

AN AUDIT OF TRANSFERS INTO THE PICU AT THE RED CROSS CHILDRENS WAR MEMORIAL HOSPITAL: A FOLLOW UP STUDY

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Declaration

This research is based on independent work performed by Dr Konstantinos Dimitriades for the requirement of the degree - Masters in Philosophy in Paediatric Critical Care, and neither the whole work nor any part of it has been, is being, or is to be submitted for another degree to any other university. This work has not been reported or published prior to registration for the above-mentioned degree.

Abstract

Background: Children are transferred from various facilities into the paediatric intensive care unit (PICU) at the Red Cross War Memorial Children's Hospital for critical care, without a specialised paediatric transfer service. A previous audit in 2003 reported a high incidence of technical, clinical and critical adverse events during transfers.

Objective: To conduct a follow-up audit on interfacility transfers into PICU to determine practice and outcome changes.

Methodology: Prospective observational study of all patients transferred into PICU between 1 December 2013 and 30 November 2014 and compared to the 2003 audit by Hatherill et al.

Results: Analysis was performed on 204 transfers (median (IQR) age 1.8 (0.2 – 12.6) months and compared to results reported by Hatherill et al (2003). The proportion of medical transfers decreased (49% to 34.3% $p=0.003$) as well as the referrals from metropolitan hospitals (34.7% to 17.6%, $p = 0.0001$), whilst the number of referrals from academic hospitals increased from 35.1% to 44.6% ($p = 0.05$). Staff accompanying transfers and transfer times remained unchanged. The proportion of fixed wing transfers increased from 14.4% to 25.5% ($p=0.006$) whilst Helicopter transfers decreased from 9.9% to 1% ($p <0.0001$). 58.4% of patients were intubated for transfer in 2003 compared to 69.1% in 2014 ($p = 0.02$). The rate of technical (35.6% to 39.7%, $p = 0.4$), clinical (26.7% to 31.9%, $p = 0.25$), and critical (8.9% to 8.8%, $p = 0.97$) adverse events remained unchanged. PICU Mortality decreased from 16.8% to 9.45% ($p=0.03$) with a decrease in Standardized Mortality Rate from 1.11 to 0.68. Three children died on arrival to PICU. The communication tool was used in 45.1% of transfers and its use was noted to be associated with significantly less critical adverse events (4.3% vs. 12.5%, $p = 0.048$). Technical adverse events were positively correlated with the clinical adverse events (Spearman's $R = 0.3$; $p=0.000008$) and critical adverse events (Spearman's $R = 0.1$; $p = 0.03$). In turn the total number of clinical adverse events were positively correlated with the total number of critical adverse events (Spearman's $R = 0.5$; $p < 0.000001$). The multiple regression analysis for PICU mortality found the total number of clinical adverse events to be independently associated with ICU mortality (adjusted OR 95% CI 2.8 (1.7 -4.7); $p = 0.0001$)

Conclusion: The rate and staffing structure of interfacility transfers into PICU have remained unchanged, and associated adverse event rates remain high. Changes are noted in the profile of transferred patients as well as adverse events. Efforts to formalize the paediatric transfer service must be strengthened whilst using interim measures to improve the current standard through education, improved skills and PICU support.

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Abbreviations

AE	- Adverse Events
APLS	- Advanced Paediatric Life Support
BP	- Blood Pressure
CI	- Confidence Interval
ECG	- Electrocardiography
ECLS	- Extra Corporeal Life Support
EMRS	- Emergency Medical and Rescue Services
EMS	- Emergency Medical Services
ETT	- Endotracheal Tube
HREC	- Human Research Ethics Committee
ICU	- Intensive Care Unit
IQR	- Inter Quartile Range
LOS	- Length of Stay
OR	- Odds Ratio
PICU	- Paediatric Intensive Care Unit
PIM	- Paediatric Index of Mortality
PRISM	- Paediatric Risk of Mortality Index
PRT	- Paediatric Retrieval Team
RCWMCH	- Red Cross War Memorial Children's Hospital
SMR	- Standardised Mortality Rate
TRAPS	- Transport Risk Assessment in Paediatrics

Chapter 1 - Introduction

1.1 Context

History

In 2003, the first audit on paediatric transfers and adverse events in the Western Cape Province of South Africa was published. This study found a high incidence of technical, clinical and critical adverse events. In their conclusion the authors suggested that training in Advanced Paediatric Life Support (APLS) might reduce the incidence of adverse events. They also proposed that the establishment of a paediatric retrieval team may reduce the incidence of technical adverse events as well as cardio-respiratory adverse events during these transfers[1]. More than ten years later, the Emergency Medical Service (EMS), has not formalised a specialised paediatric retrieval team for the transfer of critically ill children in to the PICU.

The need for paediatric transfers is closely linked to the centralisation of paediatric intensive care units. Approximately twenty years ago, subsequent to the publication of the Trent-Victoria study, centralization of paediatric intensive care has increased in countries such as the United Kingdom[2,3]. In South Africa, paediatric intensive care began in Academic Hospitals in major centres of the country and the service has remained centralized. Due to South Africa's history and size, the country comprises both underdeveloped and developed areas. Patients in rural areas have limited access to primary health care services and must travel long distances to access regional and tertiary care services, thus impacting morbidity and mortality[4]. In 2012, the South African under-5 mortality was between 50 and 75 per 1000 live births[5], however in the Western Cape Province (2011) this was estimated to be lower at 24.1 (www.mrc.ac.za)[6]. This could be attributed in part to the higher per capita spending on health in the Western Cape (www.hst.org.za)[7]. The Western Cape therefore does not represent the general condition of South Africa's health service. Yet, even in this region, which has seen a reduction in overall mortality, the transfer service remains unchanged, without the formation of a specialized retrieval team.

Outcomes Prior to Specialised Retrieval Teams

Paediatric retrieval teams were introduced in developed countries in response to the high incidence of adverse events associated with retrievals performed by inexperienced teams. A number of studies performed prior to the year 2000 indicated the need for the establishment of specialized paediatric retrieval teams (SPRT). In 1992, Kanter noted a significantly increased risk of adverse events in children who underwent interhospital transfers versus children who underwent intrahospital transfers, and this was associated with longer travel distance as well as higher level of required therapy[8]. Other studies have noted adverse events from 20% to 75% of transferred patients[9,10]. The 1992 study demonstrated that 23% of their transfers suffered a major cardiorespiratory event requiring

intervention. This study also showed an association between inexperience and adverse events[9].

Outcomes of Specialised Retrieval Teams

Over the last two decades numerous studies have been performed looking at the outcomes of patients transferred by specialised retrieval teams. Britto et al in 1995 noted that through the interventions of the SPRT, the severity of illness improved en route. No adverse technical events were seen in their study[11]. From 2004 to 2010, a number of studies were performed looking at the difference in outcomes between SPRT and non-specialized retrieval teams as well as transfers performed by the referring specialist. These studies noted better monitoring, a reduction in adverse events and improved mortality with SPRT's[12-14]. Orr et al also noted that transportation by air was associated with a higher risk of an unplanned event, which in turn was associated with 28-day mortality[13]. However, the establishment of SPRT's has not completely removed the occurrence of adverse events as noted by Lim and Ratnavel, who noted an adverse event in 36% of neonatal transfers. The majority of these adverse events occurred during the preparation and communication phase of the transfer process[15].

Pre-Transfer Communication

In the early nineties a few studies indicated that pre-transfer communication was an important factor in avoiding problems related to transfer of patients. Henning et al in 1991 found that 28 percent of problems that occurred during the transfer process could have been avoided with improved communication[16]. The literature indicates that the communication process and quality may be improved with the use of communication checklists, which may also result in shorter communication times[15,17,18].

Information Regarding Specialised Retrieval Units

Many of the papers reviewed have given examples of the composition of specialist retrieval teams. Clinicians with paediatric intensive care training and experience or training in transportation are noted in many studies[11,12,14,19,20]. Orr et al noted that a fellow in the ICU would accompany the paediatric critical care transport team only for extremely high-risk cases. Their team comprised a dedicated critical care transport nurse and a respiratory therapist with 3 years of paediatric critical care experience. The training of this team included advanced airway skills, air medical physiology and safety in the transport environment, as well as communication skills[13]. In 2007 the United Kingdom introduced the first group of trained Nurse Practitioners for critical care transport. Their training consisted of 3 years part time training in core skills such as advanced airway management, patient assessment, and central venous and arterial cannulation. Supervised retrievals were performed until they were signed off as proficient by two different consultants on at least 3 occasions. The need for nurse practitioner-led retrieval teams arose from the increased demand on this service[21]. Other team members of paediatric retrieval teams include nurses and or paramedics[11,12,14,19-21].

Equipment requirements for paediatric transfers are not standardized. The study by Vos et al. published in 2004 noted that there was a significant difference in the equipment available to specialised retrieval teams relative to the referring specialists[12]. Vos et al. in 2003 suggested the minimum equipment and consumables required for a transfer should consist of a monitor with continuous measurements of vital signs, a defibrillator, tools for airway and ventilator management; an oxygen source; suction unit; fluid and electrolyte management; medication; a resuscitation chart and communication system. In this paper the authors looked at a novel system of applying the equipment required during a transfer to the transport trolley, thus allowing for an approximation of the care given in PICU[22]. As transport medicine develops, so the equipment required during transfers becomes more sophisticated. The use of point-of-care blood analysers was shown to result in the implementation of appropriate interventions en route[23]. An extreme example of advanced equipment used in specialised paediatric transfers includes extra corporeal life support (ECLS) equipment. This type of super-specialised transfer required its own set of equipment as well as further specialised staff such as a paediatric intensivist, ECLS trained nurse, perfusionist and cardiothoracic surgeon[24]. The future of transport medicine is likely to see more innovation in terms of equipment use as well as further introduction of specialised and super-specialised retrieval teams.

Perceptions Surrounding Specialised Retrieval Teams

In the literature review we also looked at the perceptions of different groups towards the introduction of specialised retrieval teams. In 2008, Carmo et al. published their quality audit on the services delivered by the New South Wales Neonatal and Paediatric Transport Service. They noted that both referring and accepting doctors as well as parents were positive about the service[25]. In 2011 Davies et al. looked at the attitudes of paediatric intensive care nurses to the development of a nurse practitioner role for critical care transport and noted that nurses were predominantly positive to the implementation of this role. The authors also noted that 100% of polled nurses felt that the nurse practitioners were sufficiently trained[21]. Davies et al. also conducted a study looking at the attitudes of staff and parents towards parental accompaniment during the transfer of critically ill children. The authors noted that the majority of parents found the experience to be safe and beneficial and as a result experienced less stress during the transfer. The staff perceived little or no stress with parental accompaniment and were able to perform interventions without any hindrance[26].

Concerns Regarding Specialised Retrieval Teams

Although perceptions surrounding the implementation of specialised retrieval teams are predominantly positive, some concerns have been raised in the literature regarding the possibility of deskilling staff in smaller hospitals[11,27,28]. Two papers were identified investigating this particular concern. In 2003, Ramnaryan et al. performed a retrospective study looking at the skills used by referring institutions in two periods before and after the implementation of specialised retrieval teams. This study found an increase in the

rate of intubation by the referring institution and unchanged rate in central venous and arterial cannulation, thus refuting this concern[29]. In 2010, Lampariello et al. concluded that District General Hospital staff performed the majority of initial stabilisation procedures appropriately prior to the arrival of a retrieval service[30].

Standardization of Mortality Using PIM

To allow for the standardization of mortality and to remove the possibility of skewing the results by patients who are transported with a low mortality risk the studies quoted throughout this review have used either the Paediatric Risk of Mortality Score (PRISM) or the Paediatric Index of Mortality (PIM) scoring systems. The PRISM score looks at 14 variables collected over 24 hours from the time of admission, whereas the PIM score is a point of care scoring system that consists of only 8 variables. The PIM variables must be collected within 1 hour of encountering the ICU team. Tibby et al. assessed which of the Mortality Risk Scores were least affected by the retrieval process and studied 928 critically ill children retrieved for intensive care from South East England. The authors found that complete data collection for calculation of scores was performed in 88% for PIM scoring, 24% for pre-ICU PRISM and 60% for PRISMII. This is likely due to the fewer number of variables required for PIM as well as their simplicity. All three scoring systems over-predicted mortality. The authors concluded that PIM was more suitable due to its ease of data collection and that point-of-care data would not be affected by the retrieval process[31]. For this study PIM2 is in use as it was the latest version of the index available at the time of data collection. Solomon et al. assessed this index and found it to be well calibrated[32].

Previous Study Results on Paediatric Transfers in the Western Cape

The study by Hatherill et al. was used as the starting point to compare where the retrieval service in the Western Cape finds itself ten years down the line. The authors collected data on all children transferred in to the PICU at Red Cross Children's War Memorial Hospital from other institutions[1].

Adverse events were classified as Technical, Clinical and Critical Adverse Events. In total there were one or more technical adverse events in 36% of transferred children, with one or more clinical adverse events having occurred in 27% of transferred children. The authors noted that there was a trend towards experiencing a clinical adverse event in patients in whom an adverse technical event had already occurred, although this did not reach statistical significance. In the group of critical adverse events 6% of all transferred children suffered a respiratory or cardiorespiratory arrest and one or more critical events were noted in 9% of all transferred children[1].

When analysing the adverse events by staff category there was no difference in the critical or adverse events that occurred. However, when PICU staff transferred children, they were less likely to experience technical adverse events as seen by 0% versus 40% in the non-PICU staff $p=0.0002$. More adverse events across all

the categories occurred in children transferred from Metropolitan hospitals versus Academic and Rural hospitals[1].

Non-survivors were more likely to have been shocked or hypoxic, thus the authors suggested that there might be a lack of training amongst paramedic staff. Although the authors felt that an intervention to improve the quality of PICU transfers was warranted, they recognized that this would be difficult in the face of limited resources and other competing health care priorities. The findings of this study are similar to those discussed in the section on outcomes prior to specialised retrieval services[1].

Significance Of Performing This Study

The above studies assist in delineating the history and growth of specialised paediatric retrieval teams. Many countries not limited by resources have opted for the establishment of SPRT's. The compositions of these teams are heavily weighted with physicians, though a move towards nurse practitioner led teams has been noted. Although there were concerns of losing vital stabilisation skills with the formation of these teams it has been shown that this is not the case [29,30].

South Africa's transfer service remains unchanged since Hatherill et al's study (2003) and has not developed a specialised paediatric retrieval service to the PICU. We would thus not expect a change in findings since 2003. However, as all transfers are performed by the emergency medical and rescue services and as their experience of transferring critically ill children is likely to have increased over time, we hypothesize a decrease in adverse events occurring during transfers as well as improved outcomes. This study could thus assist in planning and improving the transfers of critically ill children in to the PICU.

References

1. Hatherill M, Waggle Z, Reynolds L, Argent A. Transport of critically ill children in a resource-limited setting. *Intensive Care Medicine*. 2003 Sep;29(9):1547–54.
2. Pearson G, Shann F, Barry P, Vyas J, Thomas D, Powell C, et al. Should paediatric intensive care be centralised? Trent versus Victoria. *The Lancet*. 1997 Apr 26;349(9060):1213–7.
3. Ramnarayan P, Polke E. The state of paediatric intensive care retrieval in Britain. *Archives of Disease in Childhood*. 2012 Jan 11;97(2):145–9.
4. Coovadia H, Jewkes R, Barron P, Sanders D, McIntyre D. The health and health system of South Africa: historical roots of current public health challenges. *Lancet*. 2009 Sep 5;374(9692):817–34.

5. Nannan N, Dorrington R, Laubscher R, Zinyakatira N, Prinsloo M, Darikwa T, et al. UNDER-5 MORTALITY STATISTICS IN SOUTH AFRICA: Shedding some light on the trend and causes 1997-2007. Cape Town: South African Medical Research Council; 2012 May pp. 1–107.
6. Groenewald P, Msemburi W, Morden E, Zinyakatira N, Neethling I, Daniels J, et al. Western Cape Mortality Profile 2011. www.mrc.ac.za. Cape Town: South African Medical Research Council; 2014 Jul. Accessed 08 December 2015.
7. Per Capita Health Expenditure - Health Indicators [Internet]. Health Systems Trust; pp. 1–2. Available from: <http://www.hst.org.za/content/health-indicators> Accessed 08 December 2015
8. Kanter RK, Boeing NM, Hannan WP, Kanter DL. Excess morbidity associated with interhospital transport. *Pediatrics*. 1992 Dec;90(6):893–8.
9. Barry PW, Ralston C. Adverse events occurring during interhospital transfer of the critically ill. *Archives of Disease in Childhood*. BMJ Publishing Group Ltd and Royal College of Paediatrics and Child Health; 1994;71(1):8–11.
10. Edge WE, Kanter RK, Weigle CG, Walsh RF. Reduction of morbidity in interhospital transport by specialized pediatric staff. *Crit Care Med*. 1994 Jul;22(7):1186–91.
11. Britto J, Nadel S, Maconochie I, Levin M, Habibi P. Morbidity and severity of illness during interhospital transfer: impact of a specialised paediatric retrieval team. *BMJ*. 1995 Sep 30;311(7009):836–9.
12. Vos GD, Nissen AC, Nieman FHM, Meurs MMB, van Waardenburg DA, Ramsay G, et al. Comparison of interhospital pediatric intensive care transport accompanied by a referring specialist or a specialist retrieval team. *Intensive Care Medicine*. 2004 Feb;30(2):302–8.
13. Orr RA, Felmet KA, Han Y, McCloskey KA, Dragotta MA, Bills DM, et al. Pediatric specialized transport teams are associated with improved outcomes. *Pediatrics*. 2009 Jul;124(1):40–8.
14. Ramnarayan P, Thiru K, Parslow RC, Harrison DA, Draper ES, Rowan KM. Effect of specialist retrieval teams on outcomes in children admitted to paediatric intensive care units in England and Wales: a

- retrospective cohort study. *Lancet*. 2010 Aug 28;376(9742):698–704.
15. Lim MTC, Ratnavel N. A prospective review of adverse events during interhospital transfers of neonates by a dedicated neonatal transfer service. *Pediatric Critical Care Medicine*. 2008 May;9(3):289–93.
 16. Henning R, McNamara V. Difficulties encountered in transport of the critically ill child. *Pediatric Emergency Care*. 1991 Jun 1;7(3):133.
 17. Goh AY, El-Amin Abdel-Latif M. Transport of critically ill children in a resource-limited setting: alternatives to a specialized retrieval team. *Intensive Care Medicine*. 2004 Feb;30(2):339.
 18. Yamamoto LG, Wiebe RA, Maiava DM, Merry CJ. A one-year series of pediatric prehospital care: I. Ambulance runs; II. Prehospital communication; III. Interhospital transport services. *Pediatric Emergency Care*. 1991 Aug 1;7(4):206.
 19. Crabtree I. “A bridge to the future”: impact on high dependency and intensive care. *J Child Health Care*. 2001;5(4):150–4.
 20. Doyle YG, Orr FE. Interhospital transport to paediatric intensive care by specialised staff: experience of the South Thames combined transport service, 1998-2000. *Archives of Disease in Childhood*. 2002 Sep;87(3):245–7.
 21. Davies J, Bickell F, Tibby SM. Attitudes of paediatric intensive care nurses to development of a nurse practitioner role for critical care transport. *J Adv Nurs*. 2011 Feb;67(2):317–26.
 22. Vos GD, Buurman WA, van Waardenburg DA, Visser TPL, Ramsay G, Donckerwolcke RAMG. Interhospital paediatric intensive care transport: a novel transport unit based on a standard ambulance trolley. *Eur J Emerg Med*. 2003 Sep;10(3):195–9.
 23. Vos G, Engel M, Ramsay G, van Waardenburg D. Point-of-care blood analyzer during the interhospital transport of critically ill children. *Eur J Emerg Med*. 2006 Oct;13(5):304–7.
 24. Perez A, Butt WW, Millar KJ, Best D, Thiruchelvam T, Cochrane AD, et al. Long-distance transport of critically ill children on extracorporeal life support in Australia. *Crit Care Resusc*. 2008 Mar;10(1):34.

25. Browning Carmo KA, Williams K, West M, Berry A. A quality audit of the service delivered by the NSW Neonatal and Paediatric Transport Service. *J Paediatr Child Health*. 2008 May;44(5):253–72.
26. Davies J, Tibby SM, Murdoch IA. Should parents accompany critically ill children during inter-hospital transport? *Archives of Disease in Childhood*. 2005 Dec;90(12):1270–3.
27. Raffles A. Intensive care provided by local hospitals should be improved. *BMJ*. 1996 Jan 13;312(7023):120–1.
28. Goh AY-T, Abdel-Latif ME-A, Lum LC-S, Abu-Bakar MN. Outcome of children with different accessibility to tertiary pediatric intensive care in a developing country – a prospective cohort study. *Intensive Care Medicine* [Internet]. Springer; 2003;29(1):97–102.
29. Ramnarayan P, Britto J, Tanna A, Thomas D, Alexander S, Habibi P. Does the use of a specialised paediatric retrieval service result in the loss of vital stabilisation skills among referring hospital staff? *Archives of Disease in Childhood*. 2003 Oct;88(10):851–4.
30. Lampariello S, Clement M, Aralihond AP, Lutman D, Montgomery MA, Petros AJ, et al. Stabilisation of critically ill children at the district general hospital prior to intensive care retrieval: a snapshot of current practice. *Archives of Disease in Childhood*. 2010 Sep;95(9):681–5.
31. Tibby SM, Taylor D, Festa M, Hanna S, Hatherill M, Jones G, et al. A comparison of three scoring systems for mortality risk among retrieved intensive care patients. *Archives of Disease in Childhood*. 2002 Nov;87(5):421–5.
32. Solomon LJ, Morrow BM, Argent AC. Paediatric Index of Mortality scores: An evaluation of function in the paediatric intensive care unit of the Red Cross War Memorial Children's Hospital. *Southern African Journal of Critical Care*. 2014 Aug;30(1):8–13.

1.2 ETHICAL CONSIDERATIONS

POTENTIAL RISKS AND BENEFITS

This was an observational study at a particular point in the patients' care process, with no interventions and thus no direct physical risk of harm but also no foreseeable direct benefits to individual participants.

There was a potential for a breach of confidentiality. To minimize this risk, data collected was anonymised and stored securely.

Being enrolled in the study did not affect the patient's care in the PICU and considering that patients were enrolled after transfer was complete, it also did not affect the quality of care received during the inter-facility transport.

The results of this study will provide information on the transfer of critically ill children in order to assist in improving patient outcomes. Thus, although there was no direct benefit for individual patients enrolled in this study, the results of this study may benefit future children being transferred into PICU.

If an adverse event were identified during a transfer, our responsibility was to ensure that clinical staff were made aware of this.

CONSENT

Considering the non-interventional, minimal risk nature of this study, the investigators requested that the need for written informed consent be waived for this study. The waiver of informed consent was approved by the institutional Faculty of Health Sciences Human Research Ethics Committee (HREC) (see appendices). No patient will be identified in any output arising from this study and the study itself did not collect any characteristics that could be used to identify patients. As stated above this study did not pose any direct risks or future benefits to the studied patients.

This study conformed to the requirements outlined in the Declaration of Helsinki (2013) revision.

HREC approved the study 702/13

Chapter 2 – Publication-Ready Manuscript

AN AUDIT OF TRANSFERS INTO THE PICU AT THE RED CROSS WAR MEMORIAL CHILDRENS HOSPITAL (RCWMCH): A FOLLOW UP STUDY

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Abstract

Purpose: Children are transferred from various facilities in South Africa into Paediatric Intensive Care Unit without a specialised paediatric transfer service. A 2003 audit reported a high incidence of technical, clinical and critical adverse events during transfers. We aimed to conduct a follow-up audit on interfacility transfers into PICU to determine practice and outcome changes.

Methodology: Prospective observational study of all patients transferred into the RCWMCH PICU between 1 December 2013 and 30 November 2014.

Results: Analysis was performed on 204 transfers (median (IQR) age 1.8 (0.2 – 12.6) months and compared to results reported by Hatherill et al (2003). The proportion of medical transfers decreased (49% to 34.3% $p=0.003$) as well as the referrals from metropolitan hospitals (34.7% to 17.6%, $p = 0.0001$), whilst the number of referrals from academic hospitals increased from 35.1% to 44.6% ($p = 0.05$). Staff accompanying transfers and transfer times remained unchanged. The proportion of fixed wing transfers increased from 14.4% to 25.5% ($p=0.006$). 58.4% of patients were intubated for transfer in 2003 compared to 69.1% in 2014 ($p = 0.02$). The rate of technical (35.6% to 39.7%, $p = 0.4$), clinical (26.7% to 31.9%, $p = 0.25$), and critical (8.9% to 8.8%, $p = 0.97$) adverse events remained unchanged. PICU Mortality decreased from 16.8% to 9.45% ($p=0.03$), however three children died on arrival to PICU.

Conclusion: The rate and staffing structure of interfacility transfers into PICU have remained unchanged, and associated adverse event rates remain high. Efforts to formalize the paediatric transfer service must be strengthened whilst using interim measures to improve the current standard.

Introduction

The transfer of critically ill children to Paediatric Intensive Care Units (PICU) has developed over time into a formalized discipline, in many countries. In 2003 Hatherill et al, published their experience regarding the transfer of paediatric patients into the PICU at Red Cross War Memorial Children's Hospital (RCWMCH) over a one year period (1st November 2000 to 31st October 2001).[1] They reported a high rate of adverse events, particularly when compared with results from centres using Specialized Paediatric Retrieval Teams (SPRTs)[2-4].

With the centralization of paediatric critical care services, the need for formalized paediatric retrieval services arose[5,6]. Early studies in the mid 1990's attested to the fact that non-specialized teams experienced a high number of adverse events during transport of critically ill children, and that the incidence of these events increased with the duration of transfer and were more common when performed by inexperienced staff[7,8]. In the late 1990s the establishment of SPRTs was associated with a decrease in adverse events, particularly in intensive care related adverse events such as loss of intravenous access or accidental extubation during the retrieval [9,10]. In 2004, Vos et al also noted a significant improvement in transfers performed by SPRT over transfers accompanied by the referring specialist.[2].

The ethos of mobile intensive care, as suggested by Britto et al (1995), has continued to grow with further development of transfer teams and equipment [10]. Clinicians with paediatric intensive care training and experience, or training in transportation, were included as members of the transportation team in many studies [2,4,6,10,11]. The particular combination of clinicians in transport teams varies. Many teams are nurse led, while others include other clinicians, and the seniority of the team may be related to the perceived risk of the transfer [3,12]. There is considerable variation in the literature regarding the minimum levels of equipment required to transport a critically ill child. This may relate to the fact that not all critically ill children require the same level of skills and equipment for their safe transfer. Monitors with continuous measurement of vital signs, a defibrillator, resources for airway management and vascular access, ventilator, suction and oxygen supply, as well as fluids and medications may all be required [13]. In settings such as the transportation of patients on extra corporeal life support, the team membership may comprise a cardiothoracic surgeon, intensivist, perfusionist and an intensive care nurse with far more advanced equipment being required [14].

Concerns about implementing SPRTs included the possibility of deskilling the hospitals served by the teams, particularly if the number of critically ill patients seen were already low, and that this could impact the care of patients when the teams were not available[15,16]. Two studies have refuted this, showing that since the implementation of SPRT's the emergency skills of doctors at the referring hospitals have improved, with increased numbers of endotracheal intubations, central line placements and commencement of inotropes [17,18]. The establishment of SPRTs has been perceived as being positive from both referring and receiving clinicians as well as accompanying parents [12,19,20].

Despite the mounting evidence that SPRTs result in improved outcomes and better quality of care, South Africa has yet to formalize a pediatric retrieval service. We therefore repeated the audit, as it was performed 10 years ago [1], with the aims of describing and comparing the management, adverse events, and outcomes of children transferred into the PICU at RCWMCH.

Methodology

This was a prospective observational study over a one-year period from 1st December 2013 to 30th November 2014. All patients transferred directly into the PICU of the RCWMCH, which treats approximately 1500 children a year, from an outside institution were enrolled. Institutional research ethics committee approval was obtained, and the requirement for informed consent was waived owing to the non-interventional nature of the study (HREC Rec/Ref: 702/13).

We mirrored the design of Hatherill et al's (2003) study[1], in order to accurately reflect changes in patient management, complications and outcomes over the intervening period. Transfer data were collected prospectively within 24 hours of admission to the PICU and were extracted from the admission record, nursing notes, the ambulance voucher and/or in discussion with the admitting doctor and attending paramedic. Data collected included patient demographics and admission characteristics; Paediatric Index of Mortality 2 (PIM 2) score on admission; details on the referring institution; duration of the transfer (time from initial telephonic request to the ICU or from the request for Emergency Medical and Rescue Services (EMRS) to PICU admission); transferring personnel; mode of transport; the use of a pre-transfer communication tool and whether advice was given and followed; duration of PICU stay and all-cause mortality (Table 1). A few deviations from the original study were required in order to reflect the unit's current practice as well as to reflect the current standard of care. PIM2 was used for this study as compared to PIM in Hatherill's study[1]. Other changes included the addition of capnography to monitoring, the removal of inotropes as a clinical adverse event, the addition of hypothermia and seizures under clinical adverse events, and the addition of hyperthermia in neonates transferred in an incubator. Information regarding the communication process was collected, which was not present within the previous study. In an effort to try and understand where in the transfer process adverse events take place, data was collected to reflect if adverse events took place en route or on arrival.

For the purposes of this study, adverse events were classified using previously described definitions (Table 1)[1].

Table 1. Definitions of Descriptive Data

Institution Category:
<ul style="list-style-type: none"> Academic Hospitals – Hospitals in the greater Cape Town Metropolitan area with 24 hour paediatric registrar cover.
<ul style="list-style-type: none"> Metropolitan Hospitals – Hospitals in the greater Cape Town Metropolitan area without 24 hour paediatric registrar cover. This includes private hospitals
<ul style="list-style-type: none"> Rural Hospitals – Hospitals beyond the greater Cape Town Metropolitan area, it includes District and Regional Hospitals
Transferring Personnel:
<ul style="list-style-type: none"> Registrar – Paediatric, Anaesthetic, Emergency Medicine trainees who are receiving critical care training as part of their speciality.
<ul style="list-style-type: none"> Senior Registrar – A Paediatrician currently training to sub-specialise in Paediatric Critical Care.
<ul style="list-style-type: none"> Referring Doctor – Any grade of doctor that is accompanying a patient from the referring institution.
<ul style="list-style-type: none"> Paramedic – This includes any grade of Paramedic who may be trained in Intermediate Life Support, Advanced Life support or may have completed a Bachelor’s degree in emergency medical care.
Duration of Transfer:
<ul style="list-style-type: none"> The difference between time of referral and time of admission. Time of Referral: Collected as the time the telephonic request was placed to the PICU. In elective transfers this was collected as the time the request was placed with the Emergency Medical Rescue Services. Time of Admission: The documented admission time.
Mode of Transport:
<ul style="list-style-type: none"> Road – refers to transport predominantly by Ambulance
<ul style="list-style-type: none"> Helicopter – Refers to transfer predominantly by Helicopter (No road transfer is required to RCWMCH from the helicopter)
<ul style="list-style-type: none"> Fixed Wing Aircraft – Refers to transfer predominantly by aeroplane
Diagnosis:
<ul style="list-style-type: none"> The admission diagnosis was classified under the heading of General Medical, General Surgical, Trauma and Burns, Cardiac, Neonatal Surgical or Other (Diagnosis not classified in the above e.g. Anesthetic complications).
Technical Adverse Events:
Defined as failure to commence monitoring, site intravenous access, correctly position an endotracheal tube or failure or loss of the following during transfer or on admission to the PICU:
<ul style="list-style-type: none"> Oxygen Saturation monitoring
<ul style="list-style-type: none"> Electrocardiography
<ul style="list-style-type: none"> Blood Pressure monitoring
<ul style="list-style-type: none"> Endotracheal Tube (ETT): Placement may be nasal or oral. Malposition was documented if the tube was deeper than expected for age/weight at the

nose/mouth using the formula described by the APLS (Advanced Paediatric Life Support) manual; if chest radiograph shows the ETT at the carina or below or if direct laryngoscopy or auscultation suggests this.
<ul style="list-style-type: none"> ○ APLS ETT Formula[21] <ul style="list-style-type: none"> ▪ Oral: Age/2 + 12 ▪ Nasal: Age/2 + 15
<ul style="list-style-type: none"> • End Tidal CO₂
<ul style="list-style-type: none"> • Ventilation
<ul style="list-style-type: none"> • Intravenous Access: Failure to insert, Blocked/dislodged en route or on admission to ICU. Types of vascular access include Peripheral, Central, or Intraosseous.
Clinical Adverse Events:
One or more of the following events occurring during the transfer or on arrival to the PICU.
<ul style="list-style-type: none"> • Shock: Defined as Capillary Refill Time of more than 4 seconds or Hypotension for age, and requiring either fluid resuscitation or the commencement of inotropes[1]. <ul style="list-style-type: none"> ○ Hypotension – Systolic Blood Pressure less than the 5th centile for age using the APLS formula. $65 + (\text{age} \times 2)$ outside the neonatal period [21]. ○ For neonates including preterm - Blood Pressure was compared against the normograms for Mean Blood Pressure and diastolic blood pressure in Nelsons Textbook of Pediatrics 19th Edition. (Table 62-1 and Figure 88-2)[22]
<ul style="list-style-type: none"> • Hypoxia: Defined as peripheral Oxygen saturation less than 80% in the absence of a cyanotic heart defect.
<ul style="list-style-type: none"> • Hypoglycaemia: Defined as Blood glucose less than 2.5mmol[1]
<ul style="list-style-type: none"> • Hypothermia: Defined as temperature of less than 35 degrees Celsius either by axillary or rectal measurements.
<ul style="list-style-type: none"> • Hyperthermia: Defined as temperaure more than 38.5 degrees Celsius either by axillary or rectal measurements.
<ul style="list-style-type: none"> • Seizures: Uncontrolled movement documented by clinical staff as convulsions or seizures.
Critical Adverse Events:
Defined as cardiorespiratory arrest or the need for emergency intubation during the transfer or on arrival at the PICU
<ul style="list-style-type: none"> • Cardiorespiratory arrest – Defined as the loss of circulation requiring cardiopulmonary resuscitation.
<ul style="list-style-type: none"> • Emergency Endotracheal Intubation – Defined as any unplanned intubation during the transfer or on arrival to the PICU
<ul style="list-style-type: none"> • Death: Defined as observed death en route or on arrival in the ICU

Data analysis

Data were tested for normality using Shapiro-Wilks W test, and presented as median (interquartile range, IQR) or n (%) as appropriate to nonparametric data, unless otherwise stated. Continuous data were compared using Mann-Whitney U tests and categorical variables using Chi square (or Yates corrected Chi square tests). Raw data from Hatherill's study was not available; therefore, only where sufficient data were available were results of the previous study [1] compared with those of the current study. Correlations between continuous data were analysed using Spearman Rank correlation tests and variables identified as being associated with the primary outcome (mortality) on univariate analysis were entered into a backward stepwise multiple logistic regression model. A significance level of $p < 0.05$ was used. Data were analysed using Statistica version 11 (StatSoft Inc, USA).

Results

Two hundred and four transfers of children (median age 1.8 months, IQR 0.2 - 12.6 months) were undertaken over the period of the study (Table 3).

Transfer details

General medical illness remained the major reason for transfers, but this was significantly reduced since 2003 ($n=99$ vs $n=70$) ($p=0.003$). Neonatal surgical cases were the second major reason for transfer into the PICU and the rate of cases remained unchanged. Cardiac cases were the third most common reason for transfer, with a significant increase from 2003 ($n=22$ vs $n=41$) ($p=0.01$), which may indicate increased recognition at referring hospitals (Table 2). Other conditions included transfers post anaesthetic complications, transfers for otorhinolaryngology management and other conditions that did not comply with the identified major categories. A significant increase was noted in transfers from academic institutions; whilst there was a significant decrease in transfers from metropolitan hospitals (Table 3). Four cases were transferred from primary care clinics. There was no change between the proportion of PICU and non-PICU staff accompanying transfers, however, within the non-PICU staff category there was a significant decrease in the number of cases transferred by the referring physician. Road transfers remained the predominant mode of transport, however a significant increase in the proportion of fixed wing transportation of patients was noted, and only two transfers were performed by helicopter (Table 2).

Table 2: Details of transfers comparing data from 2003 to the present study.

	Hatherill 2003 n=202 [1]	Dimitriades 2014 n=204	P (where possible*)
Age (months)	2.8 (1.1 - 14)	1.8 (0.2 - 12.6)	
Weight (kg)	3.5 (2.5 - 8.1)	3.5 (2.3 - 9.3)	
PIM2 (risk of mortality) (PIM1 in 2003)	0.15 (0.13-0.18)	0.14 (0.12 - 0.16)#	
Type of illness			
Medical	99 (49%)	70 (34.3%)	0.003
Surgical	15 (7.4%)	5 (2.5%)	0.02
Trauma	7 (3.5%)	12 (5.9%)	0.3
Cardiac	22 (10.9%)	41 (20.1%)	0.01
Neonatal surgical	52 (25.7%)	52 (25.5%)	0.95
Other	7 (3.5%)	24 (11.8%)	0.001
Referring Hospital			
Academic	71 (35.1%)	91 (44.6%)	0.05
Metropolitan	70 (34.7%)	36 (17.6%)	0.0001
Rural	61 (30.2%)	73 (35.8%)	0.2
Transport personnel			
PICU staff	20 (9.9%)	26 (12.7%)	0.4
Non-PICU staff	182 (90.1%)	178 (87.3%)	0.4
Referring physician	17 (8.4%)	2 (1%)	0.0003
Paramedics	165 (81.7%)	162 (79.4%)	0.6
EMRS Doctor		14 (6.9%)	-
Transport mode			
Road	153 (75.7%)	150 (73.5%)	0.6
Helicopter	20 (9.9%)	2 (1%)	<0.0001
Fixed wing aircraft	29 (14.4%)	52 (25.5%)	0.006
Duration of transport (hours)	3.5 (2 - 6)	4.0 (2.2 - 9.0)	

Data are median (IQR) or n (%)

* P values could not be calculated on continuous data as raw data from Hatherill's study[1] was not available.

PIM2 Calculated out of 201 patients (Excluded 3 deaths on arrival)

Adverse events

There was no difference in the total number of technical adverse events that occurred in 2003 compared to 2014 (Table 3). However, a shift was noted in the type of technical adverse events that occurred, with a significant improvement being noted in vascular access but a reduction in monitoring, which may be related to the addition of the requirement for capnography (Table 3). More patients were transferred intubated in 2014 and most of them were nasally intubated, however, there was no change in the rate of endotracheal tube (ETT) malposition. (Table 3).

Table 3: Adverse Events comparing data from 2003 to current study

	Hatherill 2003 n=202 [1]	Dimitriades 2014 n=204			P (where possible)
Technical adverse events	72 (35.6%)	81 (39.7%)			0.4
No functional venous access (total)	38 (18.8%)	2 (1%)			<0.0001
Venous access lost during transfer	26 (12.9%)	6 (2.9%)			0.0002
Venous access placed	190	202			0.07
1 peripheral	159 (83.7%)	60 (29.4%)			<0.0001
2 peripheral	19 (10%)	109 (53.4%)			<0.0001
Central venous	6 (3.2%)	30 (14.7%)			<0.0001
Umbilical venous	5 (2.6%)	0			0.03
Intraosseus	1 (0.5%)	3 (1.5%)			0.6
No functional monitoring (total)	26 (12.9%)	98 (48%)			<0.0001
Absent Saturation Monitor		4 (2%)			
Absent ECG Monitor		8 (4%)			
Absent BP Monitoring		52 (25.5%)			
Absent Capnography		65/141 (46.1%)			
Intubated for transfer	118 (58.4%)	141 (69.1%)			0.02
Oral	74 (62.7%)	52 (36.9%)			<0.0001
Nasal	44 (37.3%)	89 (63.1%)			<0.0001
ETT malpositioned	30 (25.4%)	32 (22.7%)			0.8
	Totals	Transfers (Totals)	En Route	Arrival	
Clinical adverse events	54 (26.7%)	65 (31.9%)			0.25
Shock	28 (13.9%)	22 (10.8%)	9	20	0.048
Inotrope	12 (5.9%)				
Hypoxia	27 (13.4%)	25 (12.3%)	15	17	0.2
Hypoglycaemia	12 (5.9%)	13 (6.4%)	3	11	0.8
Hypothermia		24 (11.8%)	4	24	
Hyperthermia		5 (2.5%)	0	5	-
Seizures		1 (0.5%)	0	1	-
	Totals	Transfers	En Route	Arrival	
Critical adverse events	18 (8.9%)	18 (8.8%)			0.97
Immediate intubation	11 (5.4%)	14 (6.9%)	3	11	0.6
Cardiac and/or respiratory arrest	13 (6.4%)	7 (3.4%)	1	6	0.1
Death on arrival		3 (1.5%)	-	3	
Mortality all cause	34 (16.8%)	19/201* (9.45%)			0.03
Standardized Mortality (actual/mean predicted)	1.11 (0.83-1.39)	0.68 (0.60 - 0.84)*			
Length of stay ICU		4.1 (2.0 - 9.1)#			-

* Excluding deaths on arrival (n=3)

Median (IQR)

Similarly there was no significant difference in the rate of clinical adverse events between 2003 and 2014 (Table 3). The most common clinical adverse events were hypoxia, hypothermia and shock, with the rate of shock decreasing significantly from 2003 to 2014, but remaining high (Table 3). Of the 65 transfers that experienced clinical adverse events in this study, forty-five (69.2%) had an increase in adverse events on arrival to PICU compared to those experienced during the transfer; eight (12.3%) had fewer adverse events on arrival (indicating appropriate recognitions and management of clinical adverse events); and 14 (21.5%) had the same number of adverse events en route as on arrival into the PICU.

Critical event rates were statistically unchanged between the two study periods. Three patients were noted to be dead on arrival during the hand over process, two in asystole and the third one arrived in respiratory failure and bradycardic (immediate resuscitation was unsuccessful). PIM2 values were not calculated on these patients. All three patients were transferred within the metropole with a transfer time from hospital referral that ranged from 135 – 265 minutes. A longer delay in referring case 109 to EMRS compared to the other two cases was noted and this was secondary to multiple telephonic conversations between the referring hospital and the PICU. The transfers took place by road and were accompanied only by paramedics (Table 4).

Table 4: Summary of Mortality on arrival

	Case 18	Case 109	Case 129
<u>Age</u>	6 days	87 months	154 months
<u>Hospital</u>	Academic	Academic	Metropolitan
<u>Diagnosis</u>	Necrotising Enterocolitis	Post Streptococcal Glomerulonephritis	Meningitis (Suspected coning post Lumbar Puncture)
<u>Duration transfer hospital referral/EMRS referral (minutes)</u>	135/Not available	265/98	150/124
<u>Communication</u>	Pre transfer communication tool not used, minimal communication with ICU (referral via surgery)	Pre transfer communication tool not used, advice given documented, advice not followed	Pre transfer communication tool not used, advice given documented, advice not followed
<u>Technical adverse events</u>	Absent capnography	Nil	Absent capnography
<u>Clinical adverse events</u>	Shocked en route, asystolic on arrival, hypoglycaemic on arrival	Hypoxic en route and on arrival, hypothermic en route and on arrival	Shocked en route
<u>Critical adverse events</u>	Asystole on handover leading to CPR	Bradycardic on arrival leading to Emergency intubation, CPR, but proceeded to asystole	Asystole on handover leading to CPR

EMRS – Emergency Medical and Rescue Services, ICU – Intensive Care Unit, CPR – Cardio-Pulmonary Resuscitation

There was a significant decrease in overall ICU mortality and the Standardized Mortality Rate (SMR) decreased from 1.11 in 2003 to 0.68 in 2014 (Table 3).

The number of technical adverse events en route were positively correlated with the total number of clinical (Spearman's R = 0.3; p = 0.000008) and critical adverse events occurring en route and on arrival to ICU (Spearman's R = 0.1; p = 0.03). The total number of clinical adverse events was also positively correlated with the total number of critical adverse events (Spearman's R = 0.5; p < 0.000001). Excluding those who were dead on arrival, there was a greater total number of clinical (median 1 (1-2) vs. 0 (0-1) events; p <0.000001) and critical adverse events (median 0 (0-1) vs. 0 (0-0); p = 0.0005) in those who subsequently died in ICU.

These last variables were entered into a multiple regression analysis, for the outcome of ICU mortality. The total number of clinical adverse events was found to be independently associated with ICU mortality, after excluding those who were pronounced dead on arrival to the ICU (adjusted odds ratio (95% confidence interval) 2.8 (1.7 - 4.7); p = 0.0001).

Table 5: Effects of Communication and PICU Staff on transfers

Dimitriades 2014 n=204			
	Pre transfer communication tool: Yes n=92	Pre transfer communication tool: No n=112	p
Technical AE	37 (40%)	44 (39.3%)	0.9
Clinical AE	23 (25%)	42 (37.5%)	0.06
Critical AE	4 (4.3%)	14 (12.5%)	0.048
Total mortality	10 (10.9%)	12 (10.7%)	0.97
	Advice given n=79	No advice given n=125	
Technical AE	28 (35.4%)	53 (42.4%)	0.3
Clinical AE	22 (27.8%)	43 (34.4%)	0.3
Critical AE	7 (8.9%)	11 (8.8%)	0.98
Total mortality	12 (15.2%)	10 (8%)	0.2
	PICU staff on transfer n=26	No PICU staff on transfer n=178	
Age (months)	4.667 (0.5 - 17.53)	1.633 (0.1667 - 11.5667)	0.049
Weight (kg)	5.1 (2.5 -9.8)	3.45 (2.2. 9.0)	0.2
Duration of transfer (minutes)	1372.5 (378 - 3510)	192.5 (126 - 420)	<0.0001
Risk of mortality on arrival in PICU (n=201)	0.112 (0.0682 - 0.180)	0.0778 (0.0290 - 0.1641)*	0.04
Length of stay ICU (days) (n=201)	7.6 (3.04 - 14.19)	5.06 (2.0 - 9.1)*	0.002
Technical AE	3 (11.5%)	78 (43.8%)	0.001
Clinical AE	4 (15.4%)	61 (34.3%)	0.07
Critical AE	2 (7.7%)	16 (9.0%)	0.9
Total mortality	3 (11.5%)	19 (10.8%)	0.8
Dead on arrival	0	3	0.3

AE - Adverse Events, Data are median (IQR) or n (%)

* Results exclude deaths on arrival (n=3).

The pre-transfer communication tool was used in 45.1% of transfers and was not associated with fewer technical events, however there was a trend towards fewer clinical adverse events and there were significantly fewer critical adverse events when it was utilized (Table 5). Informal reasons for its lack of use included – telephonic conversation occurred away from the forms, forms had run out, and new staff were not aware where the forms were kept. Advice was given in 79 cases and this advice was followed in 70 transfers. PICU staff were available to transfer twenty-six patients: twenty four patients were transferred by fixed wing and two by road; three transfers were undertaken by a consultant, twenty-three by a senior registrar and two by a registrar. When PICU staff was used to transfer patients there were fewer technical adverse events (11.5% vs. 43.8% $p=0.001$). Though there were fewer clinical adverse events when PICU staff was used, this did not reach statistical significance (15.4% vs. 34.3% $p=0.07$). PICU staff on transfer did not impact the rate of critical adverse events occurring.

Discussion

This study describes the transfer practices in a resource-constrained environment and compares them to those documented 12-13 years previously. Our major findings include new events of mortality occurring *en route*, although no significant changes in the rate of adverse events have occurred.

In contrast to the study in 2003[1], the mortality on arrival to PICU is concerning. The common factors in those three cases include the lack of a doctor accompanying the transfer, insufficient monitoring in two cases, as well as poor communication and a failure to follow advice. All three cases had clinical adverse events *en route*, which were not corrected at the time of arrival. This may be either due to the lack of recognition of a critically ill child or a lack of clinical skills to manage them effectively. The decrease in overall PICU mortality and improvement in standardized mortality rates may be indicative of improved PICU care, insufficient calibration of PIM2 or may in fact suggest an effect of transfer on these patients. Tibby et al noted a similar finding in their 2002 study into scoring systems for mortality risk in retrieved patients[23]. However Solomon et al. found that both PIM and PIM2 were good discriminators of death but that PIM was poorly calibrated as indicated by Hosmer-Lemeshow goodness of fit. Good calibration was noted for PIM 2 in 2006[24].

Although we noted that there was no change in the rate of technical adverse events since Hatherill et al's study[1], there was a shift in the nature of the events. More patients had appropriate intravenous access in our study, however there was a significant decrease in the quality of monitoring. A large portion of this is due to the lack of blood pressure monitoring. At the same time the standards regarding capnography and transportation of ventilated patients have also changed. Thus, the increase in the number of patients transferred intubated and ventilated without capnography *en route* added to the decline in monitoring. Since 2006 the American Academy of Pediatrics has advised the use of capnography to confirm endotracheal intubation, during transportation and whenever the patient is moved [25]. In this study approximately half (8/15) of

the intubated patients who suffered a critical adverse event had no capnography during the transfer.

This study also did not observe a significant change in the overall rate of clinical adverse events. We deviated from Hatherill's original study[1] in terms of the clinical adverse events that could be observed as per the methodology of this study. The observed decrease in shock may be due to improved vascular access or improved stabilization of patient's prior to transfer.

The overall rate of clinical and critical adverse events remained high in the current study. To combat the lack of SPRT for complex cases, the PICU continued its historical practice of sending PICU staff to accompany the transfer of those patients where possible. This practice is voluntary and dependent on staffing levels. Although a small increase in transfers by PICU staff was noted, this did not reach statistical significance. The staff categories accompanying the transfers were not of equal training, ranging from paediatric registrars to critical care trainees to consultant intensivists. The decrease in technical adverse events with PICU staff in attendance may be linked to the greater duration of transfer ($p > 0.0001$), predominantly by fixed wing transport, which also corresponded to increased monitoring, as the Western Cape Red Cross Air Mercy Service undertakes those transfers with its own set of equipment. The proportion of clinical adverse events was lower when PICU staff accompanied transfers, but this did not reach statistical significance, possibly due to the small number of transfers by PICU staff. The two critical adverse events that occurred with PICU staff involved the same staff member (critical care trainee) and both involved airway management.

Auditing the communication process was a challenge. Telephonic requests for assistance may come to the unit either through a consultant, a senior registrar or a paediatric registrar. The information is captured on a communication tool, discussed with a consultant and advice is relayed to the referring hospital. The communication tool was used in fewer than half the transfers, which relates to the informal communication process used within the unit. Although the use of the standardized communication tool resulted in fewer clinical and critical adverse events, this has to be interpreted with caution, as the quality of the communication process was not audited. Studies have noted that structured pre-defined communication tools are useful in limiting the occurrence of errors in the transfer process and in optimizing patients for transfer [26-28]. The use of pre-defined checklists ensures that important information is collected timeously to assist in patient stabilization and preparation for transfer [29].

Looking To The Future

It was interesting to note the positive correlations between technical, clinical and critical adverse events. From this data the hypothesis could be made that minimizing adverse events along this chain should result in improved transfer outcomes: decreasing technical events should result in fewer clinical adverse events, which in turn should result in fewer critical adverse events. Standards for

minimum levels of equipment should be established, in order to reduce the number of technical adverse events. A common factor in an American study evaluating ambulance personnel's perceptions of factors contributing to near miss episodes was the use of incorrect equipment size[30]. A similar study could be performed to identify local factors that may be associated with adverse events. In this study, the lack of capnography was common in ventilated patients. Specialised equipment and other resources could be pooled centrally, as suggested in a study from the Nordic Atlantic Cooperation[31], and through good pre-transfer communication allocated appropriately according to need. Unfortunately this study did not evaluate the equipment that was available for transfer, or the contribution of inappropriate equipment to adverse events. Previous studies have highlighted the need for equipment to be paediatric specific and designed for a range of age groups[30,32-34]. In addition specific training may be required to ensure that staff are appropriately skilled with paediatric equipment. [30].

In South Africa, paediatric intensive care within the public healthcare sector has always been centralized. Due to South Africa's sociopolitical history and geographic size, the country comprises both underdeveloped and developed areas. Patients in rural areas may have limited access to primary health care services and must travel long distances to access regional and tertiary care services, with associated morbidity and mortality[35,36]. In 2012, the South African under 5 mortality was between 50 and 75 per 1000 live births [37], however in the Western Cape Province this is estimated to be lower at 24.1 [38] This could be attributed in part to the higher per capita spending on health in the Western Cape (www.hst.org.za)[39]. The Western Cape therefore does not represent the general condition of South Africa's health service. Yet, even in this region, which has seen a reduction in overall mortality, the transfer services continue to have a high rate of adverse events as compared to other studies[2,3].

Efforts would have to be made to support and improve the current system. As suggested by Hatherill et al[1], the skills of the current service would need to be strengthened through education and skills training, as this remains the backbone of paediatric transfers. Support from the PICU for complex cases would have to continue as the current load of retrieved patients to the PICU remains below the suggested threshold of 250 cases per annum required to justify a separate service[40]. However, the upcoming expansion of the PICU at RCWMCH could result in an increase in the number of direct ICU transfers. Feasibility studies should be performed, to look at the sustainability of a formalized regionalized retrieval service. It is possible that if this were to include neonatal retrievals, feasibility may improve. Retrieval support, either regionalized or as given by individual units, should be provided by appropriately trained staff, skilled in the management of critically ill and injured children[3].

Appropriate cases for transfer using PICU staff need to be identified through robust communication and the role of scoring systems such as the Transport Risk Assessment in Paediatrics (TRAPS) could be investigated in this regard[41]. The communication processes should also be improved. This could be achieved by providing a single dedicated point of communication for the day which attends to

all in- and out-going communication and which also acts as the lead liaison for the paramedic service. Communication tools should be developed further and advice documented. Once the transfer is completed, feedback to the local units and the transferring team could assist in building relationships [19] as well as forming part of the outreach of intensive care. Finally, quality improvement is of outmost importance. Standards for the service and metrics to measure it need to be maintained[42,43].

The strengths of this study are that it was a prospective collection of data allowing for direct comparison with the study performed in 2003[1]. A number of limitations exist within this study. The data available did not allow for the collection of the exact time period that transfer services were in direct attendance. Thus the definition of duration of transfer was kept unchanged from the original study. The deviation in the definition of shock was allowed in this study so that data would be comparable to the original study. The large number of subgroups with small individual sample sizes limits it further. Another limitation in both the current study and the 2003 study[1] is that they describe the state of critically ill children transferred into the PICU only. These transfers are limited by the number of PICU beds available, thus many critically ill children would have been transferred directly in to the medical emergencies department by the same teams. It is recommended that the outcomes of these transfers also be investigated.

Conclusion

The rate of transfers into the PICU has remained largely unchanged since 2003 with a similar rate of adverse events, despite cases of child death now being observed during the transfer process. Changes are noted in both the profile of transferred patients as well as the observed adverse events. Although a specialized paediatric retrieval service is not considered feasible with the current available resources, efforts to formalise paediatric transfer services must be strengthened particularly in the context of the declining under-5 mortality and increased referral of more complex cases. In the interim, current services should be improved through education, improvement of skills, formalised PICU support and communication.

References

1. Hatherill M, Waggie Z, Reynolds L, Argent A (2003) Transport of critically ill children in a resource-limited setting. *Intensive Care Med.* 29(9):1547–54.
2. Vos GD, Nissen AC, Nieman FHM, Meurs MMB, van Waardenburg DA, Ramsay G, et al. (2004) Comparison of interhospital pediatric intensive care transport accompanied by a referring specialist or a specialist retrieval team. *Intensive Care Med.* 30(2):302–8.
3. Orr RA, Felmet KA, Han Y, McCloskey KA, Dragotta MA, Bills DM, et al. (2009) Pediatric specialized transport teams are associated with improved outcomes. *Pediatrics* 124(1):40–8.
4. Ramnarayan P, Thiru K, Parslow RC, Harrison DA, Draper ES, Rowan KM (2010) Effect of specialist retrieval teams on outcomes in children admitted to paediatric intensive care units in England and Wales: a retrospective cohort study. *Lancet* 376(9742):698–704.
5. Pearson G, Shann F, Barry P, Vyas J, Thomas D, Powell C, et al. (1997) Should paediatric intensive care be centralised? Trent versus Victoria. *Lancet* 349(9060):1213–7.
6. Crabtree I (2001) “A bridge to the future”: impact on high dependency and intensive care. *J Child Health Care* 5(4):150–4.
7. Kanter RK, Boeing NM, Hannan WP, Kanter DL (1992) Excess morbidity associated with interhospital transport. *Pediatrics* 90(6):893–8.
8. Barry PW, Ralston C (1994) Adverse events occurring during interhospital transfer of the critically ill. *Arch Dis Child* 71(1):8–11.
9. Edge WE, Kanter RK, Weigle CG, Walsh RF (1994) Reduction of morbidity in interhospital transport by specialized pediatric staff. *Crit Care Med.* 22(7):1186–91.
10. Britto J, Nadel S, Maconochie I, Levin M, Habibi P (1995) Morbidity and severity of illness during interhospital transfer: impact of a specialised paediatric retrieval team. *BMJ* 311(7009):836–9.
11. Doyle YG, Orr FE (2002) Interhospital transport to paediatric intensive care by specialised staff: experience of the South Thames combined transport service, 1998-2000. *Arch Dis Child* 87(3):245–7.
12. Davies J, Bickell F, Tibby SM (2011) Attitudes of paediatric intensive care nurses to development of a nurse practitioner role for critical care transport. *J Adv Nurs.* 67(2):317–26.
13. Vos GD, Buurman WA, van Waardenburg DA, Visser TPL, Ramsay G,

- Donckerwolcke RAMG (2003) Interhospital paediatric intensive care transport: a novel transport unit based on a standard ambulance trolley. *Eur J Emerg Med.* 10(3):195–9.
14. Perez A, Butt WW, Millar KJ, Best D, Thiruchelvam T, Cochrane AD, et al. (2008) Long-distance transport of critically ill children on extracorporeal life support in Australia. *Crit Care Resusc.* 10(1):34.
 15. Raffles A (1996) Intensive care provided by local hospitals should be improved. *BMJ* 312(7023):120–1.
 16. Goh AY-T, Abdel-Latif ME-A, Lum LC-S, Abu-Bakar MN (2003) Outcome of children with different accessibility to tertiary paediatric intensive care in a developing country – a prospective cohort study. *Intensive Care Med.* 29(1):97–102.
 17. Ramnarayan P, Britto J, Tanna A, Thomas D, Alexander S, Habibi P (2003) Does the use of a specialised paediatric retrieval service result in the loss of vital stabilisation skills among referring hospital staff? *Arch Dis Child* 88(10):851–4.
 18. Lampariello S, Clement M, Aralihond AP, Lutman D, Montgomery MA, Petros AJ, et al. (2010) Stabilisation of critically ill children at the district general hospital prior to intensive care retrieval: a snapshot of current practice. *Arch Dis Child* 95(9):681–5.
 19. Browning Carmo KA, Williams K, West M, Berry A (2008) A quality audit of the service delivered by the NSW Neonatal and Paediatric Transport Service. *J Paediatr Child Health* 44(5):253–72.
 20. Davies J, Tibby SM, Murdoch IA (2005) Should parents accompany critically ill children during inter-hospital transport? *Arch Dis Child* 90(12):1270–3.
 21. ALS Group (2012) *Advanced Paediatric Life Support The Practical Approach.* Fifth Edition. Wiley-Blackwell
 22. Kliegman RM, Stanton BMD et al. (2012) *Nelson Textbook of Pediatrics.* 19 ed. Saunders
 23. Tibby SM, Taylor D, Festa M, Hanna S, Hatherill M, Jones G, et al. (2002) A comparison of three scoring systems for mortality risk among retrieved intensive care patients. *Arch Dis Child* 87(5):421–5.
 24. Solomon LJ, Morrow BM, Argent AC (2014) Paediatric Index of Mortality scores: An evaluation of function in the paediatric intensive care unit of the Red Cross War Memorial Children's Hospital. *Southern African Journal of Critical Care* 30(1):8–13.
 25. Kleinman ME, de Caen AR, Chameides L, Atkins DL, Berg RA, Berg MD, et al.

- (2010)Part 10: Pediatric Basic and Advanced Life Support: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Circulation* 122(16_suppl_2):S466–S515.
26. Henning R, McNamara V (1991) Difficulties encountered in transport of the critically ill child. *Pediatr Emerg Care* 7(3):133.
 27. Goh AY, El-Amin Abdel-Latif M (2004) Transport of critically ill children in a resource-limited setting: alternatives to a specialized retrieval team. *Intensive Care Med* 30(2):339.
 28. Yamamoto LG, Wiebe RA, Maiava DM, Merry CJ (1991) A one-year series of pediatric prehospital care: I. Ambulance runs; II. Prehospital communication; III. Interhospital transport services. *Pediatr Emerg Care* 7(4):206.
 29. Lim MTC, Ratnavel N (2008) A prospective review of adverse events during interhospital transfers of neonates by a dedicated neonatal transfer service. *Pediatric Critical Care Medicine* 9(3):289–93.
 30. Cushman JT, Fairbanks RJ, O’Gara KG, Crittenden CN, Pennington EC, Wilson MA, et al. (2010) Ambulance personnel perceptions of near misses and adverse events in pediatric patients. *Prehosp Emerg Care* 14(4):477–84.
 31. Gunnarsson B, Jensen NSK, Garði TI, Harðardóttir H, Stefánsdóttir L, Heimisdóttir M (2015) Air ambulance and hospital services for critically ill and injured in Greenland, Iceland and the Faroe Islands: how can we improve? *Int J Circumpolar Health* 74:25697.
 32. Macrae DJ (1994) Paediatric intensive care transport. *Arch Disease Child*. 71(2):175-178.
 33. Roberts K, Jewkes F, Whalley H, Hopkins D, Porter K (2005) A review of emergency equipment carried and procedures performed by UK front line paramedics on paediatric patients. *Emerg Med J*. 22(8):572–6.
 34. Bohn D, Kanter RK, Burns J, Barfield WD, Kissoon N (2011) Task Force for Pediatric Emergency Mass Critical Care. Supplies and equipment for pediatric emergency mass critical care. *Pediatric Critical Care Medicine* 12(6 Suppl):S120–7.
 35. Coovadia H, Jewkes R, Barron P, Sanders D, McIntyre D (2009) The health and health system of South Africa: historical roots of current public health challenges. *Lancet* 374(9692):817–34.
 36. D’Andrea PA, van Hoving DJ, Wood D, Smith WP (2014) A 5-year analysis of the helicopter air mercy service in Richards Bay, South Africa. *S Afr Med J*. 104(2):124–6.

37. Nannan N, Dorrington R, Laubscher R, Zinyakatira N, Prinsloo M, Darikwa T, et al. (2012) Under-5 Mortality Statistics In South Africa: Shedding some light on the trend and causes 1997-2007. Cape Town: South African Medical Research Council pp. 1-107.
38. Groenewald P, Msemburi W, Morden E, Zinyakatira N, Neethling I, Daniels J, et al. (2014) Western Cape Mortality Profile 2011. www.mrc.ac.za. Cape Town: South African Medical Research Council Accessed 08 December 2015.
39. Per Capita Health Expenditure - Health Indicators [Internet]. Health Systems Trust; pp. 1-2. Available from: <http://www.hst.org.za/content/health-indicators>. Accessed 08 December 2015.
40. Ramnarayan P, Polke E (2012) The state of paediatric intensive care retrieval in Britain. *Arch Dis Child* 97(2):145-9.
41. Kandil SB, Sanford HAS, Northrup V, Bigham MT, Giuliano JS (2012) Transport disposition using the Transport Risk Assessment in Pediatrics (TRAP) score. *Prehosp Emerg Care* 16(3):366-73.
42. Bigham MT, Schwartz HP (2013) Ohio Neonatal Pediatric Transport Quality Collaborative. Quality metrics in neonatal and pediatric critical care transport: a consensus statement. *Pediatric Critical Care Medicine* 14(5):518-24.
43. Schwartz HP, Bigham MT, Schoettker PJ, Meyer K, Trautman MS, Insoft RM, et al. (2015) Quality Metrics in Neonatal and Pediatric Critical Care Transport: A National Delphi Project. *Pediatric Critical Care Medicine* DOI 10.1097/PCC.0000000000000477

Appendices - Protocol

AN AUDIT OF TRANSFERS INTO THE PICU AT the RED CROSS CHILDRENS WAR MEMORIAL HOSPITAL: TEN YEARS LATER

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INTRODUCTION

As centralisation of intensive care services was introduced in the mid-nineties, paediatric retrieval services underwent a vital transformation towards specialised services. South Africa as a middle income country did not conform to this international shift in practice. Thus in South Africa paediatric retrievals of critically ill children in to the paediatric intensive care unit are still undertaken by the Emergency Medical and Rescue Services using teams of advanced and intermediate life support paramedics who have not specialised in the transfer of children, and may have little training in this process. The study performed by Hatherill et al, published in 2003 documented the adverse events and outcomes of children transferred in this service. Ten years later the service has not changed its mode of operation thus begging the question whether the care of transferred children has changed over the last ten years.

PURPOSE OF THE STUDY

To perform an audit on transfers in to the paediatric intensive care unit (PICU) at Red Cross Children's War Memorial Hospital and to describe adverse events as well as their effect on outcomes.

PRIMARY OBJECTIVE

To describe the adverse events that occurred during the transfer process.
Adverse Events will be categorised as follows

1. Technical Adverse Events
2. Clinical Adverse Events
3. Critical Adverse Events

(Refer to appendix for definitions)

SECONDARY OBJECTIVE

To describe the mortality of patients transferred into the PICU from other institutions

- Mortality will be standardized using the PIM2 score.

TERTIARY OBJECTIVE

To describe the effect of category of staff, mode of transport used, as well as the duration of the transfer on adverse events and outcomes and to describe adverse events and outcomes according to the level of the referral institution.

BACKGROUND

History

In 2003 Hatherill et al. published the first audit on paediatric transfers and adverse events in the Western Cape Province of South Africa. This study found a high incidence of technical, clinical and critical adverse events. In their conclusion the authors suggested that training in Advanced Paediatric Life Support might reduce the incidence of adverse events. They also proposed that the establishment of a paediatric retrieval team may reduce the incidence of technical adverse events as well as cardio-respiratory adverse events during these transfers.¹ In 2013, ten years later the Emergency Medical Services have not formalised a specialised paediatric retrieval team for the transfer of critically ill children in to the PICU.

The need for paediatric transfers is closely linked to the centralisation of paediatric intensive care units. Approximately twenty years ago, subsequent to the publication of the Trent-Victoria study, this centralisation has been increasing in developed countries such as the United Kingdom.^{2,3} In South Africa, paediatric intensive care units began in Academic Hospitals in major centers of the country and the service has remained centralized. Due to South Africa's history and size, the country comprises both underdeveloped and developed areas. Patients in rural areas have limited access to primary health care services and must travel long distances to access regional and tertiary care services, thus impacting morbidity and mortality.⁴ In paediatrics the under five mortality is particularly useful in setting the local scene and allowing for comparisons. In South Africa, the Medical Research Council in 2012 released a compilation of different statistics and concluded that the under 5 mortality is between 50 and 75 per 1000 live births.⁵ According to The Health Systems Trust, in 2008 the under 5 mortality rate for the country was 48.8 whilst in the Western Cape Province this was lower at 26.5. This could be attributed in part to the per capita spending on health, which in 2009 was R2206 on average for the country where as in the Western Cape this was R2606. (www.hst.org.za) The Western Cape therefore does not represent the general condition of South Africa's health problems as closely as other provinces. Yet, even here the Emergency Medical and Retrieval Services (EMRS) are responsible for transferring routine patients to their outpatient clinic appointments as well as emergency patients requiring higher levels of care; a specialised paediatric retrieval team has not been formalised.

Outcomes Prior to Specialised Retrieval Teams

Paediatric retrieval teams were introduced in developed countries in response to the high incidence of adverse events associated with retrievals performed by inexperienced teams. In their prospective study, Kanter et al. in 1992 proved that the interhospital transfer of patients had greater associated morbidity than patients admitted to the PICU directly from the emergency department. A morbidity occurred in 37 of 177 (20.9%) transported patients versus 22 of 195 (11.3%) of control patients from the emergency department $p < 0.05$. The incidence ratio 1.85 (CI: 1.12-3.06) indicates that there is a higher risk of an adverse event occurring with the interhospital transfer of a patient compared to intrahospital transfer. Increased levels of transport morbidity (adverse events) were noted in association with an increased distance of transportation as well as an increased level of therapy required by the child. In this particular study morbidity was divided between Intensive Care Related Adverse Events and Physiologic Deterioration. There was no significant difference between transported patients and the control group in terms of Physiologic Deterioration. However, there was a significant difference in the Intensive Care Related Adverse Events with 15.3% versus 7% in the control group $p < 0.05$. The intensive care related adverse events included loss of intravenous access; unplanned extubation; endotracheal tube plug; aspiration; oxygen supply exhaustion; lack of neck stabilisation and transport vehicle accident.⁶ The terminology of morbidity in this study encompasses both physiologic deterioration and intensive care related adverse events, which can lead to confusion. In later reviewed studies, these adverse events became synonymous with adverse technical events.

In 1992 an observational prospective study was performed by Barry and Ralston on children transferred in to the Intensive Care Unit (ICU) at Birmingham Children's Hospital. Fifty-six transfers were identified of which only 14 (25%) were transferred without any adverse clinical events. A total of 95 adverse clinical events occurred in 42 (75%) of transferred patients. In 23% of these transfers there was major cardiorespiratory deterioration requiring management of either the airway and or blood pressure. Twenty of the medical escorts had less than one year of paediatric experience and only 30% of transfers were performed by a paediatric registrar or consultant.⁷ This was one of the earlier studies implying a correlation between experience and adverse events in transported patients.

The high number of adverse events noted in the above studies required an intervention that could limit these from occurring. Edge et al. in 1994, prospectively compared transport by specialised teams consisting of a paediatric resident, intensive care nurse and respiratory therapist versus a non-specialised team. One hundred and forty-one patients were transported and their morbidities were divided under the categories of physiologic deterioration or intensive care related adverse events. Once again there was no difference in physiologic deterioration. However, there was a significant difference in intensive care related adverse events between the two teams. This was noted in 2% of 49 children transferred by the specialised team versus 20% of 92 children transferred by the non-specialised team $p < 0.05$.⁸ This was the first study that sought to compare specialised and non-specialised retrieval teams.

In his review article in 2001 Crabtree summarised the above studies in his section under retrieval teams and concluded that there was a need for adequately staffed and equipped retrieval teams. He raised the concern that retrieval teams may be busy and therefore, may not attend to patients timeously, thus it is important that facilities are prepared and able to resuscitate, stabilise and provide immediate care whilst awaiting transfer.⁹

Outcomes of Specialised Retrieval Teams

Over the last two decades numerous studies have been performed looking at the outcomes of patients transferred by specialised retrieval teams. In their prospective study Britto et al. in 1995 assessed the outcomes of 51 critically ill children transferred in the London area of which 24 (47%) had meningococcal disease. This is highlighted as the majority of the children transferred in this study had a medical illness as compared to other studies that reviewed more trauma or surgical transfers. This study evaluated adverse events in terms of physiologic deterioration and equipment failure such as blocked endotracheal tubes. It also evaluated the paediatric risk of mortality score (PRISM) before and after transfer. The authors noted that of 51 transfers, 57% required airway intervention, 43% the addition of a vasoactive drug and that a change in ventilator setting was required in 26% by the arriving specialised retrieval team. Further interventions instituted by the retrieval team included the correction of hypoglycaemia in 18% of transfers and hypokalaemia in 31%. The severity of illness as assessed by PRISM improved in 34 (66.6%) of patients and deteriorated in 6 (11.7%) $p < 0.001$. Two patients (4%) had preventable physiologic deterioration, where one patient developed hypoglycaemia, whilst the other child became apnoeic due to Bronchiolitis.¹⁰ This study was important in noting that there were no adverse events relating to equipment thus indicating that precautions taken by experienced teams resulted in less accidental loss of intravenous access or loss of monitoring or even malfunction in equipment such as ventilators. It is interesting to note that this study was one of the early studies to describe the ethos of mobile intensive care, which in the author's words is the establishment of intensive care at the patient's bedside in the referring hospital.

The aftermath of the above study saw a number of letters written to the editor of the British Medical Journal. In their letter entitled "the Impact of Specialised Paediatric Retrieval Teams", Mok et al. stated that children are referred because clinicians recognize that further management is beyond their resources, capabilities and available support services.¹¹[9] The implication of this remains that children who require ICU are more ill, particularly if they require transfer. Raffles in his letter entitled "Intensive Care Provided by Local Hospitals Should be Improved" raised a concern that would later be studied in detail. His concern regarded the implied failure of life supportive skills as indicated by the high number of patients requiring airway management in Britto's study.¹²

In 2004, Vos et al. released their study from the Netherlands comparing the outcomes of children transported by specialist retrieval teams versus the referring specialist. As is mirrored in the other discussed studies, there is a significant difference in the adverse events noted in children transferred by the

referring physician. The adverse events in this study were divided in two categories: critical and serious events. Significant critical events included Hypotension in 16 of 137 (19%) of patients transferred by the referring specialist versus 7 of 112 (6.3%) transferred by the specialised retrieval team $p=0.015$. Another significant critical event in the children transferred by the referring specialist included the presence of cyanosis in 4.4% of patients versus 0% in those by the specialist retrieval team $p=0.025$. There were also more Serious Events occurring in the patients transferred by referring specialist, these included desaturation in 12.6% versus 1.8% in those transferred by specialised retrieval teams $p=0.002$; tachycardia in 7.3% versus 1.7% by specialised retrieval teams $p=0.04$ and neurological deterioration in 6.6% versus 0.9% by specialised retrieval teams $p=0.02$. Of interest is that unlike the previous reported studies there were less critical events in terms of endotracheal tube obstruction and dislodgment in the children transferred by the referring physician (2/137 1.5%) in comparison to non-specialised retrieval teams (10/177 5.6% in Kanter et al). This is as a result of the transfer being performed by either a paediatrician or anaesthetist. Per definition however, these physicians had received no paediatric intensive care training. It is important to note that there was a difference in the equipment that was available to the teams, with less monitoring and therapeutic equipment being available to the referring specialist teams. An example of this is the lack of ventilators for children less than 15kg, necessitating manual ventilation. This study added more information indicating that specialised retrieval teams who are trained in this capacity have less adverse events than even specialists who are transferring patients. This study was one of the first studies to categorise adverse events according to severity.¹³

In 2009, Orr et al. published their prospective cohort study performed between 2001 and 2002 in Pittsburgh. In this study they compared unplanned events and outcomes of children transferred by specialised and non-specialised transport teams. Unplanned events were categorized as airway related; cardiopulmonary arrest; sustained hypotension; or loss of single intravenous access for inotrope or vasopressor. Their study indicated that risks for an unplanned event included air transport with a Relative Risk (RR) of 3.3 (95%CI 1.7-6.5) as well as use of a non-specialised transport team RR 41.5 (95%CI 24.2-71.1). Risk factors associated with death during a transfer or within 28 days of admission included transport by a non-specialised team RR 3.5 (95% CI 2.3-5.2) or an unplanned event RR 4.5 (95% CI 2.5-8.3). Non specialised transport teams had significantly shorter transport times. This was attributed to the specialised transport team's practice which is to provide goal directed therapy from the first call for transfer up to admission in the PICU in keeping with the ethos of mobile intensive care. The shorter transfer times by the non-specialised transport teams indicate that a scoop and run philosophy was employed. In this study it was clear that a shorter transfer time translated in to greater mortality and morbidity rates.¹⁴

Designing a randomized controlled study to assess specialised paediatric retrieval teams against non-specialised retrieval teams would be considered unethical. Ramnaryan et al.¹⁵ in their study published in 2010, looked at a cohort of children less than 16 years admitted in 29 paediatric intensive care units in England and Wales. Although this was a retrospective study, data was collected prospectively as part of the PICANet program. This study focused on unplanned admissions

from other facilities as well as within the hospitals themselves. The children referred from other facilities were further divided in to transfer by specialised retrieval teams and non-specialised retrieval teams. Characteristics of children transferred by specialised retrieval teams included that they were older, more acutely ill, more resource intensive and stayed longer in the ICU. Although specialised retrieval teams and non-specialised retrieval teams had a similar crude mortality rate, adjusted multivariate analysis revealed a significantly reduced risk of mortality with specialist retrieval team transfers, with an Odds Ratio of 0.58 (95%CI 0.39-0.87). There was no increase in mortality or the paediatric index of mortality score (PIM) with distance. The authors highlighted the fact that specialist retrieval teams give early telephonic advice thus providing an outreach service and assisting in the continuum of care.¹⁵

Although the studies above indicate improved outcomes in terms of morbidity and mortality, it is important to note that this may be in the face of a general reduction in standardized mortality rate (SMR). Thus studies using historical control groups prior to the establishment of SRT may have comparatively different outcomes if mortality were standardized to severity of illness. White et al. performed a prospective observational study looking at the outcomes of critically ill children, divided in to transported and non-transported; they further divided those transported pre and post the establishment of a specialised paediatric retrieval service. Children were stratified in two groups with a predicted mortality rate of more than 15% or less than 15% and according to transportation with or without a paediatric retrieval team for transported patients. Non-transported patients were divided according to Paediatric Intensive Care Units or General Intensive Care Units and were used as a control in the Standardized Mortality Rate. The design of this study allowed for comparison of observed versus predicted mortality rates at the different levels of transfer as well as hospitalisation. This study noted a decrease in the standardized mortality ratio of transferred patients from 1.09 pre paediatric retrieval services to 0.74 after the establishment of paediatric retrieval services. This coincided with a significant decrease in standard mortality in Paediatric Intensive Care units from 1.59 to 0.60 and in General Intensive Care Units from 1.11 to 0.81. The concern that this study raised is that mortality rate as a crude indicator of the effectiveness of specialised retrieval services allows the bias of an improvement in the rest of patient care to directly affect this outcome.¹⁶

The establishment of a specialised retrieval service is unlikely to completely remove the occurrence of adverse events. Lim and Ratnavel (2008) looked at adverse events occurring during the interhospital transfer of neonates by a dedicated neonatal transfer service. Their prospective study over six months noted that 125 of 346 (36.1%) emergency neonatal transfers had at least one adverse event. 139 out of a total of 205 (67%) adverse events were due to avoidable human error. The majority of the events were found in the preparation and communication processes. The authors concluded that these processes could be targeted through education aimed at pre-transfer communication, training and risk management interventions which include debrief sessions post-transfer and ongoing assessments and in the future a repeat audit.¹⁷ Transfers to paediatric

intensive care units include neonates and it is likely that similarities would be found as seen in the above studies.

Pre-Transfer Communication

In the early nineties a few studies indicated that pre-transfer communication was an important factor in avoiding problems related to transfer of patients. Henning et al in 1991 performed a prospective study on 100 transfers in to their unit and noted 394 problems occurring during different stages of the process. Twenty eight percent of these could have been avoided by improving pre-transfer communication through the use of tools such as telephonic check lists which would assist in picking up clinical derangements not noted at the time of referral.¹⁸ In his correspondence to Intensive Care Medicine in 2003, Goh et al presented their findings that with the introduction of their pre-transport checklist, patients received more fluid boluses; earlier inotropes and were intubated appropriately. This led to patients presenting with less airway compromise and shock.¹⁹ The quality of the communication is equally important as noted by Yamamoto et al the same year. In their study they looked at transfers in Hawaii and noted that poorer communication clarity resulted in longer communication times.²⁰ It is likely that a structured telephonic checklist can avoid those situations by adhering to predefined important information that is required for decision making both in stabilising and the resulting transfer of the patient. Pre-transfer communication has become an integral part of the process as indicated by the ACCEPT model used in the UK for transfers. Communication between the referring and receiving unit is facilitated and with the completion of the checklist the information required for proper planning of the transfer is attained.¹⁷

Information Regarding Specialised Retrieval Units

Many of the papers reviewed have given examples of the members of specialist retrieval teams. A clinician with paediatric intensive care training and experience or training in transportation is noted in many studies.^{9,10,13,15,21} In Orr et al (2009) it was noted that a fellow in the ICU would accompany the paediatric critical care transport team only for extremely high-risk cases. Their team comprised a dedicated critical care transport nurse and a respiratory therapist with 3 years of paediatric critical care experience. The training of this team included advanced airway skills, air medical physiology and safety in the transport environment, as well as communication skills. This was followed by a 6 month period of riding with a critical care physician during transport.¹⁴ In 2007 the United Kingdom introduced the first group of trained Nurse Practitioners for critical care transport. Their training consisted of 3 years part time training in core skills such as advanced airway management, patient assessment, central venous and arterial cannulation to name a few. Supervised retrievals were performed until they were signed off as proficient by two different consultants on at least 3 occasions. The need for nurse practitioner- led retrieval teams arose from the increased demand on this service.²² Other team members of paediatric retrieval teams include nurses and or paramedics.^{9,10,13,15,21,22}

Equipment requirements for paediatric transfers are not standardized. The study by Vos et al. published in 2004 noted that there was a significant difference in the equipment available to specialised retrieval teams then was available to the referring accompanying specialists. The only piece of equipment that was available for every transfer by a referring specialist was electrocardiographic monitoring. Accompanying referring specialists were lacking oxygen saturation monitoring in 2.9% of transfers, invasive blood pressure monitoring in 93.4% of transfers and non-invasive blood pressure monitoring in 42.3% of transfers. Equipment for intubation was not available in approximately 30% of transfers and medication for intubation in 48.9% of patients transferred by the referring specialist. Equipment not available to the specialised retrieval team included End Tidal CO₂ monitoring in 33% of cases, temperature monitoring in 22.3% and an intraosseous needle in 13.4%.¹³ Vos et al. in 2003 suggested the minimum equipment required for a transfer should consist of a monitor with continuous measurements of vital signs, a defibrillator, tools for airway and ventilator management; an oxygen source; suction unit; fluid and electrolyte management; medication; a resuscitation chart and communication system. In this paper the authors looked at a novel system of applying the equipment required during a transfer to the transport trolley, thus allowing for an approximation of the care given in PICU.²³ As transport medicine develops further so will the equipment required during transfers become more sophisticated. In 2006 Vos et al. published their report on the use of point-of-care blood analysers during the interhospital transport of critically ill children. On 51 blood samples run on 29 children during their transportation it was noted that 86.2% of those patients required at least one intervention on the basis of those results. Only 42.9% of all interventions were based purely on the results. The most common interventions included a change in ventilator settings; correction of hypokalaemia and the ordering of blood products.²⁴ An example of even more advanced equipment used in specialised paediatric transfers includes extra corporeal life support (ECLS) equipment. Perez et al. conducted a retrospective review of 8 children requiring ECLS during transportation. This type of super specialised transfer required its own set of equipment as well as further specialised staff such as a paediatric intensivist, ECLS trained nurse, perfusionist and cardiothoracic surgeon.²⁵ The future of transport medicine is likely to see more innovation in terms of equipment use as well as further introduction of specialised and super-specialised retrieval teams.

Perceptions Surrounding Specialised Retrieval Teams

In the literature review we also looked at the perceptions of different people towards the introduction of specialised retrieval teams. In 2008, Carmo et al. published their quality audit on the services delivered by the New South Wales Neonatal and Paediatric Transport Service. This service consists of specialist intensive care nurses and doctors. Questionnaires were sent to referring physicians, parents and receiving consultants. Approximately 90% of 288 referring doctors were positive about this particular service and noted an improvement in time management with telephonic communication, stabilisation as well as feedback on patient outcomes. They noted that 98% of polled parents found the service supportive. 93% of polled receiving consultants found the

conferencing calls to be appropriate whilst 98% of them felt that their advice had been carried out correctly by this service. Only in a minority was concern raised regarding ventilation and the type of sedation that was used.²⁶ In 2011 Davies et al. released their article on the attitudes of paediatric intensive care nurses to the development of a nurse practitioner role for critical care transport. It was noted that nurse were predominantly positive to the implementation of this role in 2007. The authors also noted that 100% of polled nurses felt that the nurse practitioners were sufficiently trained.²² In 2004, Davies et al. conducted a study looking at the attitudes of staff and parents towards parental accompaniment during the transfer of critically ill children. The authors noted that the majority of parents found the experience to be safe and beneficial and as a result experienced less stress during the transfer. The staff perceived little or no stress with parental accompaniment and were able to perform interventions without any hindrance.²⁷

Concerns Regarding Specialised Retrieval Teams

Although perceptions surrounding the implementation of specialised retrieval teams are predominantly positive, some concerns have been raised in the literature. In his letter to the British Medical Journal Dr Raffles raised the concern regarding the types of interventions early retrieval teams performed on arrival to the referring institution in Brittos's et al study. The question he raised regards the skills of the referring clinician and in effect his concern is one of losing skills at the referring institution.^{10,12} Goh et al in 2003 showed in their study that the possibility exists that smaller hospitals may not have the number of patients required to maintain critical care skills.²⁸ Two papers were identified investigating this particular concern. In 2003, Ramnaryan et al. asked the question whether or not the use of specialised retrieval services resulted in the loss of vital stabilisation skills among referring hospital staff. The authors performed a retrospective study looking at the skills used by referring institutions in two periods before and after the implementation of specialised retrieval teams. In 1993, 31 out of 52 (59.6%) patients were intubated by the referring hospital's staff, in 2001 post specialised retrieval team introduction, 227 out of 269 (84.4%) patients were intubated by the referring hospital's staff $p < 0.001$. The rate of central venous access and arterial catheterization remained unchanged in between the two periods. The authors concluded that there was no loss of vital stabilisation skills with the introduction of specialised retrieval teams.²⁹ In 2010, Lampariello et al. released their study on the stabilisation of critically ill children at the District General Hospital prior to intensive care retrieval. They found that District General Hospital staff performed endotracheal intubations in 93.7% of patients, mechanical ventilation was commenced in 76.9%, central venous access was inserted in 67.4% and inotropes were commenced in 43.7% of patients. The authors came to the conclusion that District General Hospital staff performed the majority of initial stabilisation procedures appropriately prior to the arrival of the retrieval service.³⁰ Thus it appears from these studies that there is no loss of stabilisation skills with the introduction of specialised retrieval teams.

Standardization of Mortality Using PIM

To allow for the standardization of mortality and to remove the possibility of skewing the results by patients who are transported with a low mortality risk the studies quoted throughout this review have used either the Paediatric Risk of Mortality Score (PRISM) or the Paediatric Index of Mortality (PIM) scoring systems. The PRISM score looks at 14 variables which may be collected over 24 hours from the time of admission, whereas the PIM score is a point of care scoring system that consists of only 8 variables. The PIM variables must be collected within 1 hour of encountering the ICU team. Tibby et al. created a study to assess which of the Mortality Risk Scores were less affected by the retrieval process. They studied 928 critically ill children retrieved for intensive care from South East England. The authors found that complete data collection for calculation of scores was performed in 88% of patients for PIM scoring, 24% for pre-ICU PRISM and 60% for PRISMII. This is likely due to the fewer number of variables required for PIM as well as the simplicity of those variables. All three scoring systems over-predicted mortality, which is likely due to improved ICU care. The authors concluded that PIM was more suitable due to its ease of data collection and that point-of-care data would not be affected by the retrieval process.³¹

Previous Study Results on Paediatric Transfers in the Western Cape

The study by Hatherill et al. (2003) was used as the starting point to compare where the retrieval service in the Western Cape finds itself ten years down the line. This study was performed as a prospective study over one calendar year period. The authors collected data on all children transferred in to the PICU at Red Cross Children's War Memorial Hospital from other institutions but excluded children with a low mortality risk of less than 1% by PIM scoring. Referring hospitals were divided in to Academic, Metropolitan and Rural Hospitals, while staff transferring patients included PICU staff, Non-PICU staff which were categorised as paramedics or referring doctors. Patients were transported either by road, helicopter or fixed wing aircraft. Data were extrapolated from referral letters, admission forms, as well as transfer logs and in conversation with staff that looked after the patient; within 24 hour of admission.

Adverse events were classified as Technical Adverse Events, Clinical Adverse Events and Critical Adverse Events. In terms of technical adverse events the authors noted that there was no venous access in 6% of children and that venous access was lost or not functional in 13% of transferred children. 13% of transferred children had insufficient monitoring and 25% of intubated children had a malpositioned endotracheal tube with 6% being placed in the oesophagus. In total there were one or more technical adverse events in 36% of transferred children. Clinical adverse events that were noted included 14% of children were shocked, 13% were hypoxic and 6% were hypoglycaemic. One or more clinical adverse events occurred in 27% of transferred children. The authors noted that there was a trend towards experiencing a clinical adverse event in patients in whom an adverse technical event had already occurred, this however did not reach statistical significance. Under critical adverse events 13% of unintubated children required immediate resuscitation and intubation on arrival to the PICU.

6% of all transferred children suffered an arrest. One or more critical events were noted in 9% of all transferred children.

When analysing the adverse events by staff category there was no difference in the critical or adverse events that occurred. However, when PICU staff transferred children, they were less likely to experience technical adverse events as seen by 0% versus 40% in the non-PICU staff $p=0.0002$. Comparing the institution categories children were transferred out of; the authors noted that there was a higher likelihood of experiencing a technical adverse event in children from Metropolitan hospitals (44%) versus Academic Hospitals (38%) versus Rural Hospitals (23%) $p=0.034$. Children were also more likely to experience a clinical adverse event from Metropolitan Hospitals (39%) than from Academic Hospitals (18%) or Rural Hospitals (23%) $p=0.018$. This trend was repeated with critical adverse events occurring more in children from Metropolitan Hospitals (17%) than in Academic Hospitals (3%) or Rural Hospitals (7%) $p=0.009$.

When survivors were compared to non-survivors it was noted that non-survivors were more likely to have been shocked (32% vs. 10% $p=0.004$) or to have been hypoxic (26% vs. 11% $p=0.04$). The authors suggested that there may be a lack of training amongst paramedic staff which would highlight a deficiency in the system. The observation was made that there was a difference in the type of patient transferred from the different categories of hospital. The concern in this study was raised regarding the use of PIM to standardize mortality rates as the first contact with PICU was different depending on whether or not children were transferred by PICU staff. This was refuted by Tibby et al as discussed earlier.³¹

Although the authors felt that an intervention to improve the quality of PICU transfers was warranted, they recognized that this is difficult in the face of limited resources and other competing health care priorities. Due to the limited data they could not project the effect the establishment of a paediatric retrieval team would have on PICU outcomes.¹ The findings of this study are similar to those discussed in the section on outcomes prior to specialised retrieval services.

SIGNIFICANCE OF PERFORMING THIS STUDY

The above studies assist in delineating the history and growth of specialised paediatric retrieval teams. Many countries not limited by resources have opted for the establishment of these teams as the benefits of less adverse events and possibly improved outcomes have been documented. The composition of these teams are heavily weighted with physicians though a move towards nurse practitioner led teams has begun to grow. Although there were concerns of losing vital stabilisation skills with the formation of these teams it has been shown that this is not the case.

South Africa's transfer service remains unchanged since Hatherill et al's. study and has not developed a specialised paediatric retrieval service to the PICU. We would thus not expect a change in findings since 2003. However as all transfers

are performed by the emergency medical and rescue services and as their experience over time, in transferring critically ill children is likely to have increased we may well document a decrease in adverse events occurring during transfers as well as improved outcomes. This study could thus assist in planning and improving the transfers of critically ill children in to the PICU.

METHODOLOGY

Study Design

To be able to best show a change if indeed there is one we will mirror the study performed in 2003 with some adaptation to the current service.

Type of Study

Prospective Observational Study

Time Period

One calendar year (1 October 2013 – 31 September 2014)

Characteristics of the Study Population

Population: Critically ill children 0 days to 16 years of life

Sample: All patients who meet the inclusion criteria

Approximate sample size: In 2003 this consisted of 202 children with a median age of 2.8 months. The exact number of patients transferred directly in to the ICU is unclear, however a tally from 2012 approximated 180 patients with data that had gaps. We thus expect our numbers to be similar to the study performed in 2003.

Vulnerability: The above population is a particularly vulnerable group. However, considering that this study aims to look directly at paediatric critical care transfers, in order to improve the care we offer these children, it would not be suitable to extrapolate information from adult studies. In order to protect these patients, the study is purely observational and no interventions or deviation from current care will be performed.

Inclusion and Exclusion Criteria

Inclusion: All children transferred to the PICU at Red Cross Children's War Memorial Hospital from any other institution in whom transfer processes were initiated.

Exclusion:

1. Children transferred in to the PICU from within the Hospital
2. Children with a PIM score of < 1%

Recruitment and Enrolment

This will be performed by PICU staff, predominantly the Senior Registrar (PI)- Dr K Dimitriades

Research Procedures and Data Collection Methods

- All patients transferred to the PICU will be identified at the time of arrival through the admission register and the referral file, or the following morning if they were transferred in overnight.
- Data will be extracted from the patient file and paramedic transfer logs to the attached data collection sheet.
- Missing data will be acquired from the admitting doctor, nurse or transferring paramedic if possible.

Data Safety and Monitoring

Paper Based Data will remain in a file to be accessed by the PI in a locked cupboard in the PICU. All data entered in to the excel spread sheet or shared with the co-authors will be de-identified.

Paper based data collection forms will be entered into a password protected excel spreadsheet to be accessed by the student or supervisors only.

Data Analysis

Data will be analysed using Statistica version 10 (StatSoft Inc, USA). Appropriate parametric or nonparametric univariate analyses will be conducted according to data distribution, using the binary outcomes of mortality and adverse event categories. Variables identified as being associated with the primary outcome will be entered into a backward stepwise multiple logistic regression model. A significance level of $p < 0.05$ will be used.

ETHICAL CONSIDERATIONS

POTENTIAL RISKS AND BENEFITS

As this is an observational study at a particular point in the patients' care process there are no risks or further clinical benefits to the patients who are enrolled in the study.

There is a potential for a breach of confidentiality. To minimise this risk, data collected will be de-identified and stored securely.

Being enrolled in the study will in no way affect patient care in the PICU and considering that patients will be enrolled after transfer is complete, it will also not affect the quality care during inter-facility transport.

The results of this study will provide information on ways in which the transfer of critically ill children could be changed in order to improve patient outcome. Thus, although there will be no direct benefit for individual patients enrolled in this study, the results of this study may benefit future children being transferred into PICU.

If an adverse event is identified during a transfer our responsibility would be to ensure that clinical staff are made aware of this.

CONSENT

Considering the non-interventional, minimal risk nature of this study, the investigators request that the need for written informed consent be waived for this study. No patient will be identified in any output arising from this study and the study itself will not collect any characteristics that could be used to identify patients. As stated above this study does not pose any risks or future benefits to the studied patients.

RESOURCES

A budget will not be required for this study. The study will be run out of the PICU, and no reimbursements will be required for patients.

CONFLICTS OF INTEREST

There are no conflicts of interest to be declared.

DECLARATION

This study conforms to the principles stated in the Declaration of Helsinki (2008).

REFERENCES

- 1 Hatherill M, Waggie Z, Reynolds L, *et al.* Transport of critically ill children in a resource-limited setting. *Intensive Care Medicine* 2003;**29**:1547–54.
- 2 Pearson G, Shann F, Barry P, *et al.* Should paediatric intensive care be centralised? Trent versus Victoria. *The Lancet* 1997;**349**:1213–7.
- 3 Ramnarayan P, Polke E. The state of paediatric intensive care retrieval in Britain. *Archives of Disease in Childhood* 2012;**97**:145–9.
- 4 Coovadia H, Jewkes R, Barron P, *et al.* The health and health system of South Africa: historical roots of current public health challenges. *Lancet* 2009;**374**:817–34.
- 5 Nannan N, Dorrington R, Laubscher R, Zinyakatira N, Prinsloo M, Darikwa T, *et al.* (2012) Under-5 Mortality Statistics In South Africa: Shedding some light on the trend and causes 1997-2007. Cape Town: South African Medical Research Council pp. 1–107.
- 6 Kanter RK, Boeing NM, Hannan WP, *et al.* Excess morbidity associated with interhospital transport. *Pediatrics* 1992;**90**:893–8.
- 7 Barry PW, Ralston C. Adverse events occurring during interhospital transfer of the critically ill. *Archives of Disease in Childhood* 1994;**71**:8–11.
- 8 Edge WE, Kanter RK, Weigle CG, *et al.* Reduction of morbidity in interhospital transport by specialized pediatric staff. *Crit Care Med* 1994;**22**:1186–91.

- 9 Crabtree I. "A bridge to the future": impact on high dependency and intensive care. *J Child Health Care* 2001;**5**:150–4.
- 10 Britto J, Nadel S, Maconochie I, *et al.* Morbidity and severity of illness during interhospital transfer: impact of a specialised paediatric retrieval team. *BMJ* 1995;**311**:836–9.
- 11 Mok Q, Tasker R, Macrae D, *et al.* Impact of specialised paediatric retrieval teams. Intensive care provided by local hospitals should be improved. *BMJ* 1996;**312**:119–21.
- 12 Raffles A. Intensive care provided by local hospitals should be improved. *BMJ* 1996;**312**:120–1.
- 13 Vos GD, Nissen AC, Nieman FHM, *et al.* Comparison of interhospital pediatric intensive care transport accompanied by a referring specialist or a specialist retrieval team. *Intensive Care Medicine* 2004;**30**:302–8.
- 14 Orr RA, Felmet KA, Han Y, *et al.* Pediatric specialized transport teams are associated with improved outcomes. *Pediatrics* 2009;**124**:40–8.
- 15 Ramnarayan P, Thiru K, Parslow RC, *et al.* Effect of specialist retrieval teams on outcomes in children admitted to paediatric intensive care units in England and Wales: a retrospective cohort study. *Lancet* 2010;**376**:698–704.
- 16 White M, Weir PM, Garland L, *et al.* Outcome of critically ill children before and after the establishment of a pediatric retrieval service as a component of a national strategy for pediatric intensive care. *Pediatric Critical Care Medicine* 2002;**3**:255–60.
- 17 Lim MTC, Ratnavel N. A prospective review of adverse events during interhospital transfers of neonates by a dedicated neonatal transfer service. *Pediatric Critical Care Medicine* 2008;**9**:289–93.
- 18 Henning R, McNamara V. Difficulties encountered in transport of the critically ill child. *Pediatric Emergency Care* 1991;**7**:133.
- 19 Goh AY, El-Amin Abdel-Latif M. Transport of critically ill children in a resource-limited setting: alternatives to a specialized retrieval team. *Intensive Care Medicine* 2004;**30**:339.
- 20 Yamamoto LG, Wiebe RA, Maiava DM, *et al.* A one-year series of pediatric prehospital care: I. Ambulance runs; II. Prehospital communication; III. Interhospital transport services. *Pediatric Emergency Care* 1991;**7**:206.
- 21 Doyle YG, Orr FE. Interhospital transport to paediatric intensive care by specialised staff: experience of the South Thames combined transport service, 1998-2000. *Archives of Disease in Childhood* 2002;**87**:245–7.

- 22 Davies J, Bickell F, Tibby SM. Attitudes of paediatric intensive care nurses to development of a nurse practitioner role for critical care transport. *J Adv Nurs* 2011;**67**:317–26.
- 23 Vos GD, Buurman WA, van Waardenburg DA, *et al.* Interhospital paediatric intensive care transport: a novel transport unit based on a standard ambulance trolley. *Eur J Emerg Med* 2003;**10**:195–9.
- 24 Vos G, Engel M, Ramsay G, *et al.* Point-of-care blood analyzer during the interhospital transport of critically ill children. *Eur J Emerg Med* 2006;**13**:304–7.
- 25 Perez A, Butt WW, Millar KJ, *et al.* Long-distance transport of critically ill children on extracorporeal life support in Australia. *Crit Care Resusc* 2008;**10**:34.
- 26 Browning Carmo KA, Williams K, West M, *et al.* A quality audit of the service delivered by the NSW Neonatal and Paediatric Transport Service. *J Paediatr Child Health* 2008;**44**:253–72.
- 27 Davies J, Tibby SM, Murdoch IA. Should parents accompany critically ill children during inter-hospital transport? *Archives of Disease in Childhood* 2005;**90**:1270–3.
- 28 Goh AY-T, Abdel-Latif ME-A, Lum LC-S, *et al.* Outcome of children with different accessibility to tertiary pediatric intensive care in a developing country – a prospective cohort study. *Intensive Care Medicine* 2003;**29**:97–102.
- 29 Ramnarayan P, Britto J, Tanna A, *et al.* Does the use of a specialised paediatric retrieval service result in the loss of vital stabilisation skills among referring hospital staff? *Archives of Disease in Childhood* 2003;**88**:851–4.
- 30 Lampariello S, Clement M, Aralihond AP, *et al.* Stabilisation of critically ill children at the district general hospital prior to intensive care retrieval: a snapshot of current practice. *Archives of Disease in Childhood* 2010;**95**:681–5.
- 31 Tibby SM, Taylor D, Festa M, *et al.* A comparison of three scoring systems for mortality risk among retrieved intensive care patients. *Archives of Disease in Childhood* 2002;**87**:421–5.

Protocol Appendices

Definitions

Age: Collected as age in months at time of admission.

Weight: Collected in Kilograms as weight at time of admission or referral. In unweighed children the calculated weight used in the ICU will be collected.

Institution Category:

- Academic Hospitals – Hospitals in the greater Cape Town Metropolitan area with 24 hour paediatric registrar cover.
- Metropolitan Hospitals – Hospitals in the greater Cape Town Metropolitan area without 24 hour paediatric registrar cover. This includes private hospitals
- Rural Hospitals – Hospitals beyond the greater Cape Town Metropolitan area, it includes District and Regional Hospitals

Time of Referral: Collected as the time the telephonic request was placed to the PICU. In elective transfers this will be collected as the time the request was placed with the Emergency Medical Rescue Services.

Time of Admission: Collected from the patient file, this will either be the documented admission time or if not documented according to the earliest time entry in the file.

Transferring Personnel: PICU staff includes Registrar's or Senior Registrar's. Information will be collected from the transfer forms.

- Registrar – Paediatric, Anaesthetic, Emergency Medicine trainees who are receiving critical care training as part of their speciality.
- Senior Registrar – A Paediatrician currently training to sub-specialise in Critical Care.
- Referring Doctor – Any grade of doctor that is accompanying a patient from the referring institution.
- Paramedic – This includes any grade of Paramedic who may be trained in Basic Life Support, Intermediate Life Support, Advanced Life support or may have completed a Bachelor's degree in emergency medical care. Their registration category will be collected from the transfer log.

Mode of Transport: Information will be collected from the transport forms.

- Road – refers to transport predominantly by Ambulance
- Helicopter – Refers to transfer predominantly by Helicopter
- Fixed Wing Aircraft – Refers to transfer predominantly by aeroplane

Diagnosis: The admission diagnosis will be collected and then classified under the heading of General Medical, General Surgical, Trauma and Burns, Cardiac, Neonatal Surgical or Other.

PIM Score: The Paediatric Index of Mortality will be collected from the admission notes. This score is calculated within 1 hour of admission in to the ICU or if transported by PICU staff it will be calculated using the variables on first encounter with the ICU staff. Missing variables will be collected as soon as the child is admitted in the ICU. If transferred by PICU personnel PIM will be recalculated for comparison purposes.

Pre-Transfer Communication Tool: Refers to the request for transfer form that is used in the PICU. This tool documents clinical data of the patient prior to transfer and is used to give advice in stabilising the patient and planning the transfer. Data is collected from the Requests for Transfer file in the Unit.

Technical Adverse Events: Defined as failure to commence monitoring, site intravenous access, correctly position an endotracheal tube or failure or loss of the following during transfer or on admission to the PICU. Minimum monitoring

requirements include, Oxygen Saturation, Electrocardiography, Blood Pressure monitoring and if ventilated End Tidal CO₂. A minimum of two functional IV lines are expected in transferred patients.

- Oxygen Saturation monitoring: Monitoring present, not commenced or failure of equipment
- Electrocardiography: Monitoring present, not commenced or failure of equipment
- Blood Pressure: Monitoring present, not commenced or failure of equipment
- Endotracheal Tube: Placement may be nasal or oral. Tube may be placed correctly or malpositioned. Malposition will be documented if the tube is deeper than expected for age/weight at the nose/mouth using the formula described by the APLS manual; if chest radiograph shows the ETT at the carina or below or if direct laryngoscopy or auscultation suggests this.
 - APLS ET Formula
 - Oral: $\text{Age}/2 + 12$
 - Nasal: $\text{Age}/2 + 15$
- End Tidal CO₂: Monitoring present, not commenced or failure of equipment
- Ventilation: Present and functioning, Not Present or failure of equipment or Oxygen source.
- Intravenous Access: Present, 1 line or 2 lines, Failure to insert, Blocked/dislodged on route or on admission to ICU. Types of vascular/ access include Peripheral, Central, or Intraosseous.

Clinical Adverse Events: One or more of the following events occurring during the transfer or on arrival to the PICU.

- Shock: Defined as Capillary Refill Time of more than 4 seconds or Hypotension for age, and requiring either fluid resuscitation or the commencement of inotropes.
 - Hypotension – Systolic Blood Pressure less than the 5th centile for age using the APLS formula. $65 + (\text{age} \times 2)$ outside the neonatal period.
 - For neonates including preterm - Blood Pressure will be compared against the normograms for Mean Blood Pressure and diastolic blood pressure in Nelsons Textbook of Pediatrics 19th Edition. (Table 62-1 and Figure 88-2)
- Hypoxia: Defined as saturation less than 80% in the absence of a cyanotic heart defect.
- Hypoglycaemia: Defined as Blood glucose less than 2.5mmol
- Hypothermia: Defined as less than 35 degrees Celsius either by axillary or rectal measurements.
- Hyperthermia: Defined as temperature more than 38.5 degrees Celsius either by axillary or rectal measurements.
- Seizures: Uncontrolled movement documented by clinical staff as convulsions or seizures.

Protocol Appendix 2

Data Collection Form

Case No: _____

Age: _____

Weight: _____

Referring Institution Name: _____

Academic Hospital: Y/N
Metropolitan Hospital: Y/N
Rural Hospital: Y/N
Clinic: Y/N

Time of Referral: _____ **Time of EMRS Referral:** _____

Time of Admission to PICU: _____

Duration of Transfer in hours: _____

Type of Referral: Urgent/Elective

Comment on Type of Referral:

Transferring Personnel

PICU Staff Y/N

Registrar Y/N
Senior Registrar Y/N

Non PICU Staff Y/N

Paramedic Y/N Qualification: _____
Referring Doctor Y/N
EMRS Doctor Y/N

Mode of Transport

Road Y/N

Helicopter Y/N

Fixed Wing Y/N

Diagnosis: Primary _____ **Co Morbidity:** _____

General Medical Y/N
General Surgical Y/N
Trauma and Burns Y/N
Cardiac Y/N
Neonatal Surgical Y/N
Other Y/N

PIM Score: _____

Pre-Transfer Communication Tool Completed: Y/N

Advice Given: Y/N Advice Followed: Y/N

Comment on Communication:

Technical Adverse Events

	Yes	No	Malfunction
Oxygen Saturation Monitor			
Electrocardiography Monitor			
Blood Pressure Monitor			
End Tidal CO ₂ Monitor			
Ventilation			

Venous Access: Y/N/Obstructed or Dislodged
Obstructed/Dislodged: On Route/On Arrival to PICU
Type of Vascular Access: Peripheral/Central/Intraosseous
No of Intravascular lines: 1/2/3
Endotracheal Tube: Nasal/Oral or Not Required
Position: Correct/Malpositioned
Malpositioned: On Route/On Arrival to PICU

Clinical Adverse Events

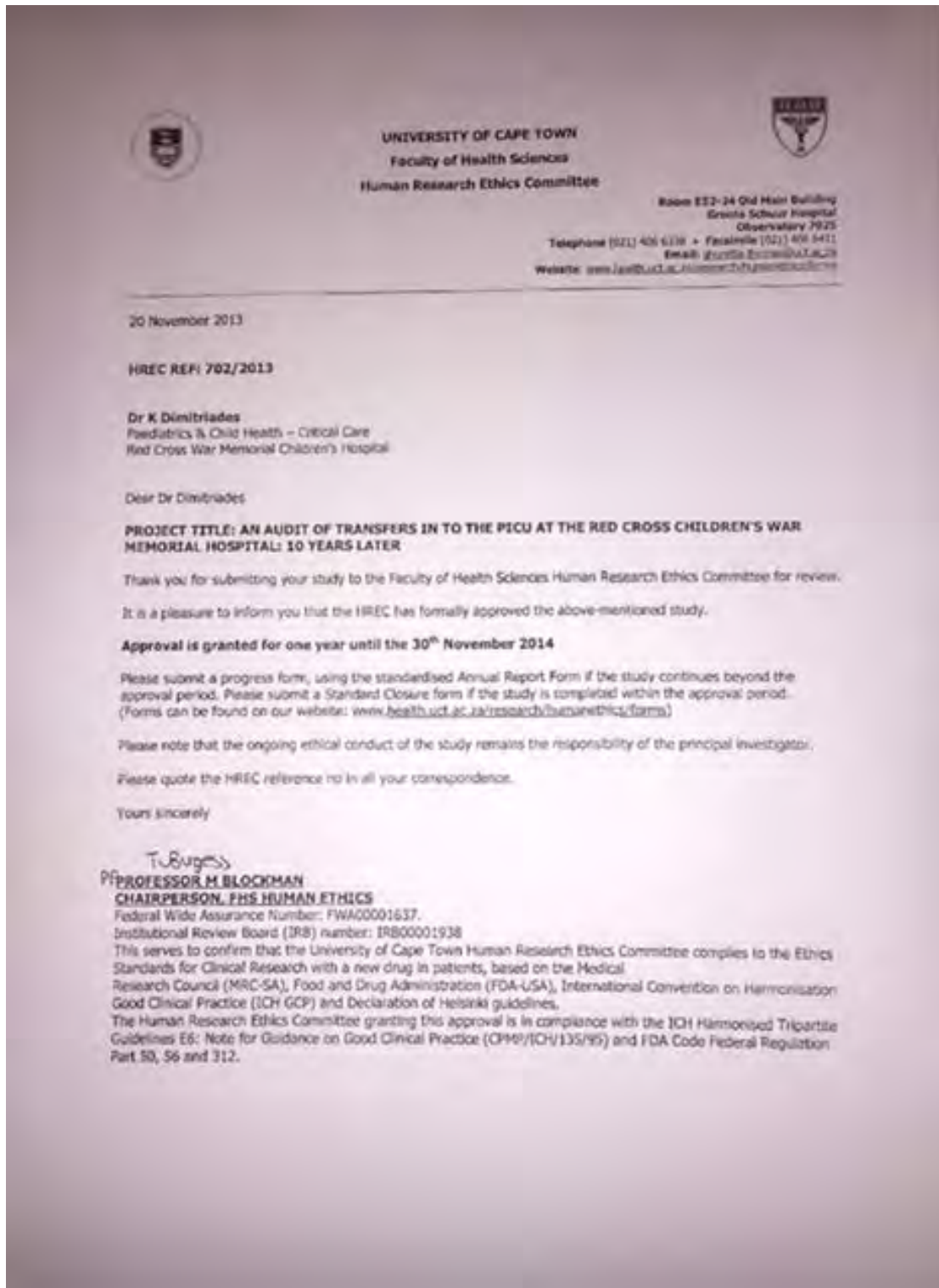
	Yes	No	On Route	On Arrival to PICU
Shock				
Hypoxia				
Hypoglycaemia				
Hypothermia				
Hyperthermia if in Incubator				
Seizures				

Critical Adverse Events

	Yes	No	On Route	On Arrival to PICU
Cardiorespiratory Arrest				
Emergency Intubation				
Death				

Mortality: Y/N
No of Days post admission to mortality: _____

Appendices – Ethics Approval (Original and Renewal)





FHS017: Annual Progress Report / Renewal

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

HREC office use only (PWA0001837; JRD0001838)

This serves as notification of annual approval, including any documentation described below.

<input checked="" type="checkbox"/> Approved	Annual progress report	Approved until next renewal date	30/03/2016
<input type="checkbox"/> Not approved	See attached comments		

Signature Chairperson of the HREC	FF T. Burgess	Date Signed	17/02/2015
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Principal Investigator to complete the following:

1. Protocol Information

Date when submitting this form	11/2/2015		
HREC REF Number	702/2013	Current Ethics Approval was granted until	30/11/2014
Protocol title	An Audit of Transfers Into The PICU At GEC Cross Children's Memorial Hospital 10 year later		
Principal Investigator	Konstantinos Dimitriadis		
Department / Office	G. Picu		
Internal Mail Address	GEC Cross War Memorial Childrens Hospital Klipfontein		

1.1 Does this protocol receive US Federal funding? Yes No

2. Protocol status (tick ✓)

Research-related activities are ongoing (Data collection completed 30/11/2014)

Data collection is complete: data analysis only (Data Analysis completed - Project currently being written up)

Please indicate (in the block below) the titles and HREC reference numbers of any projects currently making use of the Database/registry/repository

W1

3. Protocol summary

Total number of records or specimens collected, reviewed or stored since the original approval	11 FEB 2015	204
Total number of records or specimens collected, reviewed or stored since last progress report		0
Have any research-related outputs (e.g. publications, abstracts, presentations) resulted from this research? If yes, please specify		<input type="checkbox"/> No

4. Signature

Signature of PI		Date	11/2/2015
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Appendices – Author Guidelines for Intensive Care Medicine

Instructions to Authors

ICM is a critical care journal that publishes studies covering all aspects of critical care from every country. The journal publishes studies that include critically ill patients or patients at very high risk of becoming critically ill and, in addition to those investigating critically ill patients in the ICU, welcomes studies of high-risk patients in the Emergency Department and during the perioperative period.

All papers providing pre-clinical data (experimental, animal, in-vitro, bench studies or studies without patients) should be submitted to [ICM Experimental](#).

All manuscripts undergo review. An initial check is conducted soon after submission to ensure that all manuscripts comply with the guidelines outlined in the Instructions for Authors. A pre-evaluation is then performed by the Editor-in-Chief and one or more Editors to determine which papers are sent for external peer review.

Research articles must meet the following criteria:

- The manuscript presents the results of primary scientific research.
- The results have not been published in full elsewhere.
- Analyses are performed to a high technical standard and are described in full in the manuscript.
- Conclusions are presented in a clear and concise manner and are supported by the data.
- Manuscripts must be written in English using standard scientific terms.
- The research meets all applicable ethical standards.
- The article adheres to appropriate reporting guidelines and community standards for full data disclosure.
- All conflicts of interest should be clearly stated in the manuscript.
- According to the Uniform Requirements for Manuscripts Submitted to Biomedical Journals, designation as an author must satisfy three conditions. The author must have:
 - - Contributed substantially to the conception and design of the study, the acquisition of data, or the analysis and interpretation of the data
 - - Drafted or provided critical revision of the article
 - - Provided final approval of the version submitted for publication
 -
 - Authors of original papers and reviews are requested to provide the following information:
 -
 - - A "Take-home message" (two-sentences) which summarizes how the manuscript adds to current knowledge. This will appear in the final published version of the paper.
 - - A 140-character Tweet that may appear online via the Intensive Care Medicine website or social media platforms. This Tweet will not form part of the print version of the manuscript.

- The role of authors and contributors has recently been clarified by the [ICMJE](#)

ICM does not have any publication fees, and color figures are produced free of charge. Open access is available if required; please consult Springer's website for further information.

For further details, or to submit an outline of your manuscript, please contact the Intensive Care Medicine Managing Editor at journal.icm@sls.aphp.fr

Format instructions

All submissions must include references formatted according to the ICM standard:

53. Brown KL, MacLaren G, Marino BS (2013) Looking beyond survival rates: neurological outcomes after extracorporeal life support. *Intensive Care Med* 39:1870-1872.

If you use Zotero, the ICM styling template can be found [here](#). Figures should be in color if possible. Please use shades of blue for PowerPoint-style data presentations. Technical information about figures' format can be found below.

Types of papers

Original papers

- Original papers must not exceed 3,000 words and should include no more than 5 illustrations or tables.
- Up to 40 references are permitted.
- When reporting the results of a randomized controlled trial, author(s) should use the CONSORT statement as a guide to preparing the manuscript (<http://www.consort-statement.org/>).
- If authors consider that their manuscript needs to be longer than 3,000 words or contain more figures or tables, the reasons for this should be justified in the cover letter to the Editor-in-Chief.
- Supplementary information can be published in electronic supplements without limitation.

7-day profile publications

- High-quality manuscripts providing new findings from large prospective observational or interventional studies can be submitted as a 7-day profile publication, allowing important data to be rapidly available in the public domain.
- 7-day profile publications are initially assessed by the Editor-in-Chief and Deputy Editors, and those deemed suitable for this format sent to external reviewers. A decision will be notified to the authors within 7 working days.
- Manuscripts will either be provisionally accepted, rejected or transferred to

the standard peer review process. In the case of provisional acceptance, authors will have one day to address the reviewers' comments and resubmit a revised manuscript.

Reviews articles, systematic reviews, meta-analyses

- Review articles should only be submitted after prior consultation with the editors, and are subject to the peer review process. The journal is primarily interested in receiving systematic reviews and meta-analyses that use high-quality methodology and address relevant clinical questions not already or completely addressed in the literature.
- Review articles must not exceed 4,000 words and 75 references. Supplementary information can be published in electronic supplements without limitation.
- Proposals for review articles should be submitted as a two-page outline so that content can be discussed agreed at an early stage. Non-systematic review articles must be state-of-the-art reviews objectively depicting the current best knowledge on a given topic.
- Review articles must include original tables, figures, graphs, and other didactic material. They must provide unique information not available elsewhere.

My paper 20 years later

Upon invitation by the editorial board, international experts who published a landmark study 20 or more years ago have the opportunity to provide readers with a global unbiased and objective perspective on how their paper contributed to changes in clinical practice and whether their findings have subsequently been confirmed or refuted by others. Such manuscripts should not exceed 4000 words, 75 references and 5 figure or tables.

The outline can be flexible but must include discussion of the following:

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- How my findings have been directly or indirectly confirmed
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- Are there any ongoing studies that will add knowledge in this area?

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LaTeX macro package

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- Gamelin FX, Baquet G, Berthoin S, Thevenet D, Nourry C, Nottin S, Bosquet L (2009) Effect of high intensity intermittent training on heart rate variability in prepubescent children. *Eur J Appl Physiol* 105:731-738. doi: 10.1007/s00421-008-0955-8
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- Book

- South J, Blass B (2001) The future of modern genomics. Blackwell, London
- Book chapter
- Brown B, Aaron M (2001) The politics of nature. In: Smith J (ed) The rise of modern genomics, 3rd edn. Wiley, New York, pp 230-257
- Online document
- Cartwright J (2007) Big stars have weather too. IOP Publishing PhysicsWeb. <http://physicsweb.org/articles/news/11/6/16/1>. Accessed 26 June 2007
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1. Davidoff F, for the CSE Task Force on Authorship (2000) Who's the author? Problems with biomedical authorship, and some possible solutions. *Science Editor* 23:111-119
2. Yank V, Rennie D (1999) Disclosure of researcher contributions: a study of original research articles in *The Lancet*. *Ann Intern Med* 130:661-670
3. Flanagan A, Fontanarosa PB, DeAngelis CD (2002) Authorship for research groups. *JAMA* 288:3166-3168

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