahim et al (2013) looked at the factors associated with children admitted to ICUs. They evaluated the adaptive behaviour, functional outcomes and Health related quality of life in children after urgent ICU admission. The study was done in Toronto at a hospital which has an 18 bed PICU and an 18 bed cardiac ICU. HRQOL was defined as the perceived physical and mental health of the patient over time by the caregivers of the patient. Ninety-one patients were enrolled in the study who were diagnosed with respiratory, neurological, circulatory and oncology diseases. They found major determinants of post ICU outcome to be the child's neurological admissions, longer ICU stay, decreased oxygen saturation and longer intense modes of resuscitations (Ebrahim et al, 2013).

Rennick and Rashotte (2009) conducted a systematic review on children's psychological sequelae following PICU hospitalisation. They described the PICU, where children are exposed to a vast array of medical technologies and highly invasive procedures. Noise levels are extremely high and they are constantly exposed to light. This results in children at risk for negative psychological outcomes and post-traumatic stress disorder.

Critical illness and ICU admission is a stressful and chaotic situation. Patients are exposed to necessary interventions for their survival. Life-saving practices include mechanical ventilation, endotracheal intubation and chest tube insertion, central venous and arterial catheterisation and intensive drug administration (Bennett, 2015; Makic, 2016). Cognitive and psychological stressors result from sleep withdrawal, sedation, pain, anxiety, fear, delusions and delirium. Patients in the ICU have feelings of loneliness and weakness (Asperberro et al, 2017).

The Society of Critical Care Medicine defined post-intensive care syndrome (PICS) as "new or worsening impairments in physical, cognitive or mental status arising after critical illness and persisting beyond acute care hospitalisation" (Needham et al, 2012; Rawal, Yadav and Kumar, 2017).

The term post-intensive care syndrome (PICS) results from the consequences that ICU survivors face. These are physical, cognitive and mental health

impairments that persist for months and years after discharge from ICU ad after critical illness (Bone, Feinglass and Goodman, 2014).

Bone et al (2014) conducted a retrospective exploratory study to investigate risk factors associated with decline in health after ICU discharge. They collected data by the virtual PICU performance system (VPS) network. The VPS database contains data on patients admitted to over 80 PICUs in the United States. Outcome measures used were change in global functional ability (Paediatric Overall Performance Category (POPC) and change in cognitive function by the Paediatric Cerebral Performance Category (PCPC). A regression analysis was done and the following risk factors were found to be the most prevalent affecting Health related quality of life; unscheduled admissions to the ICU, invasive mechanical ventilation and length of stay longer than two and half days. Heneghan and Pollack (2017) state the primary focus of critical care has evolved from saving lives by monitoring and maintaining physiological status to placing greater emphasis on prevention of secondary injuries and preservation of function.

There are 150 000 to 250 000 admissions to paediatric intensive care units every year in the United States (Board, 2005). In order to ensure that these children are not at risk of developmental delay after being discharged from the PICU and hospital, adequate follow-up is recommended (Board, 2005).

Merely looking at mortality rate, number of days on ventilation and length of hospital stay after discharge from PICU is no longer sufficient to establish quality of life (Knoester, Bronner & Bos, 2008). There are many possible long-term complications that can affect a PICU survivor; physical disability, emotional, mental as well as functional health are a few. According to Knoester et al. (2008), studies investigating physical sequelae in PICU survivors are scarce. The outcome of a PICU survivor depends on many factors. These include diagnosis, pre-existing health problems, severity of illness, standards in the ICU and the overall hospital and state health care system (Butt, 2012).

In a prospective follow-up study done between December 2002 and October 2005 at Emma children's hospital in the Netherlands (n=186; mean age= 1.4 years; follow-up time= 3months). It was found that 9% of the children had concentration problems, 15% had behavioural problems, 13% had delayed psychomotor development, 7% had temporary voice changes, 9% had eating problems, 9% sleeping problems and 9% had withdrawal symptoms. This indicates that there are many complications one could expect to see in a child post discharge from PICU (Knoester et al., 2008).

Another study done by Knoester et al (2007) reviewed twenty-seven studies consisting of 3444 PICU survivors. Studies that looked at the aspects of physical and psychological sequelae of PICU survivors were included in the study. A limitation to this study was that not all studies had the same population, follow-up time and used the same measurement tools. However, the studies that were reviewed showed distinct physical sequelae which included neurological abnormalities as well as lung, cardiac and renal abnormalities. This study concluded that PICU survivors and their parents have physical and psychological sequelae affecting their quality of life and should be followed up post discharge from PICU (Knoester et al., 2007).

A retrospective cohort study of 10 450 siblings who were born between 1999 and 2005 was conducted. Three hundred and four children without a history of developmental and behavioural disorders had been exposed to anaesthesia when they had undergone surgery (younger than 3 years of age). Ten thousand and one hundred and forty six children were included who had not been exposed to anaesthesia. Both groups were analysed and followed until diagnosis of developmental and behavioural disorder. The study concluded that the incidence of developmental and behavioural disorders was higher for the exposed group compared to the unexposed group. This study highlights the effect anaesthesia has on development of children (DiMaggio, Sun & Li, 2011).

Hospital-acquired pneumonia (HAP) is a major medical problem in most European countries. A study done in the PICU of Ain Shams University

Hospital (a medical ICU with 10 beds) investigated patients that developed HAP. Patient's demographic information and clinical information was taken into account during this study. It was found that 25 patients out of 90 developed HAP. Risk factors of HAP were found to be mechanical ventilation, reintubation, sedation by benzodiazepines and opioids, nasogastric feeding, gastro-oesophageal reflux and H2 blockers. Length of stay doubled for those patients that developed HAP. Developing HAP increases the length of ICU and hospital stay and makes the child prone to developing other conditions and infections (Mansour & Bendary, 2012).

The range of conditions with which children are admitted to PICU is potentially vast. It is imperative that each child is followed up particularly if there are known developmental risk factors

2.4.1 Neonatal ICU

Children born moderately pre-term (32-35 weeks gestational age) are susceptible to many neonatal morbidities. These morbidities include asphyxia, respiratory insufficiency, septicaemia, hypoglycaemia, hyperbilirubinemia, apnoea, hypothermia and feeding problems. Occasionally, if these morbidities are severe enough, the child may be admitted to the NICU (Kerstjens et al, 2012).

The neonatal intensive care unit (NICU) can have a major impact on the developmental outcome of its infants. The NICU's noise levels are excessively high and it is very bright. These two factors have been thought to adversely affect the growth and development of the very preterm infant (Pineda et al, 2014).

A study done by Rosie (2016) looked at the neurodevelopmental outcomes of neonatal intensive care unit survivors attending a follow-up clinic at a Gauteng

hospital. The study included 40 participants who were admitted to the NICU and then assessed with the Bayley-III. Due to the small sample size, it was difficult to discover which factor or complication posed a risk for developmental delay however the statistical analysis showed that special attention should be paid to infants diagnosed with sepsis, anaemia and those born normal vaginal delivery (NVD).

2.5. Developmental assessment

2.5.1. BSID-III

A standardised developmental test is a tool designed to measure whether an individual's development is what would be expected at a specific age (Rademeyer & Jacklin, 2013). The individual's results are compared a norm.

There are many standardised assessment tools that can be used to assess children for developmental delay. The neurodevelopmental assessment of children and infants includes examining the motor development and function (Tieman, Palisano & Sutlive, 2005). Some of the assessment tools that can be used include The Bayley Scales of Infant Development, (BSID-II). Peabody Developmental Motor Scales, 2nd Edition (PMDS-2), the Toddler Infant Motor Evaluation (T.I.M.E.), the Paediatric Evaluation of Disability Inventory (PEDI) and the Gross Motor Function Measure (GMFM) (Tieman, Palisano & Sutlive, 2005). There are many developmental assessment tools to choose from.

The Bayley Scales of Infant and Toddler Development, third edition (BayleyIII) is one of the tools used, it compares the infant to standardised norm (Ballot et al, 2017). The BSID-III is the recommended tool. The Bayley-III is the most widely used tool and it is considered the gold standard of assessment tools (Weiss et al, 2010). The Bayley-III was published in 2006 and is an updated version of the Bayley Scales of Infant and Toddler Development, 2nd edition (BSID-II) which was published in 1993 (Ballot et al, 2017).

As described in the Bayley-III manual, the Bayley-III is an individually administered tool that assesses the developmental functioning of infants and young children one month to 42 months of age. The main purpose of the Bayley-III is to identify children with developmental delay and to provide information for intervention planning. It consists of three administered scales; the Cognitive Scale, the Language Scale (including Receptive and Expressive Communication), and the Motor Scale (including Fine Motor and Gross Motor). It also has a Social Emotional and Adaptive Behaviour questionnaire; the Social Emotional Scale and Adaptive Behaviour Scale, which is completed by the parent or primary caregiver (Bayley, 2006).

The clinical use of the BSID-III was improved during its standardisation through the numerous special population studies undertaken in children diagnosed with developmental delay, at risk for developmental delay (including those born prematurely and those with genetic or congenital disorders) and/or a clinical diagnosis (Down Syndrome, Cerebral Palsy and birth asphyxia) (Bayley, 2006).

The Bayley-III is both reliable and valid. Inter-rater reliability, test-retest reliability and internal consistency were examined for reliability. Internal consistency of subscales and relationship with other outcome measures were evaluated for validity (Green at al, 2013; Pinon, 2010). An abnormal outcome on each scale is a score of less than 70 and a score between 70 and 85 is considered at risk (Ballot et al, 2012). Composite scores are used to describe the child's level of performance in qualitative terms (Bayley, 2006). The five scales of the Bayley-III are characterised according to 'very superior', 'superior', 'high average', 'average', 'low average', 'borderline' and 'extremely low'. For the language composite scores; if the score is 130 and above it is classified as 'very superior', 120-129 it is classified as 'superior', 110-119 it is 'high average', 90-109 it is 'average', 80-89 it is 'low average', 70-79 it is 'borderline' and 69 and below is classified as 'extremely low'.

These classifications are the same for the motor and cognitive scales (Bayley, 2006).

Richter et al (2015) used data generated in Birth to twenty plus. It was an on going longitudinal birth cohort study and the first in a South African context. It examined the socioeconomic, growth, health, development and overall wellbeing of urban South African children. The findings of the study suggest that the BSID mental scale at one year was the best predictor of delayed age of school entry. The BSID is the most widely used tool to assess developmental delay and is considered the 'gold standard' (Richter et al, 2015). From Richter et al's (2015) study it is clear that the BSID is very effective in identifying children at risk of late school entry.

2.5.2. The Bayley-III Cognitive Scale

The cognitive scale has a total of 91 items and it assesses the child's ability to understand and interpret symbols and information (Bayley, 2006). Of the 91 items that this scale contains, some were retained from the previous BSID-II version; some were modified, added or dropped completely. This scale is aligned with the latest developmental research on cognitive functioning (Armstong & Agazzi, 2010).

The items added to this scale assessed attention, habituation, conceptual reasoning, memory function, problem-solving and processing speed. Play is a critical role that is needed in cognitive functioning and was considered when modifying this scale (Armstong & Agazzi, 2010).

2.5.3. The Bayley-III Language Scale

The language scale includes both receptive and expressive communication and assesses the child's language development (Bayley, 2006). The receptive language scale includes 49 items and the expressive language scale includes 38 items. The receptive language scale assesses the child's auditory acuity

and ability to understand and respond to verbal stimuli. The expressive language scales assesses the child's ability to vocalise, name pictures and objects and communicate with others (Bayley, 2006). Some of the major changes made to this scale included expanding some areas like pre-linguistic, social and complex language components (Crais, 2010). The term communication refers to any means the child uses to communicate with others; eye gaze, gesture, facial expression, vocalisation and words (Crais, 2010). Language and communication are key factors in a child's overall learning (Crais, 2010).

2.5.4. The Bayley-III Motor Scale

The motor scale consists of a fine motor section and a gross motor section. The fine motor section has 66 items and assesses skills associated with eye movements, perceptual-motor integration, motor planning and motor speed (Bayley, 2006). This scale looks specifically at how a child is able to manipulate objects and toys in their hands (Case-Smith & Alexander, 2010). It specifically looks at reaching and grasping patterns, bimanual coordination and the functional use of objects (Case-Smith & Alexander, 2010).

The gross motor section has 72 items and measures the movements of the limbs and torso (Bayley, 2006). This scale looks at skills incorporating early movement, postural stability, control and balance and locomotion (Case-Smith & Alexander, 2010).

2.5.5. Validity

In the study done by Rademeyer & Jacklin (2013), the Bayley-III was used in South Africa to compare it to the United States of America (USA). The Bayley Scales of Infant development is a tool designed and normed in the USA. It is considered the gold standard of assessment tools. Rademeyer & Jacklin

(2013) investigated its validity in SA as the populations in the USA differ vastly to that of South Africa.

Richter et al (1992) also validated the use of the first version of the Bayley Scales of Infant Development (BSID I) on a group of South African children. They administered the tool to a group of urban and rural children. Although the BSID I was modelled on a group of American children, the South African children performed well on the tool and in some cases performed better than the American group of children in the motor and mental areas of development (Richter et al, 1992). Thus this developmental assessment is more than appropriate to be used on South African rural and urban children. A similar study by performed by Aina and Morakinyo (2005) on a group of Nigerian children, again confirming the appropriateness of the tool for African children. It has been thought that African children have developed abilities and seem to perform better at an earlier age (Capute et al, 1985).

2.5.6. Reliability

The reliability of a test refers to the accuracy, consistency and stability of test scores (Anastasi and Urbina, 1997). The overall average reliability coefficients of the Bayley-III subtests range from 0.86 (for fine motor) to 0.91 (for cognitive, expressive communication and gross motor). The reliability coefficient for receptive communication is 0.87 and for the composite scales are 0.93 for language and 0.92 for motor. The reliability data for cognitive, language, motor, social-emotional and adaptive-behaviour reflect a high degree of internal consistency. The Bayley-III is a reliable tool to assess individuals with different levels of development or with different clinical diagnoses (Bayley, 2006).

2.5.7. Use of Bayley Scales of Infant Development, third edition in South African setting

A number of studies have used the BSID-III in South Africa and have found it and appropriate tool in this context (Rademeyer and Jacklin, 2013; Baillieu & Potterton, 2008; Potterton et al, 2009; Whitehead, Potterton & Coovadia, 2013). A study done by Ballot et al (2017) investigated the use of the BSID-III in young children in an urban setting in South Africa. It was concluded that the BSID-III can be used and is appropriate in inner city South African children.

2.6. Conclusion of literature review

Children discharged from PICU face many factors, which could impact on their development. These may be pre-existing socioeconomic factors, factors related to their medical conditions as well as intrinsic factors such as prematurity. There are very few studies that have followed up children discharged from PICU to establish what their developmental challenges may be, especially in developing countries such as South Africa. It is important to determine what rehabilitation needs these children may have so that adequate follow up can be provided.

CHAPTER 3: Methodology

In this chapter the methodology used in this study will be described.

3.1. Study Design

This study was a cross sectional descriptive study design.

3.2. Study setting and population

Children that were part of this study were identified from the ICU database at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH). There are 15 beds in the PICU. The ICU is shared by neonates, paediatrics and paediatric surgery patients (Jardine and Ballot, 2015). It admits children up to the age of fourteen years old. According to the article by Mopeli et al (2016), a retrospective review was done between January 2013 and July 2014 reviewing the medical conditions admitted to the PICU at CMJAH. During this period 883 admissions were documented. Of these, 131 were medical patients. Sixty-four percent of these had LRTIs (Mopeli et al, 2016). Only patients that met the inclusion criteria were included in this study.

Developmental follow-up of PICU survivors is not standard care at CMJAH and thus there is a gap and a need for this study.

CMJAH is located in Parktown, Gauteng, South Africa and serves patients from across the Gauteng provinces and neighbouring provinces.

The ICU sees a variety of conditions such as traumatic brain injury, pneumonia, lower respiratory tract infection, sepsis and many others according to the unit statistics. According to the article by Mopeli et al (2016), LRTIs (64.1%) was the majority of admissions between January 2013 and July 2014. The patients were selected based on the inclusion and exclusion criteria.

3.3. Ethical clearance

Prior to commencing data collection for this study, ethical clearance (Clearance certificate number: M160479) was obtained from the Human Research Ethics Committee (Medical) of the University of the Witwatersrand (Appendix 4). Permission was granted by Prof Daynia Ballot to conduct the study in the paediatric follow-up clinic at CMJAH.

Due to the participants being too young to consent, their parents and caregivers were provided with and asked to sign written informed permission for their child's participation in the study.

The consent form was not translated into another language; however, a translator was available to translate the consent form should the parents have needed. Zulu and Sotho translators were available.

Participants were remunerated for their participation in the study. The contribution for transportation costs was in line with the National Health Research Ethics Council (NHREC) guidelines.

3.4. Inclusion Criteria PICU group

- Children previously admitted to the intensive care unit at Charlotte Maxeke Johannesburg Academic hospital.
- Children between the ages of one month and three and a half years old corrected age.
- Children admitted with a medical condition (A medical condition is a life-threatening disease that does not require surgical intervention (Mopeli et al, 2016)).
- Children who are between one and six months post discharge from the Paediatric Intensive Care Unit (PICU).

3.5. Exclusion Criteria PICU group

- Children with any pre-existing neurological problem such as cerebral palsy (CP), Down's syndrome, Hypoxic Ischaemic Encephalopathy (HIE) and hydrocephalus.

3.6. Control group

The control group was a group of healthy term neonates from CMJAH in South Africa that were discharged home with their mothers after birth. This was a database that already existed and the participants corrected age and Bayley-III scores had already been documented. Subsequently, Ballot et al (2017) published an article on the participants used for this control group. A group of well term neonates born between July 2013 and October 2013 who were discharged home with their mothers within 48 hours of birth. The mothers who had delivered in hospital were informed of the follow-up study and were invited to participate. An appropriately trained physiotherapist or paediatrician conducted BSID-III assessments. The data was then entered into a neonatal database using Research Electronic Data Capture (RED-CAP) software; it was posted into IBM SPSS 23 for further analysis. Ninety children were enrolled in this study however one was excluded as after the BSID-III the child was diagnosed with trisomy-21 and 15 were lost to follow-up. This resulted in 74 participants remaining in the database and 42 of these controls were used. The mean birth weight of the 74 children was 2674g, the mean maternal age was 27.67 years, gender distribution was equal between male and female, majority were born via vaginal delivery and almost one third of the children were HIV-exp (Ballot et al, 2017).

3.7. Sample size calculation

According to the unit statistics in PICU at CMJAH, over the past three years the PICU has had 690 admissions, 488 of these admissions are less than three years old and half of these admissions (244) are medical conditions (predominantly lower respiratory tract infections (LRTI)). This rendered and average of 10 paediatric patients under the age of three years old per month in the PICU. The patient's diagnoses were reviewed and chosen appropriately.

To have been able to detect a difference of 10 on the Bayley-III, when using a standard deviation of 15 (Bayley, 2006), a power of 90%, a confidence interval of +/- 3,08 and a significance set at 0,05; it was found that the sample for each group was 48 participants. An excel sample size calculator (v3_2).xls was used to perform the calculation.

3.8. Outcome measures and measurement tools

The Bayley Scales of Infant and Toddler Development, third edition (Bayley-III) was used to assess the development of the infants in the study.

The Bayley-III is a tool that is administered individually to assess the development of infants and young children aged from one month to 42 months of age. It is used to ascertain extent of developmental delay and to help devise an intervention plan should there be any form of developmental delay. It consists of five domains; cognitive, language, motor, social-emotional and adaptive. The first three domains are tested by administering certain items to the child and the last two are tested by administering a questionnaire to the primary caregiver. There is also the Behaviour-observation Inventory, which is completed by both the examiner and the primary caregiver to assess the child's behaviour during the testing session.

The goal with early intervention is to minimise the effects of developmental delay in the long term (Bayley, 2006). In addition to using the Bayley-III as an assessment tool, it can also be used to track the progress of an intervention plan.

In order for the assessment to have been effective it needed to be administered in a controlled environment so that there is nothing to distract the child. It needed to be spacious so that they could display gross motor movements effectively, quiet, have good lighting and be comfortable for the examiner, caregiver and the child.

A data collection sheet was also used to keep record the participant's demographic and clinical profiles (See appendix 1 and 2). This was based on the PICU database and the information that was available on it.

3.9. Procedure

The research began on 26th of May 2016 once ethical clearance was received on the 24th May 2016. Patient admission and discharge books from the PICU were reviewed. Only patients who were in hospital from January 2016 to July 2016 and who had been discharge for at least one month up to six months were included. The patients were chosen based on the inclusion criteria.

Once the appropriate patients were identified the parents or caregivers were contacted telephonically and invited to take part in the study. The appointment was made on a Thursday during the neonatal follow-up clinic. The transport costs were reimbursed to the patients once they arrived at the clinic and a toy and snack was given to the patients. The data collection was conducted over a six-month period from June 2016 to December 2016.

Once the caregivers arrived at the clinic with the baby, they went to the nurses' room to get the weight, height of the baby measured using standardised hospital-measuring instruments. The information collected was limited to the information routinely collected and documented by the clinicians in the PICU database. They were then invited into a treatment room by the researcher.

The caregivers were then given an information sheet explaining the research. The information was written in English but nurses were available should the participants and caregivers have needed a translator. Once they agreed and were happy to continue, informed signed consent was obtained. The demographic sheet was also filled out according to the information in the patient's hospital file and their corrected age was calculated.

The Bayley-III was explained to the parent so that they were aware of what to expect. The participants were assigned study codes (number 1-42). The Bayley III was administered by the researcher each time in a controlled environment without any distractions. Only the cognitive, motor and language facets were tested.

The results of the Bayley-III were recorded on the outcomes form and converted to composite scores. Once the assessment was completed the results were explained to the caregiver and the baby was then examined by a doctor.

Any participant scoring in the lower ranges and were at risk, were referred to the appropriate therapy (Occupational therapy, Speech and language therapy or Physiotherapy). All participant information was kept in a confidential filing system.

3.10. Statistical Analysis

All data was analysed with the assistance of a biostatistician. Data was analysed using STATA 14 (Data COFP) USA.

- Descriptive statistics such as means, standard deviations, medians and frequencies were used to describe the demographic information, which was normally distributed.
- Weight-for-age and length-for age z-scores were calculated using WHO Anthro (version 3.3.2.).
- Descriptive statistics were used to summarise the clinical data of the participants. This included frequencies, mean and standard deviations.
- Means and standard deviations were used to describe the composite scores.
- The means were compared using a Mann Whitney U test.
- Chi squared tests were run to determine if one group (the PICU group and the control group) was more likely to result in developmental delay.
- The composite scores of the Bayley-III were used to calculate the scores of the children.
- A One-Way Anova was run to determine if any facet of development was significantly different to the others.
- Independent sample t-tests were run comparing test scores against categorical dependant variables.
- A bivariate Pearson's correlation analysis was run to determine the association between test scores and the continuous demographic and clinical variables.

  Clinical significance was set at $p<0.05$.

The results of this study are presented in chapter 4.

CHAPTER 4: Results

The data from 42 participants were analysed and will be presented in this chapter. When participants were chosen from the CMJAH ICU database, the inclusion criterion was strictly adhered to. The control group was only utilised for the purpose of drawing comparisons for developmental outcomes.

4.1. Demographic data

The demographic data of the 42 participants is described in table 4.1. and 4.2. It is presented as means, standard deviations and the medians. Current below refers to the day the developmental assessment was done.

Table 4. 1 Current Demographic data (n=42)

Variable	Mean	Standard Deviation	Range	Median
Chonological age (days)	276.9	176.10	44-840	242.63
Corrected age (days)	265.2	177.10	30-840	225.42
Height (cm)	65.21	7.72	46.5-83.5	65.40
Weight (kg)	7.57	1.93	4.1-12.3	7.14

The above table shows the demographic data of all the participants. It shows the means and standard deviations of all the values. The youngest participant at the time of the assessment was 44 days old (1 month and 14 days) and the oldest was 840 days (28 months) old. The corrected age of the youngest participant was 30 days old and the oldest was the same as the actual age (840 days old or 27.61 months). The shortest participant at the time of the assessment was 46.50cm and the tallest was 83.50cm. The lowest weight at the time of the assessment was 4,06 kg and the highest was 12.34kg. The mean corrected age of the control group was 10.58 months. No significant difference was found for age between the PICU and control groups. The p-value=0.34.

The birth data of the 42 participants is represented in table 4.2. below.

Table 4. 2 Birth history demographic data (n=42)

Variable	Mean	Standard Deviation	Range	Median
Gestational age (weeks)	38	3.53	24-40	40
Birth weight (g)	2684	729.01	1030-3810	2855

The lowest birth weight was 1030g and the highest was 3810g. Eight of the 42 participants had a gestational age of less than 37 weeks. Seven of the 8 were born between 31 and 36 weeks. Only 1 participant was born at 24 weeks.

Figure 4.1. Represents the distribution of the z-scores of weight-for-age.

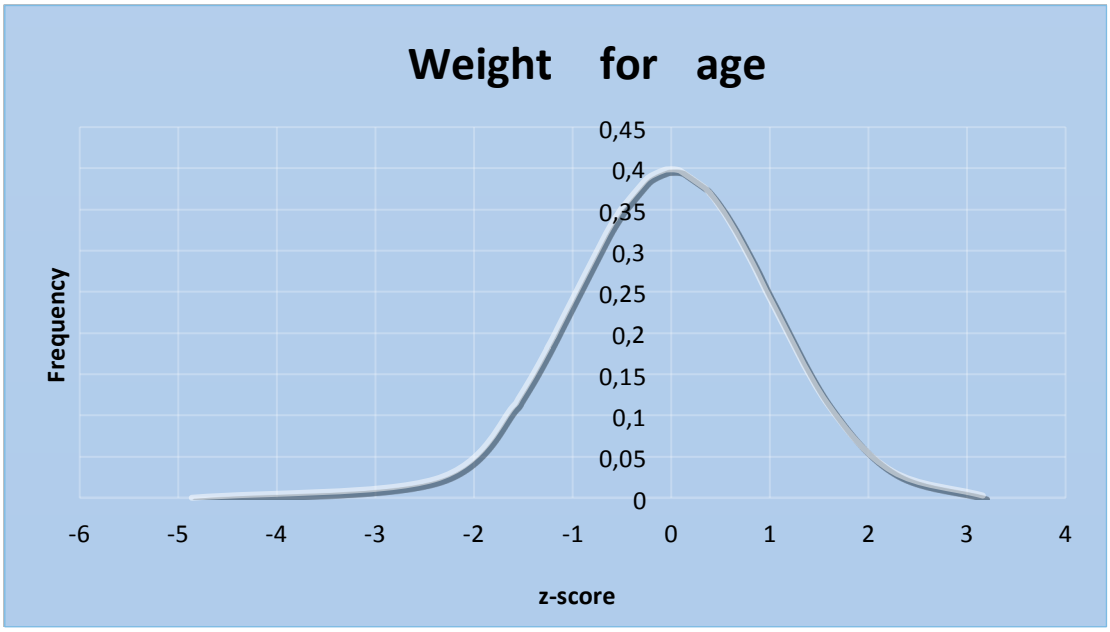

Figure 4. 1 Weight-for-age z-scores (n=42)

Figure 4.1. Displays the z-scores for weight-for-age of all 42 participants. Their corrected ages were used to calculate these scores. Two participants were

malnourished as they had z-scores of below minus two and two had z-scores of above two.

Figure 4.2. Represents the distribution of z-scores for length-for-age.

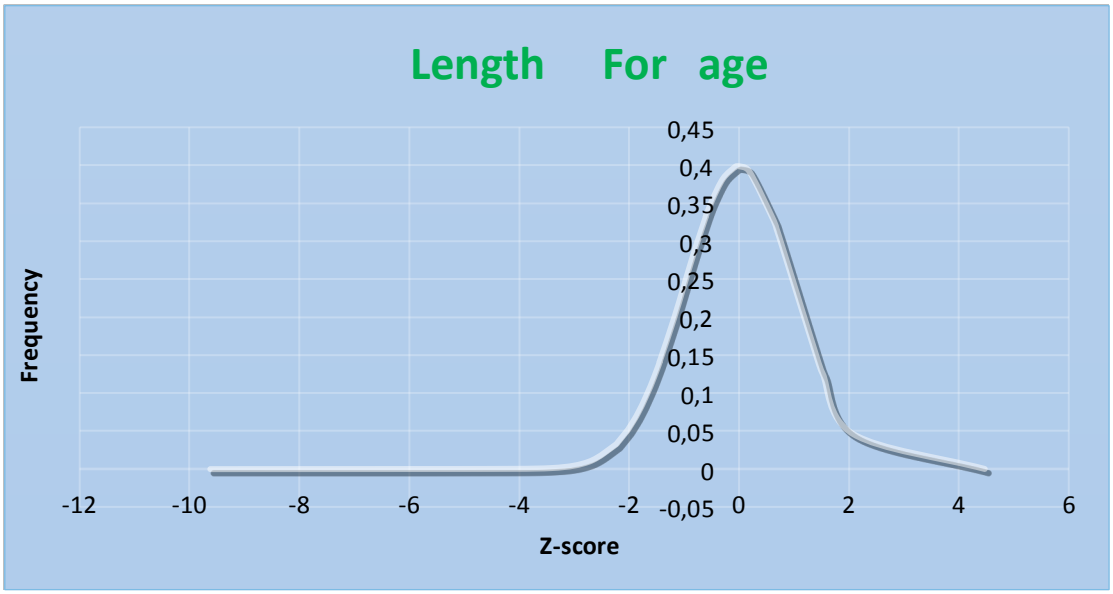

Figure 4. 2 Length-for-age z-scores (n=42)

Figure 4.2. Displays the z-scores for length-for-age of all 42 participants. Their corrected ages were used to calculate these scores. Eight participants were stunted as they had z-score of below minus 2 and two participants had z-scores of above 2.

Table 4.3. Presents demographic data of the participants that cannot be presented as means and standard deviations. They are presented as frequencies.

Table 4. 3 Demographic data as percentage (n=42)

Variable	Percentage (%)	Number (n)
Male	57.1	24
Female	42.9	18
Caesarean section	54.8	23
NVD	45.2	19
HIV exposed uninfected	31.0	13
HIV Infected	16.7	7

Table 4.3. Indicates that there were more male participants than females. The number of caesarean sections was higher than normal vaginal deliveries (NVD). Thirty one percent of the participants were HIV exposed and only 16.7% of infants were HIV positive and on ARVs. All 42 participants were of the same ethnicity (black). Twenty-four of the participants were born at CMJAH and the rest were born at other government hospitals and clinics or at home.

Table 4.4. Represents the clinical profile of the participants. It represents the amount of time the participants spent in ICU and the amount of time spent on ventilation while in the ICU.

Table 4. 4 Clinical Profile (n=42)

Variable	Mean	Standard Deviation	Median	Range
Length of ICU stay (days)	12.85	10.62	12	1-62
Length of mechanical ventilation (days)	8.61	6.73	6	1-28

Table 4.4. Indicates that the mean length of stay in the ICU was 12.85 days with the longest amount of time being at 62 days spent in the ICU. The mean time spent of ventilation was 8.61 days, which is less than the mean number of days spent in the ICU. The participant who spent the longest time on the ventilation was only admitted in the ICU for 32 days. The participant who spent the most time in ICU was only ventilated for 4 days on IPPV. All participants were ventilated during admission. Fourteen out of 42 participants had prolonged mechanical ventilation (>10 days). Only one participant had a prolonged stay in the hospital at 62 days. This particular patient was diagnosed with Bronchopneumonia, was on conventional mechanical ventilation and was the only premature participant born at 24 weeks. No information was documented on the length of stay in the hospital out of the ICU for any of the participants.

Table 4.5. Represents the type of mechanical ventilation the participants were prescribed during their stay in ICU.

Table 4. 5 Mode of ventilation (n=42)

Type of ventilation	Percentage %
IPPV	95.2
NCPAP (after IPPV)	12
O2 (after IPPV)	2.4
High frequency ventilation	4.8

Table 4.5. Shows that 95.2% (40) of the participants were put on intermittent positive pressure ventilation (IPPV), 12% (5) were then put onto nasal continuous positive airway pressure (NCPAP) after the IPPV and one of the participants was given oxygen after the IPPV. Less than 5% (2) of the participants were put onto high frequency ventilation.

4.2. Conditions

Table 4.6. Shows the primary conditions the participants were diagnosed with during their admission in ICU. They are presented according to the percentage of the population affected.

Table 4. 6 Primary admission diagnosis (n=42)

Diagnosis	Frequency	Percentage %
AGE	1	2,38
Bronchopneumonia	19	45,24
Bronchiolitis	5	11,90
Bronchospasm	1	2,38
Croup	2	4,76
Empyema	1	2,38
LRTI	6	14,29
Pneumothorax	1	2,38
Pulmonary Haemorrhage	1	2,38
Sepsis	5	11,90

AGE=acute gastroenteritis, LRTI= Lower Respiratory tract infection

Table 4.6. Represents the percentage and frequency of conditions that the participants were diagnosed with while in ICU. Some of the participants had another condition like asthma as well as one of the conditions listed above. The highest number of comorbidities experienced by one participant was 4. This participant had abdominal cellulitis, anaemia, sepsis and metabolic acidosis. The table shows that the most common condition suffered by the participants was Bronchopneumonia (45.24% of the population).

4.3. Developmental outcomes

The composite scores of the Bayley-III assessments for the PICU and control group are represented below in figure 4.3. using a box-and-whisker scatter plot.

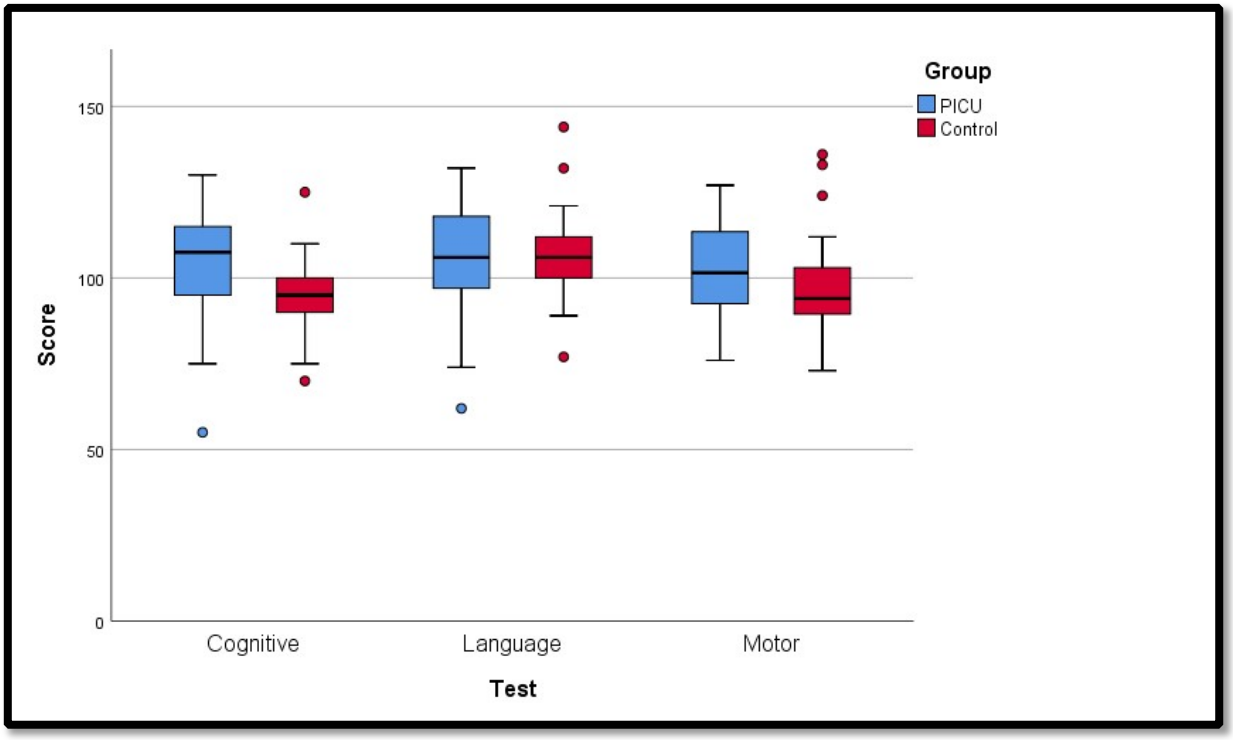

Figure 4. 3 Box-and-whisker scatter plot of the Bayley-III score for the PICU and control groups (n=42)

Figure 4.3. Presents the mean scores of the Bayley scores. It shows that scores of the PICU group are widely spread compared to those of the control group.

Table 4.7. Represents the means, standards deviations and p-values of the PICU and control groups.

Table 4. 7 Mean, standard deviations and p-values of the BSID-III for the PICU and control groups (n=42)

	PICU mean (SD)	Control mean (SD)	P-value
Cognitive	104.17 (15.81)	94.17 (9.75)	p<0.001
Language	108.17 (17.19)	103.93 (9.23)	p=0.124
Motor	104.26 (14.60)	95.45 (9.54)	p=0.007

Composite scores of Bayley-III for PICU and control group (n=42)

A z-test was done to compare the composite scores of the Bayley-III for the PICU and control groups, to see if there was a statistical significance. A p-value of 0,0000 was yielded for the cognitive, language and motor scales. This indicated that there was a statistical significance between the scores of the two groups.

Table 4.8. Presents the median and interquartile ranges of the composite scores of each scale; language, cognitive and motor.

Table 4. 8 Median and interquartile ranges of composite scores of the BSID-III for the control and PICU groups (n=42)

Scale	Median		Inter-quartile range	
	PICU	Control	PICU	Control
Cognitive	107.5	95	90-115	90-100
Language	107.5	104.5	97-124	100-109
Motor	103	94	94-115	88-100

The above table illustrates the medians and inter-quartile ranges of the Bayley-III assessment scores of the PICU and control groups.

Table 4.9. Presents the highest and lowest composite scores.

Table 4. 9 Highest and lowest composite scores of the BSID-III of the PICU and control groups (n=42)

Scale	Highest Score		Lowest Score	
	PICU	Control	PICU	Control
Cognitive	130	125	55	70
Language	144	121	62	77
Motor	136	124	76	73

This table illustrates the highest and lowest scores of the 42 participants. Table 4.8. Indicates that the cognitive scale had the lowest scores, with the highest and lowest score being lower than the motor and language scores. However, the cognitive scale had a higher mean score than the motor scale. The language scale had the highest score compared to the motor and cognitive scales and the motor scale had the highest lowest score compared to the cognitive and language scales. The participant

with the lowest cognitive score was female and born via caesarean section at 40 weeks, she had a birth weight of 2890g and her diagnosis was bronchopneumonia with empyema. The highest score of the control group is lower than the highest score of the PICU group but the lowest score of the cognitive and language scales for the control group is higher than the lowest scores of the PICU group. The lowest score for the motor scale of the PICU group is higher than the control group.

Table 4.10. Represents the qualitative descriptions of the Bayley-III composite scores. The number of children that fell into each score is represented for the motor, language and cognitive scales. The PICU and control groups are presented below.

Table 4. 10 Qualitative descriptions of the Bayley-III composite scores (n=42)

Composite score	Motor		Cognitive		Language	
	PICU	Control	PICU	Control	PICU	Control
Very superior (130+)	2	0	2	0	3	0
Superior (120-129)	5	1	6	1	8	2
High Average (110-119)	11	2	12	1	9	8
Average (90-109)	19	28	16	31	16	29
Low Average (80-89)	4	9	3	7	3	2
Borderline (70-79)	1	2	1	2	2	1
Extremely low (69 and below)	0	0	2	0	1	0

Table 4.10. Above represents the composite scores for each scale (cognitive, motor and language) for both the PICU and control group.

Table 4.11. Represents the consolidated qualitative descriptions of the Bayley-III composite scores.

Table 4. 11 Consolidated qualitative descriptions of the Bayley-III composite categories (n=42)

	Cognitive		Language		Motor	
	PICU	**Control**	**PICU**	**Control**	**PICU**	**Control**
Normal (>85)	38	39	38	42	39	38
At Risk (<85)	3	3	3	0	3	4
Delayed (<70)	1	0	1	0	0	0

Table 4.11. Represents the amount of participants in the control and PICU group that fell into the categories, normal, at risk and delayed. Should a participant fall into the category 'delayed' they should be referred immediately for Physiotherapy, Occupational Therapy or Speech and Hearing Therapy. Should they fall into the category 'At Risk' then they should be sent to one of the abovementioned categories for monitoring. The table shows us that the PICU group had two participants who needed treatment in the cognitive and language scales. It shows that there isn't a vast difference in scores between the PICU and control groups

Facets of development (n=42)

An ANOVA-F test was done to compare the three scales in the Bayley-III. The p-value yielded was less than 0.05 therefore rejecting the null hypothesis. There was statistical difference between the three facets of development (cognitive, language and motor).

The model was statistically significant F(2) = 6.346, p = .002. Bonferroni posthoc tests were used to determine where the differences lay.

Table 4. 12 Comparisons between developmental facet scores.

Post Hoc Comparisons

		Mean Difference	SE	t	Cohen's d	p bonf
Cognitive	Language	-6.810	2.104	-3.236	-0.204	0.004
	Motor	-0.690	2.104	-0.328	-0.021	1.000
Language	Motor	6.119	2.104	2.908	0.183	0.012

Note. Cohen's d does not correct for multiple comparisons.

These outcomes are illustrated in the figure on the next page:

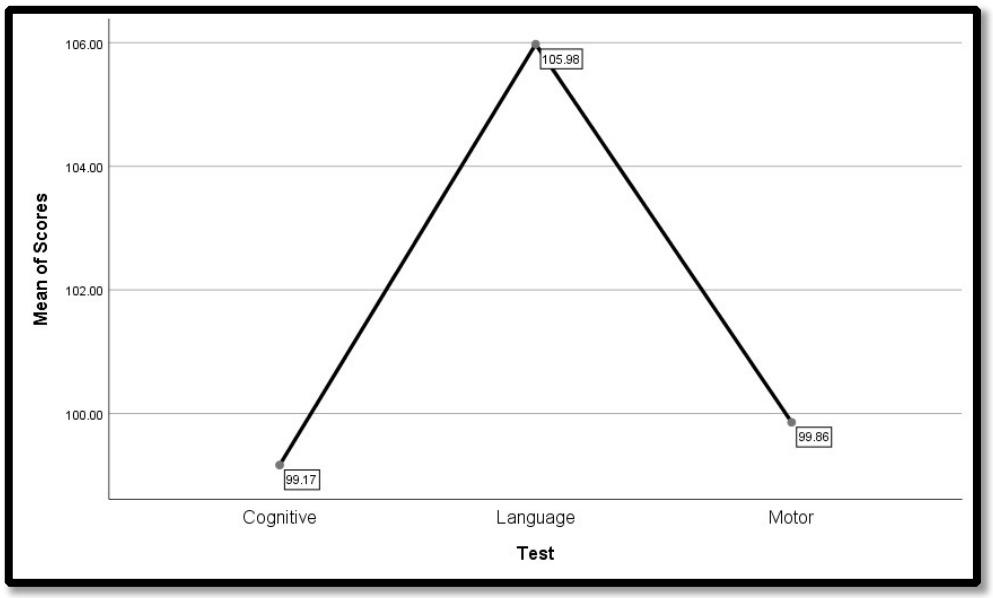

Figure 4. 4 Comparisons between developmental facet scores.

Relationship between demographic and clinical data and developmental outcome

In order to establish if any relationship exists between the demographic and clinical information of PICU survivors in relation to their developmental outcome independent samples t-tests were run comparing test scores again dependent variables (Gender, HIV Exposure, Previous Admission to ICU, Type of Delivery, Birth Asphyxia, and Neonatal Complications). Previous admission to ICU was approaching significance (p=0.061). The only statistically significant outcome was between the dependent variable of Neonatal complications, see the table below:

Table 4. 13 Description of complications for each developmental facet

Group Descriptives

	Group	N	Mean	SD	SE
Cognitive	No	26	108.85	16.511	3.238
	Yes	16	96.56	11.361	2.840
Language	No	26	113.15	17.608	3.453
	Yes	16	99.69	13.098	3.275
Motor	No	26	109.27	15.035	2.949
	Yes	16	96.13	9.563	2.391

As can be seen in table 4.13 above, a significant relationship existed between all three facets of development and neonatal complications.

A bivariate Pearson's correlation analysis was run to determine the association between test scores and the continuous socio-demographic variables (Birth weight, Age, Weight, Height, Duration of ICU stay, and Duration of ventilation). The only significant outcomes was between Motor score and Age, r = .351, p = 0.023). See table 4.14.

Table 4. 14 Relationship between neonatal complications and developmental facets

Independent Samples T-Test						
					95% CI for Cohen's d	
	t	df	p	Cohen's d	Lower	Upper
Cognitive	2.614	40.00	0.013	0.830	0.177	1.474
Language	2.638	40.00	0.012	0.838	0.184	1.482
Motor	3.122	40.00	0.003	0.992	0.327	1.646

Note. Student's t-test.

Table 4. 15 Correlations (n=42)

		Cognitive	Language	Motor	Birth Weight (g)	Age	Weight (kg)	Height (cm)	ICU stay	Ventilation
Cognitive	Pearson Correlation	1	0.981**	0.948**	-0.116	0.239	-0.016	0.037	-0.255	0.016
	Sig. (2- tailed)		0.000	0.000	0.463	0.127	0.922	0.820	0.107	0.920
	N	42	42	42	42	42	42	41	41	41
Language	Pearson Correlation	0.981**	1	0.966**	-0.054	0.226	0.002	0.072	0.261	-0.028
	Sig. (2- tailed)	0.000		0.000	0.736	0.149	0.991	0.654	0.100	0.863
	N	42	42	42	42	42	42	41	41	41
Motor	Pearson Correlation	0.948**	0.966**	1	-0.079	**0.351***	0.091	0.109	0.240	-0.061
	Sig. (2- tailed)	0.000	0.000		0.621	**0.023**	0.567	0.497	0.130	0.704
	N	42	42	42	42	42	42	41	41	41
Birth weight (g)	Pearson Correlation	-0.116	-0.054	-0.079	1	-0.185	-0.333*	-0.272	-0.445**	-0.264
	Sig. (2- tailed)	0.463	0.736	0.621		0.240	0.031	0.085	0.004	0.096
	N	42	42	42	42	42	42	41	41	41
Age	Pearson Correlation	0.239	0.226	0.351*	-0.185	1	0.635**	0.550**	0.025	-0.180
	Sig. (2- tailed)	0.127	0.149	0.023	0.240		0.000	0.000	0.876	0.260
	N	42	42	42	42	42	42	41	41	41
Weight (kg)	Pearson Correlation	-0.016	0.002	0.091	0.333*	0.635**	1	0.811**	-0.182	0.276
	Sig. (2 -tailed)	0.922	0.991	0.567	0.031	0.000		0.000	0.256	0.081
	N	42	42	42	42	42	42	41	41	41
Height (cm)	Pearson Correlation	0.037	0.072	0.109	0.272	0.550**	0.811**	1	-0.104	-0.135
	Sig. (2 -tailed)	0.820	0.654	0.497	0.085	0.000	0.000		0.523	0.408
	N	41	41	41	41	41	41	41	40	40
Duration ICU stay	Pearson Correlation		0.255	0.261	0.240	-0.445**	0.025	-0.182	-0.104	1	-0.472** **of**
	Sig. (2-tailed)	0.107	0.100	0.130	0.004	0.876	0.256	0.523		0.002
	N	41	41	41	41	41	41	40	41	41
Duration of ventilation	Pearson Correlation	0.016	-0.028	-0.061	-0.264	-0.180	-0.276	-0.135	-0.472**	1
	Sig. (2-tailed)	0.920	0.863	0.704	0.096	0.260	0.081	0.408	0.002	
	N	41	41	41	41	41	41	40	41	41

**** Correlation is significant at the 0.01 level (2-tailed) *Correlation is significant at the 0.05 level (2-tailed)**

The correlations of interest are those between developmental scores and demographic and clinical variables. The only significant association in this group was between age and motor scores.

4.3. Summary

The results show us that there were more males than females included in the study. The mean age of the PICU group was 8.84 months and of the control group 10.58 months. The Bayley-III mean composite scores of the PICU group were higher than the control group. There was a statistical difference between the three facets of development ($p=0.002$). Neonatal complications showed a statistical significance. There was also significance between age and the motor composite scores ($p=0.023$).

The results of this chapter will be discussed in chapter 5.

CHAPTER 5: Discussion

The results presented in chapter 4 will be discussed in this chapter.

Forty-two participants were included in this study based on the inclusion criteria discussed previously. According to the sample size calculation (as described in chapter three) 48 participants would give a 90% power with significance set at 0.05.. Over 60 patients were contacted and invited to participate in the study however 5 were reported to have passed away and the rest did not arrive to their appointment for no known reason. The researcher continued to invite participants to take part in the study until the sample size was reached. It was a challenge recruiting the correct amount of participants as some did not arrive or reported that could not get back to the hospital for the follow-up appointment even though there was a remuneration fee. The sample size of 42 participants yields a power of 86%, which is very good.

There were many challenges when conducting this research. Participant information was taken from the CMJAH PICU database. Once patients who met the inclusion criteria were found, they were contacted to be invited to participate in the study. Sometimes it was discovered that the patient had passed away or moved back home and unable to attend the study. Often if patients were suitable it was discovered that they were neonates and therefore not appropriate for the inclusion criteria. There were many no-arrivals on the day of the clinic for no apparent reason. It was extremely difficult to reach the sample size of 42 participants.

5.1. Demographics of participants

5.1.1. Age at developmental assessment

The mean corrected age of participants in the current study was 265,2 days (or 8,84 months). Compared to the study by Rosie (2016) who looked at neonates, the mean corrected age was 147 days. In the study by Ballot et al (2017), infants and young children in an urban setting in South Africa were investigated; the mean age for the first Bayley-III assessment was 10,9 months and the mean age for the second Bayley-III assessment was 19,9 months. The findings of this study showed that all children assessed were within one

standard deviation of the norm, i.e. no child scored below 70 for any category (Ballot et al, 2017).

Rademeyer & Jacklin (2013) noted that the composite scores of children decreased with advancing age of assessment. In the article by Mopeli et al (2106) with a sample of 131 participants with medical conditions the median age of the participants was 3.8 months. The median age was slightly lower than the median age of the participants in the current study, being at 7.5 months.

When looking at the current study, the results of the Bayley-III assessments for the control group were lower than that of the PICU group. The mean age for the PICU group was 8,84 months and for the control group was 10,58 months. This could be explained from looking at what Rademeyer & Jacklin (2013) said; that the composite scores decreased with increased age of assessment. The youngest child in the PICU group was 1 month old and the oldest was 28 months old compared to the control group, the youngest was 7 months and the oldest was 21 months of age.

5.1.2 Gender

In the current study, 57,1% (24) of the population were males and 42,9% (18) were females. Compared to the study by Rosie (2016) and Ballot et al (2017) who both had an equal number of males and females. In the study by Ballot et al (2012) there were 61 female participants and 45 male participants. The results of that study showed that the females did better on the Bayley-III assessments when compared to the males. In the current study, the males did slightly better than females in their average scores for each scale of the BayleyIII, however these values were not statistically significant. However, the sample size was too small so no definite reason could be given for this.

5.1.3. Prematurity

The PICU at CMJAH does not separate infants born full term or prematurely. The NICU and PICU are one ICU (Jardine and Ballott, 2015). The guidelines for prematurity (Khan-D'Angelo et al, 2012) were discussed in the literature review and any child born at a gestational age of less than 37 weeks is considered premature. The average gestational age of the participants in the current study was 38 weeks, indicating that most of them were not born prematurely. This means that the participants would not have been predisposed to any risk factors associated with developmental delay due to prematurity. Many studies have been done on premature infants in the NICU (Rosie, 2016; Ballot et al, 2012; Ballantyne et al, 2016) and it is known that they are at increased risk for developmental delay. In the current study ten of the participants (24%) were born at a gestational age of less than 37 weeks and one in particular was born at 24 weeks. Taking the literature into consideration it would be advised that regardless of their PICU admission these children be followed up.

As mentioned in the literature, prematurity results in a decreased gestational age, which has a negative, effect on the complications experiences by these individuals (Blencowe et al., Katz et al., 2013).

5.1.4 Birth weight

The majority of the children in the current study were born at 38 weeks gestational age and the mean birth weight was 2684g. Most of the children had a normal birth weight. The study by Rosie (2016) looked at children in the NICU and the criteria for admission to this NICU was 1000 grams minimum. The study by Ballot et al (2012) looked at the developmental outcome of very low birth weight infants and therefore the birth weights of these two studies were considerably lower than the current study.

Most babies are born and develop normally, however there are a few groups of babies who are born prematurely and fall ill and do not develop normally or who require some assistance (Doyle, et al., 2014). In the study by Doyle et al

(2014), they looked at the importance and the reasons as to why these 'at risk' babies should be followed up. Some of the reasons discovered included preterm babies (a gestational age of less than 37 weeks), low birth weight babies (birth weight of less than 2500g) and term babies that received positive pressure ventilation for longer than 24 hours amongst other reasons.

Some of the children in the current study had similar factors especially that they were all ventilated and in ICU. The average birth weight amongst the PICU group was 2684g with the lowest at 1030g. The average gestational age was 38 weeks with the lowest at 24 weeks and the average time on ventilation was 8,61 days. These are the risk factors and should require follow up of these children.

5.1.5. Growth status

Most of the participants had weight-for-age and length-for-age values within normal limits (WHO, 2008). There was no association between weight for age z-score which is not surprising as most of the children had normal growth parameters. Two participants had a z-score of below minus two and two had a z-score of above two for weight-for-age. Eight participants had a z-score of below minus two and two had a z-score of above two for length-for-age. Corrected ages were used for calculation of the z-scores. A literature search was done by Keino et al (2014) on stunting and overweight among children in sub-Saharan Africa, the reported that prevalence of stunting and overweight was dependent on demographic variables, demographic and environmental factors. Many studies indicated that stunting is more common in male children and those living in a rural setting (Keino et al, 2014). In Rosie's (2016) study, the majority of the participants had a weight-for-age and length-for-age within normal limits as well.

As reviewed in the Lancet series articles, maternal and infant malnutrition and obesity are major factors in child development. Maternal nutrition and bodymass index predicts birth weight of the unborn child (Walker et al, 2011).

5.2. Clinical profile of participants

5.2.1. Days on mechanical ventilation

In the current study the mean days spent on ventilation was 8.61 days. The participant who spent the most time on ventilation (28 days) was put onto IPPV and then nasal CPAP. This participant was male and diagnosed with sepsis. His gestational age was 40 weeks and his birth weight was 3180g. This particular participant had no neonatal complications at birth.

In the study by Mopeli et al (2016) the median days on mechanical ventilation was four days for the HIV-unexposed participants and eight days for the HIVexp participants. The HIV-exp participants spent four days longer on mechanical ventilation. In the current study, the median days spent on mechanical ventilation was six days. Detailed data was not recorded from HIV-exp and HIV-unexposed participants.

The study by Ballot et al (2012), out of 106 participants, 82 of them received ventilator support (IPPV/NCPAP), the rest did not need it. Only six of the participants were in the ICU for longer than six days and 14 of them received supplemental oxygen for longer than 30 days. From the findings of the study, it showed that duration of supplemental oxygen was a borderline significant risk factor for BSID-III motor score (Ballot et al, 2012).

From this, we can deduce that infants who spend more time on the ventilator and receiving supplemental oxygen can have an impact on the results of the BSID-III assessment however in this study it was not significantly associated with developmental outcome.

5.2.2. Length of stay in Paediatric Intensive Care Unit

The mean length of ICU stay was 12,85 days. The median days spent in ICU was 12 days. In Mopeli et al (2016) the median number of days spent in the PICU was five days for the HIV-unexposed participants and eight days for the HIV-exp participants. The participant who spent the longest time in the PICU

was admitted for 62 days (two months). This participant was female, diagnosed with Apnoea and Bronchopneumonia and was ventilated for four days on IPPV. Her gestational age was 24 weeks. This could be an indication as to why she was in ICU for such a long time. In the study by Rosie (2016), the longest NICU admission was 135 days (four months and 15 days). This participant had a gestational age of 27 weeks.

The study by Ballot et al (2012) reviewed 106 infants. The mean hospital stay was 40,28 days and mean number of days in intensive care was 6 days. From these results it showed that infants who stayed in hospital between 30 to 40 days were 7.41 times more likely to have an abnormal language score on the BSID-III.

From various literature reviewed (Board, 2005; Butt, 2012; Knoester et al, 2008; DiMaggio et al, 2011) we know that the effects of PICU can be detrimental to the wellbeing and developmental outcome of the infants admitted to the PICU. The longer time spent in the PICU the greater the chances of being exposed to risk factors such as HAP, anaesthesia and longer time on mechanical ventilation. It is important to discharge these children from the PICU as soon as possible so as to avoid greater exposure.

In this study time in PICU was not significant however history of a previous PICU admission was approaching significance suggesting that infants with chronic or complex health issues such as prolonged mechanical ventilation time and URTI need more vigilant developmental follow-up.

5.2.3. Diagnosis of participants

The primary focus of these participants should be preventing secondary complications and to preserve function (Heneghan and Pollack, 2017).

Butt (2012) looked at the outcome of children after discharge from the PICU. Five hundred and seventeen children were eligible for the study after six years. Overall 21% of the children's health related quality of life (HRQoL) was unchanged, 40% improved and 38% of the children health status worsened.

The results indicated that the HRQoL was dependant on the diagnosis. Children who were diagnosed with a cardiorespiratory or musculoskeletal problem seemed to improve compared to children who were admitted with trauma or acute sepsis and shock who worsened after ICU. This study by Butt (2012) confirmed that the outcome of a child depends on different factors; the diagnosis, pre-existing health problems, severity of illness among others. In the current study, neonatal complications, diagnosis, length of ICU stay and length of ventilation were factors that played a role in the outcome of PICU survivors.

Rosie (2016) looked at developmental outcome of infants discharged from neonatal intensive care. The most common conditions experienced by the participants was sepsis (with 67,5% of the population) followed by a blood transfusion (55% of the population). Only 20% of the population had pneumonia compared to 45,24% in the current study which was the most common diagnosis.

Diarrheal disease remains the major cause of morbidity and mortality among children (Florez et al, 2016). One of the participants was diagnosed with AGE. This particular participant weighed 4,65kg and was 56cm in height. He spent 24 days in PICU and was ventilated the entire time on conventional mechanical ventilation. His gestational age was 34 weeks. The BSID-III composite scores for this participant were a cognitive score of 110, language score of 97 and motor score of 82. These results show that the participant was 'at risk' for developmental delay in the motor scale and would need to be monitored carefully. The study done by Mopeli et al (2016) showed that 4.6% of the participants had gastroenteritis.

5.2.4. HIV exposure and infection

HIV can cause developmental delay as a result of encephalopathy after it enters the CNS during pregnancy. The delays that are seen are evident in the cognitive, language and motor functions of the child (Van Rie et al, 2007). Due to the prevalence of delay being high (60%) and the possible fact that it may be present from as early as four months of age, it is necessary to take careful note

of these children (Baillieu and Potterton, 2008; Potterton et al, 2009; Van Rie et al, 2007).

Almost one third (31%) of the participants in this current study were exposed to HIV, this is comparable to 32,5% of infants who were exposed to HIV in a similar study by Rosie (2016) and 32,4% of infants who were exposed to HIV in a study by Ballot et al (2012). These two studies by Rosie and Ballot et al are different because they looked at neonatal infants, however the characteristics of the mothers were similar and they attended similar hospitals, Chris Hani Baragwanath Hospital (CHBAH) and CMJAH. These two hospitals serve patients from similar socioeconomic backgrounds in Gauteng.

Of the 13 thirteen patients who were HIV exposed in the current study, 7 seven of them were on ARVs (16.7% of the study population). Compared to Rosie (2016) and Ballot et al (2012) who had less children who were HIV exposed. Of these thirteen HIV exposed participants, only one of them scored below 85 (at risk) on the Bayley-III for the motor scale. This particular participant had a birth weight of 2870g, a gestational age of 40 weeks, the mother had a normal vaginal delivery, she was in ICU and ventilated for 15 days and her diagnosis was Pneumonia.

Another study done by Hutchings & Potterton (2013) looked at the impact of HIV infection on the development of infants. The results of this study showed that the cognitive, language and motor scores were significantly lower in the HIV-exposed and infected infants compared to the HIV exposed but not infected infants. The group of uninfected infants showed no signs of developmental delay. This supports the results of the current study where the HIV exposed participants did not show worse developmental scores on the Bayley-III (Hutchings & Potterton, 2013).

A different study by Baillieu & Potterton (2008) investigated forty HIV-positive antiretroviral-naïve children aged 18 to 30 months attending the Harriet Shezi Paediatric HIV clinic at CHBAH in South Africa using the BSID-III. The results of this study showed that these children do have cognitive impairment; their motor development, coordination and muscle tone and reflexes are affected as well as having language delays.

These above findings suggest that children who are HIV positive and those exposed to it should be followed up and assessed for developmental delay.

5.3. Developmental outcome

Ballot et al (2012) conducted a study in very low birth weight infants in a developing country (SA) at CMJAH. The infants included in this study had been admitted to the neonatal unit at CMJAH and an assessment using the Bayley-III was done to assess their developmental level. A total of 106 babies had a Bayley-III assessment. These babies had two assessments done; one at a mean age of 10,83 months and a second at a mean age of 17,74 months. Of the 106 babies, sixteen (15,1%) had a score of less than 70 (9 had isolated abnormalities, 4 had all 3 subscales less than 70 and three had two subscales below 70). The demographics of these babies was their birth weight was 1182g, their gestational age was 30,81 weeks, they had a median Apgar score of 8, their average time in hospital was 40,28 days, majority of them were black African and 61 were female and 49 male. The results of this study found that supplemental oxygen, prolonged hospitalisation, resuscitation at birth were all associated with poor outcome. The outcome of this study was that this group of children warrants long-term follow up post discharge.

When compared to the current study on PICU survivors, although the mean gestational age and birth weight are higher in this study, it shows that if there were any neonatal complications and the longer the duration in ICU, the lower the participants composite scores would be. From the current study on PICU survivors, the results yielded showed that four of the participants would need to be followed up with Physiotherapy, four would need Speech Therapy and three would either need Occupational Therapy or Physiotherapy.

A study done by Ballot et al (2017) looked at the use of the Bayley-III to assess the developmental outcome in infants and young children in an urban setting in South Africa. The Bayley-III has been used to assess developmental outcome of children in SA but there is little evidence on children with no previous admission to ICU.

The results from the study by Ballot et al (2017) show that the mean age of the participants was 19,4 months compared to 9 months and 7 days in this study. The study by Ballot et al (2017) showed that a group of South African children without neonatal risk factors achieved scores within the normal ranges of the Bayley-III.

As discussed earlier, Richter et al (1992) proved that South African children tend to perform better on the Bayley-I especially when under the age of 12 months. This is something that needs to be considered when reviewing the results of the two groups.

The study shows the mean cognitive score to be 92.2, the mean language score to be 94.8 and the mean motor score to be 98.8. This is compared to the current study where the mean cognitive, language and motor scores are 101.79; 108.02 and 104.26 respectively. The difference between the two studies is that this sample size was much smaller than the one in Ballot et al's study (42 compared to 74). The study by Knoester et al (2007) where they investigated patients with septic shock, respiratory insufficiency, meningococcal disease, central venous catheterisation, intubation, physical and psychological sequelae, post-traumatic stress disorder (PTSD), quality of life, health status and long-term outcome. It was found that neurological abnormalities were evident in these children and just like NICU survivors, standard evaluation and rehabilitation should be conducted and provided in PICU survivors.

5.3.1. Cognitive

As the literature states developmental delay is diagnosed when an infant does not reach their full developmental potential. For the Bayley-III if an infant scores between 70 and 84 on their composite scores they are considered at risk and if they score below 70 they are considered delayed (Ballot et al, 2012). A child is classified as having developmental delay if they have a low score in all three scales (Bayley, 2006). In both cases the infants should be referred on to a Physiotherapist, Occupational Therapist or Speech and

Language Therapist for further assessment and treatment if needed. Like the setting of the study by Rademeyer & Jacklin (2013), the participants of the current study also come from a poor socioeconomic background of poverty, unemployment and disease.

The mean cognitive score for the Bayley-III assessments in the current study for the PICU group was 104.17 and for the control group was 94.17. A reason for this difference in scores could be that the control group was slightly older than the PICU group and thus their scores were a more accurate representation of their developmental status.

In the current study, three out of 42 participants had a score of less than 85 (indicating at risk) and one had a score of less than 70 (indicating delay). These four infants were referred for Occupational Therapy for further investigation and assessment. When compared to the study by Rosie (2016), there were five participants that had cognitive scores lower than 70 and there were 15 participants that scored between 70 and 85.

In order for a child to be classified as 'being delayed' they should have a lower score in at least two of the three subscales. In the current study, one participant scored between 70 and 85 (at risk) in the cognitive and motor scales. This infant was female, had a birth weight of 2350g, a gestational age of 38 weeks, did suffer from respiratory distress syndrome (RDS) (neonatal complication), was diagnosed with sepsis and was on the ventilator for 14 days. Another infant (male) scored less than 85 in the cognitive scale and less than 70 in the language scale. This infant had a birth weight of 2300g, gestational age of 40 weeks, was ventilated for 1 day but spent 13 days in the ICU and was diagnosed with croup.

These results are similar to the study by Rosie (2016) where none of the infants had an abnormal result in all three areas.

5.3.2. Language

The mean language score for the current PICU group was 108.02 and for the control group 103.93. There were no children in the control group that scored below 85 (this shows us that none of these children needed to be referred on for further assessment). However there were three children in the PICU group that scored below 85 and one that scored below 70. So although the mean score for the PICU group was higher than the control group, there were four children that needed further assessment and follow-up.

5.3.3. Motor

The mean motor composite scores for the current study were 104.26 for the PICU group and 95.45 for the control group. A reason for this difference in scores could be that the children were younger in the PICU group and it has been shown that children do better in motor aspects when they are younger (Rademeyer & Jacklin, 2013).

Three of the participants in the PICU group scored below 85 and four of the participants in the control group scored below 85. A factor that was statistically significant in affecting the composite scores of the children was any form of neonatal complications. It was also found that the older the child was the worse their score on the Bayley-III motor scale, thus explaining the difference in results of the PICU and control groups.

5.4. Study Limitations

The sample selection in this study was somewhat biased and resulted in an unrepresentative sample.

Possibly should have considered the fragility of the ICU survivors and made the follow-up period a reasonable amount of time to give the patients time to heal and recover adequately. The fragility of the ICU survivors could have skewed the results and not been a true representation of the outcome of paediatric ICU survivors.

It would have been better to make the follow-up timeframe the same for all participants so as to give more accurate and true results.

Follow-up of the participants should have possibly been from hospital discharge and not just PICU discharge.

No data was collected on the socioeconomic status of the participants and their families. This would have helped to better understand the results.

A parent self-report questionnaire should have been done to get a baseline report on the participants developmental status prior to admission to ICU. It would have been better to be able to do a comparison with the outcome after PICU.

More information on the parent's state of mind and stress level would have helped to understand the home environment and dynamic and possibly give more information on the participants developmental outcome.

More detail would have been beneficial on the disease severity of PICU survivors.

The sample size of this study was relatively small and therefor the results should be interpreted with caution and not generalised. A low statistical power undermines the purpose of scientific research, it reduces the chance of detecting a true effect. It also reduces the likelihood that a statistically significant result reflects a true effect (Button et al, 2013).

This study was conducted at one government hospital which has a small paediatric ICU, it would have been better if the study had incorporated more government hospitals to be able to compare different ICUs and different kinds of patients.

The age range for this study was from 1 month to 3 and half years however the infants enrolled into the study were very young. The mean age of the participants was 8.84 months with the youngest being one month and the oldest 28 months. From the literature reviewed, we now know that these infants may yet to have reached their full potential and thus the results of the BSID-III assessments may change as the children get older.

It would have been more beneficial to assess the infants with the Bayley-III at two time points to get a comprehensive score, as sometimes children do not participate at their full potential on the day of the assessment. Only one developmental assessment was done because it was a master's study and more than one would have gone over the budget.

A longitudinal study would have been better as the functional outcome of the participants changes over time.

5.5. Recommendations for further research

From the findings of this study, it shows that nearly 10% of the study population (42) showed one or more forms of developmental delay on the BSID-III. Thus it demonstrates that neurodevelopmental assessment and screening of infants admitted to the PICU is important. Follow-up of these infants may help to eliminate developmental delay in the community.

It would be beneficial for future research to follow-up on PICUs from different hospitals as the one the study was conducted was very small. The results of the study also show that any child that has a history of neonatal complications is at risk of developmental delay and therefore should be followed up.

As the literature shows, it is more beneficial and realistic to perform the BSID-III on older children, as sometimes younger children do not perform to their full potential. It would be better to perform the same study in children over one year of age.

Study with a prospective longitudinal study would be recommended.

CHAPTER 6: Conclusion

There is limited literature on the effects of the PICU on the development of the children admitted and treated. However as many studies report the critical time (birth to 5 years) in a child's development where language, cognition, emotion, social, behaviour and physical skills develop it is important to look closely at children admitted to PICUs (Ozkan et al, 2012; Pem, D, 2012; Moura et al, 2010).

Many studies have been done on the effects of the NICU on the development of children but there is a gap in the literature on the effects of the PICU. Children are predisposed to many risk factors such as chromosal abnormalities, genetic and congenital disorders, central nervous system disturbances, severe attachment disorders, respiratory distress, brain haemorrhage, chronic infection and severe nutritional deprivation (Bayley, 2006). As the Lancet series show children from poor socioeconomic backgrounds are also exposed to poverty and malnutrition, which impact their development. The socioeconomic status of these children was not investigated.

The aim of this study was to identify if PICU survivors aged one month to three and a half years old are at risk of having developmental delay. This was assessed using the Bayley Scales of Infant and Toddler development, third edition and documenting their demographic data.

Forty two participants between the ages of one month and 42 months of age were assessed using the Bayley-III. Their corrected age was calculated and their demographic data was documented. Participants were identified from the Paediatric ICU database. The caregivers were called and a follow-up appointment was made. The Bayley-III assessments were conducted at the Neonatal follow-up clinic at Charlotte Maxeke Johannesburg Academic Hospital in Gauteng. The results were analysed and the composite scores were calculated for the Bayley-III. Intervention was implemented if the participant showed signs of developmental delay in one or more areas of the Bayley-III (Physiotherapy, Occupational Therapy and Speech therapy). The participants were not followed up after the first appointment. At the

appointment where they were assessed using the Bayley-III, they were also seen by a medical doctor and were able to voice any concerns they may have had. The control group of infants were also sourced from CMJAH and the Bayley-III assessments were performed by a trained professional.

After analysing the results of the current study it is evident that children discharged from the PICU are in fact at risk of some form of developmental delay and should be followed up. When comparing the composite scores of the PICU and control groups it was found that the results of the PICU group were slightly better than those of the control group. A reason for this could have been that the PICU group were younger and children have been known to perform better on the Bayley-III at a younger age. A key factor that stood out after performing the statistical analysis was children with a history of neonatal complications scored lower on the Bayley-III composite scores.

As stated before the sample size of this population was very small and further research is recommended. It would be beneficial for further research looking into children admitted to PICUs at different government hospitals. We can say, though, that there is a risk of developmental delay in these PICU survivors and that an appropriate follow-up plan be put into place once they are discharged from hospital.

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APPENDIX 1: Information document

Study title: The developmental status of Paediatric Intensive Care Unit survivors at an academic hospital in Gauteng.

Hello,

My name is Andrea Lentzakis and I am a research student at the university of Witwatersrand under the supervision of Prof Joanne Potterton and Prof Daynia Ballot. Research is where you try to find out an answer to a question. I want to find out what happens to children after they have been discharged from ICU.

Your child was recently admitted to the ICU at CMJAH and I would like to invite your child to participate in this study, with your permission.

In this study I will be testing neurodevelopment in children using a tool called the Bayley Scales of Infant and Toddler Development third edition. This will test their cognitive, language and motor abilities. I will give your child some toys to play with and watch what they do and I will ask them to walk, run and jump. I will show them how to do everything first.

I would also like permission to look at their hospital file to get information like their birth history, weight and height.

The results of the Bayley Scales of Infant and Toddler Development third edition and information from their hospital files will be captured using bed letters.

Risks

There are no risks with this study and there is no right or wrong answer to any of the activities they will do. We will be doing activities that are age-specific to your child so there is nothing to worry about.

Should any problems be found, we will refer your child to the right place for further assessment and treatment.

Benefits

This will help us to see if children who have been in ICU should be tested afterwards to see how they are developing.

We will pay for your transport to and from the hospital on the day of the assessment.

Participation:

Participation in this study is completely voluntary and if at any point you or your child doesn't want to do it anymore he/she may stop. Should he/she discontinue the study there will be no impact to them or their medical care.

Confidentiality:

Your child's information will be kept confidential at all times. Identifying factors such as identification number, name and surname, hospital number and birthdate will not be available to the public. A number will be assigned to your child to maintain confidentiality.

Should you have any questions or concerns please do not hesitate to contact me on the contact details below.

Thank you very much.

Andrea Lentzakis

Contact details of researcher:

Andrea Lentzakis

Physiotherapist

University of the Witwatersrand

072 186 1284

Contact details of the Human Research Ethics Committee (HREC):

Prof P Cleaton Jones

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:

Appendix 2 Consent form

Study title: The developmental status of Paediatric Intensive Care Unit survivors at an academic hospital in Gauteng.

Consent statement

I, the undersigned, _____, acknowledge that I read the information sheet and hereby give permission that my son/ daughter,

_____, may participate in the study as described (Full name and Surname)

above. I also give permission for the researcher to get information from my child's hospital file.

YES NO

Signatures:

Parent or Guardian: _____

Researcher: _____

Witness: _____

:

Appendix 3 Demographic sheet

Demographic and clinical information

Demographic and clinical information

Number assigned to patient: _____

Gender: ○ Male ○ Female

Age: _____

Weight: _____

Height: _____

Diagnosis: _____

Admission date: _____

Discharge date: _____

Duration of ICU stay: _____

HIV exposed: ○ Yes ○ No

Aids related illness: ○ Yes ○ No

On ARVs: ○ Yes ○ No

Previously admitted to ICU: ○ Yes ○ No

Intubated and ventilated: ○ Yes ○ No

Duration of ventilation: _____

Neurological history e.g. epilepsy, GBS ○ Yes ○ No

Birth history:

Birth Place: _____

Resus at birth: ○ Yes ○ No

NVD: ○ Yes ○ No

Caesarian: ○ Yes ○ No

Birth asphyxia: ○ Yes ○ No

Neonatal complications: ○ Yes ○ No

_____

Gestational Age: _____

:

Appendix 4 Ethics clearance letter

R14/49 Miss Andrea Maria Lentzakis

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M160479

NAME: (Principal Investigator)	Miss Andrea Maria Lentzakis
DEPARTMENT:	Physiotherapy Charlotte Maxeke Johannesburg Academic Hospital
PROJECT TITLE:	The Development Status of Paediatric Intensive Care Unit Survivors at an Academic Hospital in Gauteng
DATE CONSIDERED:	06/05/2016
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Prof Joanne Potterton and Prof Daynia Ballot

APPROVED BY: Professor P Cleaton-Jones, Chairperson, HREC (Medical)

DATE OF APPROVAL: 10/06/2016

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 Research Office Secretary in Room 10004, 10th floor, Senate House/2nd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand. 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**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in April and will therefore be due in the month of April each year.

Principal Investigator Signature

Date 12/6/2016

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix 5: Letters of permission

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG | FACULTY OF HEALTH SCIENCES

14 April 2016

To Whom It May Concern

RE: The Developmental Status of Paediatric Intensive Care Unit Survivors at an Academic Hospital in Gauteng"

I hereby give permission for Ms Andrea Lentzakis to access the neonatal REDCAP database at CMJAH for the purpose of obtaining a control group of infants for the above study. I am the gatekeeper of the database and am also one of her supervisors. Prof Joanne Potterton from the Wits Department of Physiotherapy is the other supervisor.

Yours Truly

Daynia Ballot (Prof)

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UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG | FACULTY OF HEALTH SCIENCES

14 April 2016

To Whom It May Concern

RE: The Developmental Status of Paediatric Intensive Care Unit Survivors at an Academic Hospital in Gauteng"

I hereby give permission for Ms Andrea Lentzakis to conduct the above study in the Paediatric Department at CMJAH. Her supervisors are Prof Daynia Ballot who is a member of our staff and Prof Joanne Potterton from the Wits Department of Physiotherapy.

Yours Truly

Peter Cooper (Prof)

HOD

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Appendix 6: Turn it in report