Paediatric Acute Kidney Injury Management in an African Setting.

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Declaration of own work

I hereby declare that the entirety of the work contained in this thesis is my own original work, both in concept and execution; that I am the sole author thereof, aside from the normal guidance received from my supervisors and contributions by those acknowledged.Published manuscripts form part of this thesis. I confirm that I have been granted permission by the University of Cape Town's Doctoral Degrees Board to include the following publications in my PhD thesis, and where co-authorships are involved, my co-authors have agreed that I may include the publication(s). The assistance and contributions received from co-authors of publications is described with each publication as it appears in the thesis.

1. McCulloch MI, Argent AC, Morrow B, Nourse P, Coetzee A, Du Buisson C, Reddy D, Buckley J, Sinclair PJ, Gajjar P, Semanska L, Eddy A, Feehally J, Cano F, Warady BA. Lessons learned from regional training of paediatric nephrology fellows in Africa. Pediatr Nephrol. 2023 Nov;38(11):3757-3768. doi: 10.1007/s00467-023-06022-9. Epub 2023 Jun 6. PMID: 37278919; PMCID: PMC10243235.

2. McCulloch MI, Nourse P, Argent AC. Use of locally prepared peritoneal dialysis (PD) fluid for acute PD in children and infants in Africa. Perit Dial Int. 2020 Sep;40(5):441-445. doi: 10.1177/0896860820920132. Epub 2020 Apr 23. PMID: 32323622.

3. McCulloch MI, Luyckx VA, Morrow B, Nourse P, Coetzee A, Reddy D, Du Buisson C, Buckley J, Webber I, Numanoglu A, Sinclair G, Nelson C, Salie S, Reichmuth K, Argent A. Dialysis for Paediatric Acute Kidney Injury in Cape Town, South Africa (Submitted to Pediatric Nephrology, in review).

This dissertation includes 4 original papers, Chapters 2 and 3 have already been published, as has Chapter 1 now but for the purposes of this PhD we included the original version and Chapter 4 is a manuscript in preparation.No part of the thesis has been submitted in the past, or is being, or is to be submitted for a degree at this or any other University. I grant the University of Cape Town free licence to reproduce the thesis in whole or part, for the purpose of research. This thesis is presented for examination for the degree of PhD.

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Mignon McCulloch
Date: 6 November 2024
Student Number: MCCMIG001

Unsigned Plagiarism Declaration
Declaration of own work
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Mignon McCulloch(16.11.2024)

Abstract

Kidney disease is a growing public health concern, affecting adults but also children who face challenges of access in low-resource settings including Africa. We studied our own paediatric dialysis results, our fellows training in the field of acute kidney injury (AKI) and reviewed innovative techniques for acute peritoneal dialysis, which also included costing of forms of acute dialysis in children.

Dialysis for Paediatric AKI in Cape Town, South Africa

A review of our dialysis database of over 593 cases for AKI at Red Cross War Memorial Children's Hospital (RCWMCH) over 20 years focusing on 'Peritoneal dialysis (PD) first for our paediatric AKI program' whereby most children received PD as a first modality, despite having extracorporeal dialysis available. Types of dialysis were reviewed, as well as complications with acceptable outcomes described.

Lessons learned from regional training of paediatric nephrology fellows in Africa

There is a significant shortage of staff managing children with AKI in Africa and this is a review of our training program (1999 – 2021) of 38 African paediatric nephrology fellows. The emphasis is on training in paediatric AKI, including a review of hands-on training and length of training time in our unit, including subspecialty exams and research. Although a 100% return rate was noted to their home institutions, a survey was performed of our trainees on return home. This survey identified specific challenges faced and allowed for appropriateness of our training.

Use of locally prepared peritoneal dialysis fluid for acute PD in children and infants in Africa including documentation of innovation of PD catheters and fluid, in the absence of conventional equipment, with good outcomes in our centre (4% peritonitis rate).

Costing of our dialysis modalities included a short review in costing of dialysis modalities for acute kidney injury in our program.

Conclusion: My thesis presents the development of services for children with acute kidney injury in Africa over 20 years. For me the future should be that 'No child should die of acute kidney injury, without an attempt at peritoneal dialysis'.

Keywords: Acute Kidney Injury; Peritoneal Dialysis Fluid;

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In completing this thesis, I hereby wish to thank a number of people who were part of Team Mignon to get this project to fruition:

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I am also so grateful to my colleagues both in the Renal Unit and in the PICU at RCWMCH for being such an amazing team including all the kidney guys – Pete Nourse, Ashton Coetzee, Deveshni Reddy, Christel Du Buisson and Jonathan Buckley, our medical officers Theresa Abdo and Taryn Pienaar, rotating registrars as well as the wonderful nursing and allied health team specifically Nicci Collison and Shihaam Cader as well as all the cleaning and domestic staff that make up the happy team in ward E2. Prof Wiggelinkhuizen would be pleased too! A special word of awe for our training Renal Fellows from other parts of South Africa and further afield in Africa – your commitment to your quest for knowledge about children's kidney disease is truly remarkable. You give up so much time with your families to come and spend time at RCWMCH to learn your skills and teach us a lot too – I really salute you all.

Thanks also to the Saving Young Lives team from across the world who have shared my passion for bringing knowledge about treating acute kidney injury with peritoneal dialysis to even the lowest resource setting.

The best for last, a huge thanks to my sister Michelle, fur children and crazy friends but especially my partner Jean De Ville De Goyet who has been such an enormous support & help and has also put up with me working on the 'thesis' for so many of our recent holidays – you are amazing!

In closing, my parents would have been proud as I walked in my Dad's footsteps in doing a PhD but more importantly that I could do something to help children in completing this work.

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Introduction

Acute Kidney Injury

Acute kidney injury (AKI) reflects a sudden reduction in kidney function in response to an acute insult or episode (e.g. severe infection, heart failure, exposure to a nephrotoxin). Kidney function can recover rapidly if the underlying problem is corrected or removed fast or may remain abnormal or even worsen depending on the severity and duration of the insult. In some cases, AKI may be severe enough to necessitate dialysis for survival [1]. Dialysis for AKI may be required for days or weeks until some recovery of kidney function occurs. Depending on the severity, after an episode of AKI, kidney function may recover fully and rapidly (AKI, defined as recovery within 7 days), may recover slowly (acute kidney disease, AKD, defined as recovery between 7 and 90 days), or there may be some permanent loss of kidney function which over time may develop into overt chronic kidney disease (CKD, persistence of kidney dysfunction beyond 90 days) [2,3]. In some patients' kidney function never recovers and they develop end-stage kidney failure (KF). For the purposes of this PhD, for simplicity, the term AKI is used to include any acute kidney injury, and thus all acute pathology that is not CKD.

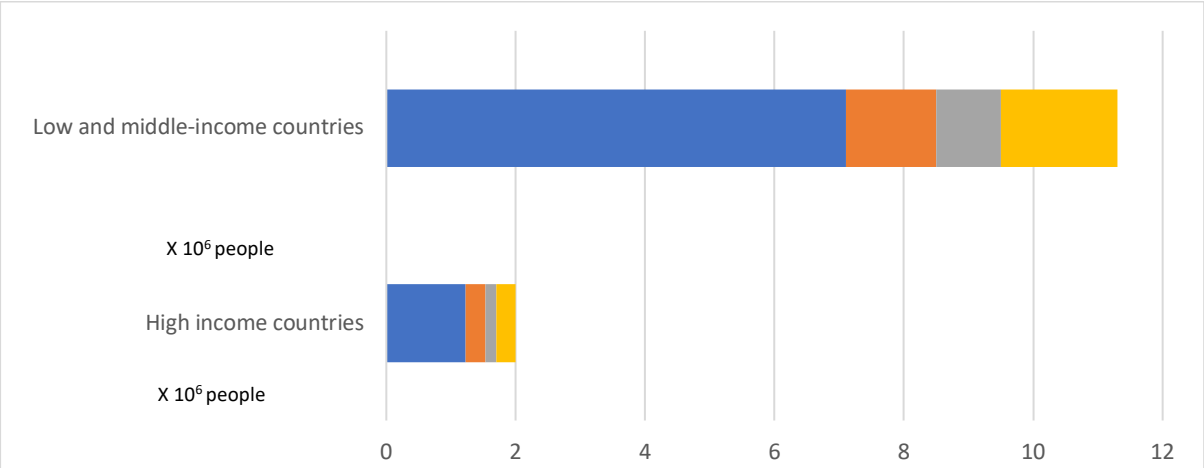
Categories of renal dysfunction:

Acute Kidney Injury (AKI)	Renal dysfunction lasting less than 7 days
Acute Kidney Disease (AKD)	Renal dysfunction lasting 7 to 90 days
Chronic Kidney Disease (CKD)	Renal dysfunction lasting more than 3 months
End-stage Kidney Failure (KF)	Permanent kidney failure

CKD indicates a permanent loss of kidney function, ranging from mild to KF, when chronic dialysis or transplantation would be required for survival. Increasingly it is being recognised in both children and adults that AKI is a risk factor for subsequent CKD and longer-term mortality - even if kidney function appears to return to baseline after the acute episode [4]. CKD in turn is as important a public health concern, affecting around 10% of the adult population world-wide and impaired kidney function is currently the 7th leading global risk factor for death [5,6].

The global burden of acute kidney injury

AKI has been estimated to occur in approximately 13.3 million people per year Figure 1, of whom 1.7 million die, 1.2 million will develop KF within 2 years and 2.1 million will develop CKD within 3 years [7].



	High income countries	Low and middle-income countries
Recovery of kidney function	1.23	7.1
Died within 3 months	0.3	1.4
Kidney failure by 24 months	0.17	1
Chronic kidney disease at 3 years	0.3	1.8

Figure 1: Global burden of acute kidney injury in millions people, estimate in 2012 *(data extracted from reference 7)*

Based on these estimates, 85% of cases occur in lower resource settings, where access to any form of dialysis may be limited or non-existent [8]. The real extent of the AKI burden is however not known, due to lack of appropriate systems to detect and track AKI, especially in lower resource settings (LRS) [1]. AKI is not tracked by the Global Burden of Disease study, few countries have registries for AKI, and if present, these are for adults [9]. Most existing studies have been conducted in high resource settings, leaving a gap in knowledge in lower resource settings [10]. Even within less well-resourced countries, available studies mainly originate from tertiary centres, with failure to capture the burden in rural areas [6]. Given the relative paucity of data in children, especially regarding longer term outcomes, there is increasing interest in better defining epidemiology as well as management of AKI in both children and neonates [1,11,12]. A global meta-analysis in 2013 reported a pooled AKI incidence of 33.7% among hospitalized children with a pooled mortality of 13.8% [13].

Based on this analysis, 1 in 5 hospitalized adults and 1 in 3 hospitalized children experience some degree of AKI. AKI is therefore an important clinical problem in 2

children. Substantial disparities in paediatric AKI mortality exist on a global scale, with children from low and lower-middle income settings, and upper middle-income settings having a 57- and 11-fold increased risk of death compared to children from high income settings [14]. In lower resource settings, children were diagnosed later, had more severe AKI and less access to dialysis. Delay or non-diagnosis of AKI in lower resource settings is due to lack of access to care for reasons such as cost (to patients and their families) distance to sites of potential care and insufficient facilities especially for children [1].

Causes and risk of AKI are multifactorial

AKI is a condition that spans the junction between infections and non-communicable diseases. Risk factors extend from the environment to society and the individual as shown in Figure 2. Climate change is increasingly being recognised as a contributor to AKI risk. Changes in global temperatures are disturbing the hydrologic cycle (movement of water from earth to atmosphere and back again) with implications for access to clean water. In addition, the weather changes are related to changes in transmission pathways of pathogens of many kinds (viral as well as waterborne), and this in turn is increasing exposure to infections related to AKI [16,17].

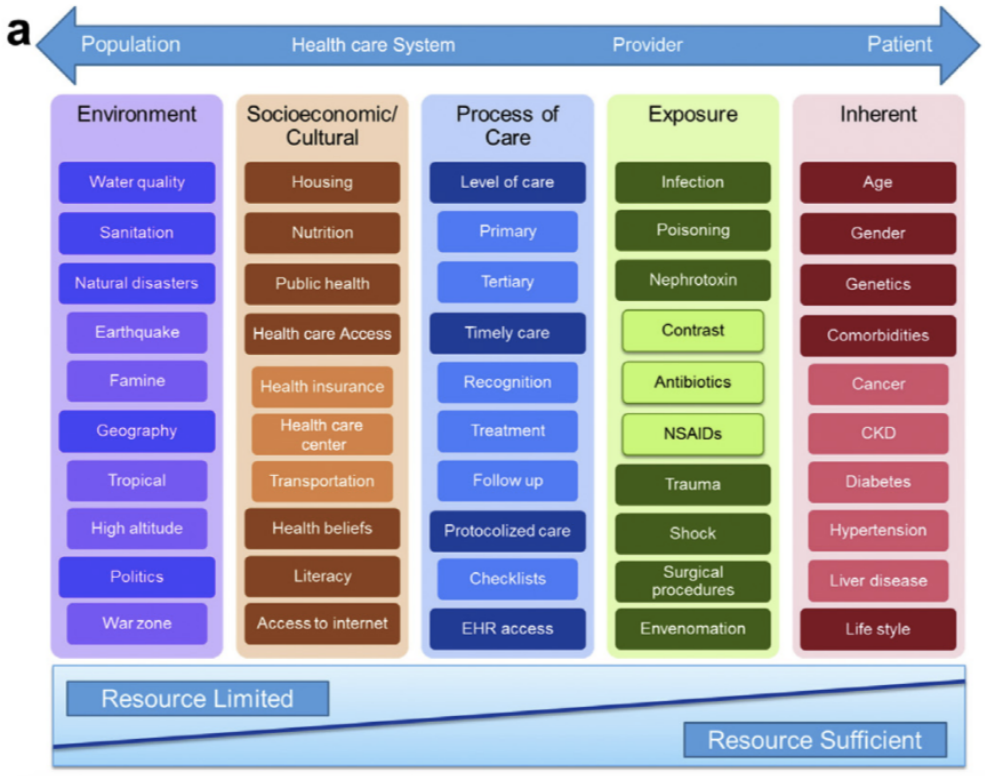


Figure 2: Risk Factors of AKI in a range of settings. (Reproduced with permission from Kashhani et al., Acute Kidney Injury Risk Assessment: Differences and Similarities Between Resource-Limited and Resource-Rich Countries. Kidney Int Rep. 2017 Jul;2(4):519-529. PMID: 28845471; PMCID: PMC5568820) [15].

In high income countries, the causes of paediatric AKI are usually hospital acquired and include septic shock, complications after cardiac surgery and solid organ transplantation [8]. Sepsis itself is associated with AKI as highlighted by various working groups, such as the Acute Disease Quality Initiative workgroup (ADQI) [18].

In lower resource settings, much of AKI in children is a result of infections such as diarrhoeal illnesses and malaria as well as HIV (causing both AKI and KF), which are associated with poor sanitation and lack of access to clean water, trauma (including burns), insufficient access to primary care and vaccination and delays in seeking care [4,15,19, 20].

A recent review has highlighted the disproportionate incidence of infections in children in LMIC and the enduring negative impact that AKI in this setting can have on a susceptible individual's life with increased susceptibility to CKD as well as impaired health related quality of life [17].

Global disparities in outcomes associated with various causes of AKI are highlighted in Table 1 as shown below.

Table 1: Relative proportions of deaths in children due to infections and kidney disease. Reproduced with permission McCulloch M et al, Challenges of access to kidney care for children in low-resource settings. Nat Rev Nephrol. 2021 Jan;17(1):33-45. PMID: 33005036 [11].

Table 1 | **Relative proportions of deaths in children due to infections and kidney disease**

Disease	Age (years)	Global (95% CI)	HIC (95% CI)	UMIC (95% CI)	LMIC (95% CI)	LIC (95% CI)
Lower respiratory tract infections	<5	15 (14.04–16.0)	2.77 (2.6–2.96)	10.65 (10.0–11.51)	16.53 (15.32–17.73)	13.86 (12.56–15.18)
	5–14	6.01 (5.32–6.64)	3.01 (2.86–3.19)	4.36 (4.14–4.85)	6.48 (5.64–7.26)	6.23 (5.72–7.2)
Diarrhoea	<5	9.9 (8.94–10.9)	1.05 (0.93–1.14)	3.02 (2.81–3.24)	10.46 (9.34–11.57)	11.11 (9.56–12.76)
	5–14	6.08 (3.78–9.98)	0.33 (0.29–0.38)	0.9 (0.63–1.36)	7.21 (4.47–11.77)	7.4 (4.24–12.03)
Typhoid and paratyphoid	<5	0.44 (0.21–0.8)	0.0093 (0.0029–0.0230	0.11 (0.049–0.2)	0.6 (0.29–1.1)	0.25 (0.11–0.47)
	5–14	7.77 (4.5–12.07)	0.2 (0.071–0.46)	1.63 (0.85–2.76)	11.48 (6.75–17.69)	3.54 (1.81–6.11)
Malaria	<5	6.57 (4.29–9.38)	0.00023 (0.000041–0.00083)	0.16 (0.078–0.25)	5.24 (3.38–7.55)	11.05 (7.01–16.06)
	5–14	7.43 (5.25–10.23)	0.0006 (0.00018-0.0017	0.12 (0.067–0.19)	7.25 (5.25–9.8)	13.57 (8.61–20.54)
HIV/AIDS	<5	1.44 (1.29–1.6)	0.27 (0.22–0.41)	1.68 (1.45–1.95)	1.16 (1.0–1.39)	1.92 (1.61–2.27)
	5–14	6.12 (5.75–6.48)	0.48 (0.44–0.54)	3.95 (3.74–4.18)	3.25 (2.97–3.51)	15.18 (13.86–16.48)
CKD	<5	0.24 (0.22–0.26)	0.31 (0.29–0.33)	0.36 (0.33–0.39)	0.22 (0.2–0.25)	0.25 (0.22–0.28)
	5–14	1.1 (1.0–1.2)	0.67 (0.64–0.72)	1.23 (1.17–1.33)	1.17 (1.05–1.3)	0.87 (0.76–0.99)
Acute GN	<5	0.0059 (0.0038–0.0077)	0.0025 (0.0023–0.0027)	0.014 (0.013–0.016)	0.0034 (0.0024–0.0043)	0.0081 (0.0033–0.013)
	5–14	0.035 (0.029–0.041)	0.0079 (0.0074–0.0086)	0.091 (0.082–0.1)	0.019 (0.016–0.023)	0.037 (0.022–0.057)
CAKUT	<5	0.2 (0.14–0.25)	1.04 (0.72–1.29)	0.38 (0.32–0.44)	0.17 (0.11–0.24)	0.18 (0.089–0.24)
	5–14	0.079 (0.065–0.098)	0.15 (0.11–0.2)	0.1 (0.09–0.13)	0.077 (0.59–0.11)	0.064 (0.035–0.092)

CAKUT, congenital anomalies of kidney and urinary tract; CKD, chronic kidney disease; GN, glomerulonephritis; HIC, high-income country; LIC, low-income country; LMIC, lower middle-income country; UMIC, upper middle-income country. Data compiled from the Institute for Health Metrics and Evaluation[18].

There is substantial evidence that the nephron endowment (i.e. the number for functioning filtering units within the kidneys) of individuals is set within the first few weeks of life, and that individuals who are born too small (with low birth weights or small for gestational age) or too soon (preterm) have reduced numbers of nephrons present in their kidneys [21]. Thus, children born in low resource settings, where rates of low birthweight and prematurity are high, may already be at increased risk of kidney disease especially if subjected to additional kidney injury and further nephron loss [21]. Importantly also, in low resource regions there may be repeated insults due to persistence of poverty and environmentally driven causes of AKI which would further increase the risk of longer-term CKD.

Combining all this information, there is an urgent need to increase awareness of the importance of preventive measures for AKI at multiple levels, including populations, professionals and policy makers [11,22]. Prevention of AKI in children requires a multi-sectoral approach to improve education (paediatric and maternal); prevent malnutrition by providing basic food and nutrition, improve housing with reduced overcrowding and access to clean water and sanitation; reduce risks of infection and trauma; provide access to immunization and basic healthcare; and addressing climate change as a consolidated approach to preventing AKI [23 – 25].

Child health has been prioritized since the launch of the millennium development goals, and it is likely that some of the progress that followed (including improved

access to clean water, malaria protection, access to vaccination, reduced poverty) has had a positive impact on AKI in children, as depicted in Figure 3. It is unclear how much of this progress has been lost during the pandemic.

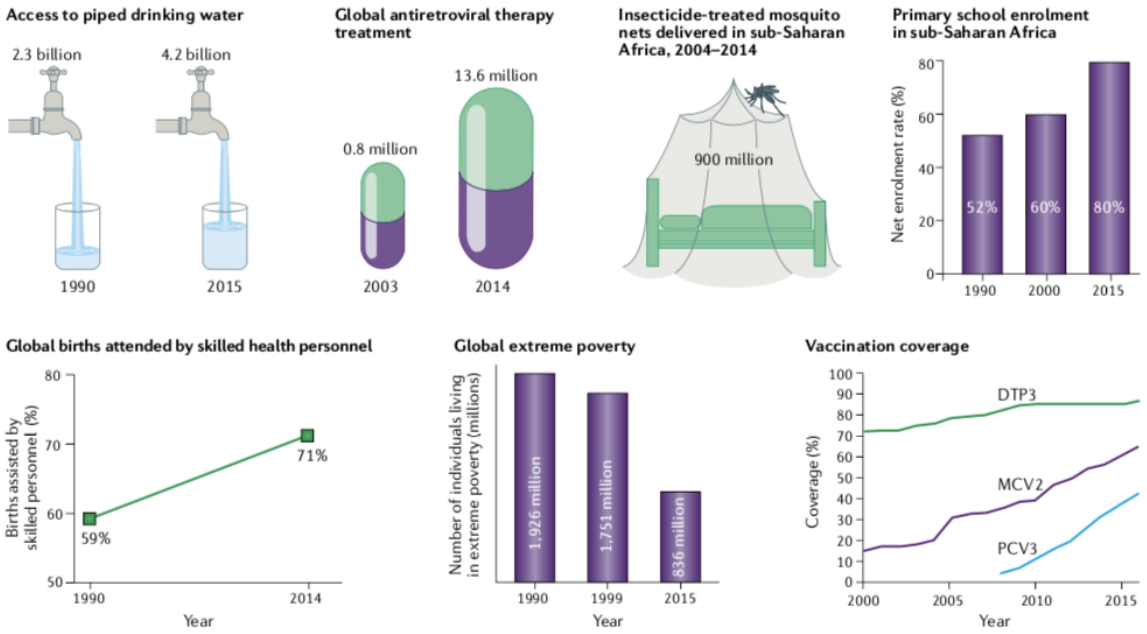


Figure 3: Successes achieved through the MDGs that might be relevant for kidney disease. (Reproduced with permission McCulloch M et al, Challenges of access to kidney care for children in low-resource settings. Nat Rev Nephrol. 2021 Jan;17(1):33-45. PMID: 33005036) [11]

The sustainable development goals (SDGs) were introduced in 2015 to build on the success of the millennium development goals. This set of 17 goals are more holistic and comprehensive. Most SDGs have relevance for kidney health, and many are associated with risk of AKI and are crucial for child health and well-being. SDG 3 and its targets, shown in Table 2, are particularly of relevance to this PhD and topic as it promotes health and well-being for all ages. Target 3.4, which aims to “reduce premature mortality from NCDs by a third by 2030 relative to 2015 levels, and to promote mental health and wellbeing”, is specifically relevant as AKI poses a threat to kidney health and may lead to premature mortality [16]. Associated with this target are the other targets: 3.2, 3.3, 3.8, 3B and 3C which are also directly relevant to this topic and PhD.

Table 2: Relevant SDG Targets for Kidney Disease.

SDG 3	Target	Relevance to AKI and this PhD
3.1	Reduce global maternal mortality ratio by 2030	Poorly nourished and cared for mothers may result in poor foetal and infant nephron endowment and increased susceptibility to AKI due to infections and environmental factors e.g. unclean water. Maternal screening for hypertension and proteinuria which will impact on foetuses. Also, maternal ultrasound screening to assess congenital kidney problems and prevent acute on chronic pathologies.
3.2	End preventable deaths of newborns and children under 5 by 2030	Prevention of infections by immunisations including e.g. Rotavirus vaccine to prevent diarrhoea, clean water supply and adequate nutrition
3.3	End epidemics of AIDS, Tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne and other communicable diseases	Screening mothers and newborns for HIV with prevention of maternal to child transmission, management of malaria which is a major cause of AKI.
3.4	Reduce premature mortality from non-communicable diseases by 1/3 by 2030, by promoting mental health and well-being	In addition to above, addressing mental health issues especially in adolescents with bladder related disabilities such as spina bifida requiring regular self-catheterisation to prevent infections and AKI
3.5	Strengthen prevention and treatment of substance abuse	Preventing all forms of toxins including non-steroidal anti-inflammatory drugs (NSAIDs) but also substance abuse which can cause AKI often on top of chronic kidney disease
3.6	Halve the number of deaths and injuries from road traffic accidents by 2020	Direct kidney injuries but also severe trauma with acute tubular necrosis due to shock
3.7	Ensure universal access to sexual and reproductive services by 2030	Prevention of teen pregnancies
3.8	Achieve universal health coverage	Rapid access for children who have AKI not only for diagnosis but also treatment
3.9	Reduce number of deaths from hazardous chemicals and pollution	Direct impact resulting in AKI
SDG 3	**Means of implementation**	**Relevance to AKI and this PhD**
3.A	Strengthen the WHO Framework Convention on Tobacco Control	Maternal smoking has impact on foetal kidneys making these more susceptible to acute insults
3.B	Support R&D of vaccines and medicines for communicable and non-communicable diseases and	Prevention of AKI is essential with comprehensive immunisations but also availability of treatment of AKI including drugs, dialysis fluids and catheters.

	provide access to essential medicines and vaccines	
3.C	Increase health financing and recruitment, development, training and retention of health care workers	Educating primary health care staff to identify AKI but also availability of appropriately trained paediatricians and specifically paediatric nephrologists to treat AKI medically and with dialysis where required
3.D	Strengthen capacity of all countries for early warning, risk reduction and management of national and global health risks	Awareness of AKI not only in adults but also in infants, children and adolescents requiring early diagnosis and treatment.

Recognition of AKI

The recognition and prompt treatment of AKI is essential to minimise kidney injury and ideally to avoid the need for dialysis. Since 2012 the definition of AKI and grading of its severity has been standardized using the KDIGO criteria (Table 3) [26]. There has also been a recent update looking at controversies in AKI and improving global outcomes [27,28].

The KDIGO criteria rely on measurement of serum creatinine, ideally knowledge of a baseline serum creatinine value, and measurement of urine output, both of which are not always available in low resource settings. For example, a recent global survey found that serum creatinine testing was only available at primary care level in one third of low-income countries [29]. Making the diagnosis of AKI in such settings, before a child would become oligo-anuric would be extremely challenging.

Table 3: KDIGO Criteria for diagnosis and severity of AKI. (Reproduced with permission from KDIGO Kellum JA, Lameire N; KDIGO AKI Guideline Work Group. Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1). Crit Care. 2013 Feb 4;17(1): 204. PMID: 23394211) [26].

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline OR ⩾0.3 mg/dl (⩾26.5 μmol/l) increase	<0.5 ml/kg/h for 6–12 hours
2	2.0–2.9 times baseline	<0.5 ml/kg/h for ⩾12 hours
3	3.0 times baseline OR Increase in serum creatinine to ⩾4.0 mg/dl (⩾353.6 μmol/l) OR Initiation of renal replacement therapy OR, In patients <18 years, decrease in eGFR to <35 ml/min per 1.73 m^2	<0.3 ml/kg/h for ⩾24 hours OR Anuria for ⩾12 hours

In lower resource settings there is often a delay in recognition of AKI, with patients presenting very late in the course of illness, and substantial challenges to testing and

monitoring of renal function [30]. Often there is a lack of access to testing for a variety of reasons including: financial (frequent need for families to pay out of pocket for investigations); organizational (biochemistry machines may not be calibrated or functional with limited capacity for repair, and reagents may not be available); and transport of specimens to a laboratory may be delayed or problematic. Even when testing is available, access to results may be extremely delayed. A recent study in Nigeria demonstrated that even in a population where more than three quarters children had deranged electrolytes and / or elevated creatinine levels on admission, results of blood tests were either not available for 48 hours post admission or were not reviewed, resulting in a delay in identification of AKI [31].

Even when AKI is recognised there is a current global shortage of healthcare workers with knowledge, training and expertise in the management of patients with AKI, and so institution of appropriate therapy may be extremely limited [32,33].

Global surveys suggest that there will be a significant shortage of nephrology health workers in the future, which will worsen the situation of increased kidney disease predicted in the future [34-37].

A South African study has specifically looked at the forecast of a worrying decrease in the nephrology workforce in 2030[38,39]. In the paediatric nephrology arena, this problem is even worse as currently paediatric nephrologists are only 10% of the number of adult nephrologists and in Africa for example, until recently there have been many countries which have had no paediatric nephrologists in the entire country (this in an area where 50% or more of the population is paediatric). This has resulted in efforts to improve the workforce dedicated to paediatric kidney care both in terms of diagnosis as well as management.

Treatment of AKI

Once the diagnosis of AKI is made, it is important to identify the cause and initiate appropriate therapy to address the cause and to prevent worsening of the AKI. Close monitoring is important to detect and treat the consequences of impaired renal function with particular attention to issues such as fluid balance and electrolyte abnormalities (potassium, bicarbonate). Treatment capacity is however dependent on locally available facilities, some of which need to be adapted for child age and size.

Initially conservative treatment includes removing the cause of AKI where possible, resuscitation using fluids where required, avoiding nephrotoxins (e.g. NSAID’s or Aminoglycosides where monitoring not available) and adjustment of medication doses

for kidney failure. Children with AKI with oliguria or anuria may require fluid restriction and drugs such as Furosemide and Aminophylline are used as first line [40]. Failing a response to conservative management, acute dialysis may be necessary to save life, but even if only required for short periods (in contrast to chronic dialysis for people with end-stage kidney failure), and despite its being routine in many places, dialysis is often inaccessible in low resource settings.

Despite the fact that dialysis is available in most countries there therefore is an important 'Dialysis Gap' between those who need dialysis and those who can access it. This gap is wide for adults in LLMICs, and is even wider for children [30,41 – 42]. Indeed, a study from Nigeria showed a mean delay of 6 days from onset of renal symptoms and presentation to hospital to the initiation of dialysis despite an indication being present on day 1 [43]. This delay reflects the family's search for resources to pay out of pocket and the hospital infrastructure being insufficient to meet the clinical need. Most health systems in low resource settings require out of pocket payment for any of the kidney treatment including consumables as well as dialysis fluid, with a study in Nigeria showing that the cost for haemodialysis (HD) and even peritoneal dialysis (PD) (which may be marginally cheaper), for 5 days may rapidly amount to more than the monthly wage.

Inadequate stocks of consumables for dialysis (e.g. dialysis catheters and / or dialysis fluid) are regular problems, for reasons ranging from supply chain problems to complications at international borders (in Africa, South Africa and Nigeria are currently the only countries with companies manufacturing dialysis fluids).

Dialysis for children with AKI

A systematic review of AKI in children in sub-Saharan Africa showed that in patients with access to dialysis, overall mortality was 34% compared to 73% in children who had no access to dialysis [8]. Pooled rate of recovery of kidney function was 75%. Dialysis therefore saves lives and "buys time" for the kidneys to recover in many children with AKI.

There are two forms of dialysis, peritoneal dialysis (PD) and haemodialysis (HD), both of which can be used in children as documented in Table 4. Peritoneal dialysis requires placement of a catheter into the abdominal cavity through which dialysis fluid is exchanged multiple times during the day. Diffusion occurs across the peritoneal membrane to remove urea, creatinine, potassium, and other uraemic metabolites from the patient, to permit bicarbonate diffusion into the patient to correct metabolic acidosis, and fluid is removed down an osmotic gradient generated by glucose in the dialysis fluid (dialysate). PD is adaptable for patients of all ages and sizes, although smaller children require smaller catheters.

HD in contrast requires access to a patient's blood via a dual-lumen catheter. The blood is circulated through a dialysis filter bathed in dialysate outside of the body, where diffusion occurs to correct metabolic derangements and fluid is removed through generation of negative pressure across the membrane. HD may not be appropriate for children and small infants unless appropriately sized catheters, blood lines, filters and machines are in place and staff are appropriately trained. Adolescents and bigger children may be eligible for treatment in adult dialysis units where adult sized PD and HD consumables may be more readily available (not always the case even for adults in all lower resource settings).

Table 4: Comparison of advantages and disadvantages of peritoneal dialysis and haemodialysis in children.

	Peritoneal Dialysis (PD)	**Haemodialysis (HD)**
Dialysis catheters	A peritoneal dialysis catheter must be placed in the abdomen. This can be performed surgically (requiring theatre infrastructure and surgeons) or using a variety of catheters which can be placed safely using Seldinger techniques at the bedside.	Requires a trained person to place venous catheter in theatre or at the bedside. Venous access can be difficult especially in small infants in terms of inserting HD catheters into veins large enough to perform effective dialysis. Specific small double lumen HD catheters with equal sized lumens for infants and neonates may not easily be available. Newer HD machine technology for neonatal dialysis (e.g. Carpe Diem) using lower flows and smaller catheters is not easily available and remains costly.
Improvised PD catheters	If standard catheters are unavailable, a variety of catheters have been used with varying success; rigid stick (which may be only PD catheter available but have potential for significant complications	Difficult to improvise if correct size HD catheter not available

	including vascular and bowel damage), soft Seldinger pigtail catheters (Cook), chest drains and even nasogastric tubes	
Dialysis Fluid	For PD requires manufacturing with increasing factories based in Africa (Adcock Ingram in Johannesburg, SA and Biomedical *sciences Laboratories Ltd Ilorin, Nigeria since 2016)*	Fluid mostly imported from Europe
Improvised PD Fluid	Can "make" PD fluid locally using commercial intravenous fluids such as Normal Saline/Ringers Lactate adding glucose as needed under sterile conditions (see Table 5)	Requires professionally manufactured haemodialysis fluid, continuous sterile water supply
Machinery	Cycling dialysis machines can even be used on the smallest of children. Does required paediatric sized consumables	HD machines require custom made consumables and frequently not appropriately sized for paediatrics available.
Electricity	PD can be done manually without electricity Electricity required for automated PD	Required
Water supply	Required for handwashing, hygiene	Required, including dialysis water "system" to generate water usable for dialysate, free of pathogens

Although PD requires less infrastructure than HD, it is still dependant on some resources including PD catheters, PD fluid and appropriate trained medical and nursing staff [44]. A technical challenge in environments where resources are limited is that for smaller children and infants under 1year and especially neonates less than a month, the appropriately sized dialysis equipment for either HD or PD may not be

available as these are often more costly; are not procured in large quantities, and usually have to be imported from other countries (often with much stronger currencies – thus adding to the expenses). Availability of PD fluid may be challenging as this is expensive to procure and to transport.

In an emergency setting, as per the ISPD guidelines, improvised techniques can be used for PD catheters, even using venous cannulae and adapted fluids to save lives where formal dialysis units may not be available for AKI [45]. Locally mixed fluids, provided mixed in a sterile fashion, can be safely used at the bedside using standard commercially available intravenous fluids as documented in Table 5. An advantage that children have here over adults is that given the small volumes required per cycle of PD, one 1 litre bag may be enough for several exchanges in a day.

Overall, this section has covered the limitations related to the generalizability of treatment of paediatric AKI for well-resourced regions where PD and HD is available. I have also discussed the challenges of less well-resourced regions and the strategies to address them including the use of the new ISPD guidelines for improvisation where equipment and fluid not available.

Table 5: Adaptation of commercial fluid to generate fluid usable for peritoneal dialysis at the bedside. (Reproduced with permission from Nourse P, Cullis B, Finkelstein F, Numanoglu A, Warady B, Antwi S, McCulloch M. ISPD guidelines for peritoneal dialysis in acute kidney injury: 2020 Update (paediatrics). Perit Dial Int. 2021 Mar;41(2):139-157. doi: 10.1177/0896860820982120. Epub 2021 Feb 1. PMID:33523772) [45].

Table A1. Suggestions for the preparation of locally mixed peritoneal dialysis fluids.[a]

Dialysis fluid can be made by adding 50% dextrose to Ringers lactate, plasmalyte B or Hartmann's solution
1 L Ringers lactate + 30 mL 50% dextrose will make a 1.5% solution 1 L Ringers lactate + 90 mL 50% dextrose will make a 4.5% solution 1 L Plasmalyte B + 30 mL 50% dextrose makes a 1.5% dialysis solution 1 L Plasmalyte B + 90 mL 90% dextrose makes a 4.5% dialysis solution 1 L Hartmann's + 30 mL 50% dextrose makes a 1.5% dialysis solution 1 L Hartmann's + 90 mL 50% dextrose makes a 4.5% dialysis solution
Using 0.45% saline + 5% dextrose + $NaHCO_3$
1 L ½ Normal saline + 40 mL 50% dextrose + 40 mL 8.4% $NaHCO_3$ + 60 mL 3% NaCl will make a 1.5% dialysis solution 1 L ½ Normal saline + 60 mL 50% dextrose + 40 mL 8.4% $NaHCO_3$ + 60 mL 3% NaCl will make a 2.5% dialysis solution
Using 0.9% saline + 5% dextrose + $NaHCO_3$
1 L Normal saline + 1 L 5% dextrose + 100 mL 8.4% $NaHCO_3$ makes a 2.5% dialysis solution
Please note the final electrolyte and glucose concentrations of the above solutions:
1 L Plasmalyte B/Ringers lactate/ Hartmanns' + 30 mL 50% dextrose (15 g) will generate a solution with the following concentrations: glucose = 1.45%, Na = 126 mmol/L, HCO_3-/Lactate = 27 mmol/L, K = 3.8 mmol/L, Mg = 1.45 mmol/L, Osmolality= 342 1 L ½ Normal saline + 40 mL 8.5% $NaHCO_3$ (40 mmol) + 40 mL 50% dextrose (20 g) + 60 mL 3% NaCl (30 mmol) will generate a solution with approximately the following concentrations: Na = ±130 mmol/L, HCO_3 = 35 mmol/L, glucose = 1.7%, osm = 345 1 L Normal saline + 1 L 5% dextrose + 100 mL 8.4% $NaHCO_3$ makes a 2.5% dialysis solution will generate a solution with the following concentration: glucose = 2.38%, Na = 121 mmol/L, HCO_3 = 48 mmol/L, osm = 374

[a]When adding more glucose, the electrolyte concentrations will change slightly but not significantly.

Improving quality of care for children with AKI

In order to successfully begin to address the AKI burden and achieve SDG 3 from the perspective of improving kidney health (previously in Table 2), a health systems wide approach is needed, which includes not only public health prevention of AKI, but also sustainable and quality disease management strategies.

Such strategies must be integrated into the health system and require political will and adequate funding for sustainability. In addition, to deliver quality and timely care, health care workers require appropriate training to be aware of AKI and how to diagnose and treat this condition. This also needs sustainable access to mediczation and technology, which in the case of acute dialysis must be appropriate not only for children and adolescents but also for neonates and infants. All of these components are integrated within the 6 health systems building blocks, Figure 4, as outlined by the World Health Organisation as prerequisites for health systems strengthening and improved health care delivery.

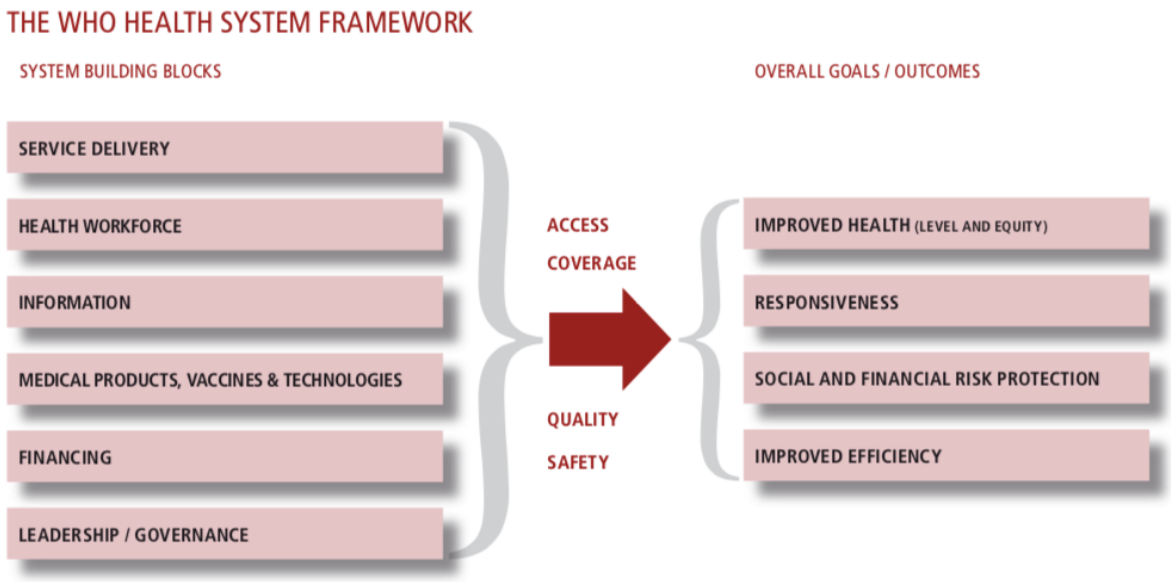


Figure 4: The Six Building Blocks of a Health System: Aims and Desirable Attributes. (Reproduced with permission from WHO: https://www.who.int/publications/i/item/everybody-s-business----strengthening-health-systems-to-improve-health-outcomes. Accessed 6.2.2024) [46].

We know that service delivery for children with AKI is challenging and dialysis is mostly not available in Africa and related to this, my thesis explores options to improve care for AKI in infants and children [47-49] Within the framework of the WHO 'building blocks' I have embarked on this African based PhD reviewing the experience of acute dialysis for children with AKI including the development of a basic database together with a review of the outcomes [50].

This has been as part of a systematic approach towards improving service delivery and quality of care for children with AKI, and build capacity among African healthcare workers to diagnose and treat AKI through:

- Review of experience in delivering dialysis and quality of dialysis for children with AKI in a low resource setting (Paper 1)
- Evaluating the impact of capacity building and the quality of care delivered by healthcare workers trained to deliver acute PD for children with AKI in low resource settings (Paper 2)
- Evaluating the safety and utility of locally made PD fluids as a means to increase access to dialysis technologies in low resource settings (Paper 3)
- Obtaining data on costing of dialysis provision in children with AKI to inform sustainable financing (Paper 4)

- Dissemination of knowledge and experience on innovation in the field of paediatric nephrology to expand PD for AKI in children which was previously unavailable in sub-Saharan Africa.

Each paper is included as a chapter of the PhD with a brief rationale for each summarized in the scope of the thesis below. The papers are included as published. The chapters are followed by a discussion summarizing the learnings from this PhD, the global significance of this work and the next steps required for clinical care and advocacy for kidney care for children in lower resource settings.

Scope and Layout of the Thesis

Chapter 1: Dialysis for Paediatric Acute Kidney Injury in Cape Town, South Africa (Paper 1)

This will combine the goals of strengthening Service Delivery and Health Information Systems.

Building block: Optimizing and Improving Service Delivery
An important objective for this thesis is to document the number of children we have dialysed for AKI, to analyse the causes of AKI needing dialysis in variably aged paediatric patients in order to identify potentially preventative factors and to assess quality and outcomes of dialysis delivered.

I have performed an analysis of outcomes among children with AKI who received PD or HD at Red Cross War Memorial Children's Hospital using the 20-year dialysis database (593 cases).

In this study I evaluated and tested the hypothesis that our 'Peritoneal Dialysis (PD) First for AKI' program (in that we attempt PD first where possible given the advantages of PD over HD in a resource limited setting) achieves acceptable outcomes when compared to the more standard extracorporeal dialysis (HD). Most children with AKI who required dialysis received PD as their first and often only dialysis modality. In later years as more equipment has become available, other forms of extracorporeal dialysis (ECD) have also been used. Outcomes were acceptable compared with international data.

The Value of Health Information
This paper is based on the simple paper-based database of acute dialysis that has been maintained at the RCWMCH over a period of 20 years. Sophisticated health

information systems are increasingly available in high income countries in addition to clinical and support services, but these are mostly lacking in lower resource settings, precluding the possibility to implement quality assurance exercises. This paper illustrates the value of keeping careful records of AKI causes, therapies performed, and complications encountered. In addition, the implementation of electronic databases is recommended not only to allow early recognition and planning but also to provide information related to quality of management of AKI and for future follow-up planning. Kidney databases for adults are few for chronic kidney diseases and even more so for children and almost non-existent for AKI, and good databases would be important not only locally but also at governmental advocacy level. Challenges with quality of data highlight how the implementation of health information systems at the clinical level could contribute to improvements processes for service delivery.

Chapter 2: Lessons learned from regional training of paediatric nephrology fellows in Africa (Paper 2)

Building block: Strengthening the Pediatric Nephrology Health Workforce in SSA

One of the main reasons that children die of AKI is lack of access to appropriate care, which in addition to being dependant on resources is crucially dependent on knowledge of health care workers trained in paediatric nephrology. Until recently there have been virtually no paediatric nephrologists in Sub-Saharan Africa.

Recognizing this we developed a training course for paediatric nephrology fellows from South Africa and various parts of Africa with international funding from many organisations including mainly the International Pediatric Nephrology Association (IPNA) and the International Society of Nephrology (ISN).

As part of this thesis, I have evaluated the impact of this training program of paediatric nephrologists (38) from 1999 – 2021. Training emphasis in paediatric acute kidney injury included a review of hands-on training skills including bedside PD catheter insertion and all the improvised techniques for managing AKI in low resource settings. The length of training time in our Red Cross War Memorial Children's Hospital unit was also reviewed and in addition the number of subspecialty Certificates of Paediatric Nephrology (CMSA)(14) as well as the number of completed Master's degrees(MPhil), University of Cape Town(UCT) Master's degrees(9) achieved.

The number of clinical projects published by the fellows were also documented.

Table 6: Publications by paediatric nephrology fellows during training at RCWMCH/UCT.

Paediatric Nephrology Fellow trained at RCWMCH/UCT	**Publication**
Isaac Ocheke	Ocheke IE, Antwi S, Gajjar P, McCulloch MI, Nourse P. Pelvi-Ureteric Junction Obstruction at Red Cross Children's Hospital, Cape Town: a Six Year Review. Arab J Nephrol Transplant. 2014 Jan;7(1):33-6. PMID: 24702532.
Chisambo Mwaba	Mwaba, C., Nourse, P., Pillay, K., & Gajjar, P (2020). Aetiology and outcomes of crescentic glomerulonephritis in South African children: a ten-year folder review. African Journal of Paediatric Nephrology, *7*, e15-e21.
Ade Solarin	Solarin AU, Nourse P, Gajjar P. Vitamin D status of children with moderate to severe chronic kidney disease at a Tertiary Pediatric Center in Cape Town. Saudi J Kidney Dis Transpl. 2019 Jul-Aug;30(4):781-794. doi: 10.4103/1319-2442.265453. PMID: 31464234.
Thembisile Mosalakatane	Mosalakatane TD, McCulloch M, Nourse P, Coetzee A, Wright A, Raad J, Lazarus J, Howlett J. A 15-year retrospective review of urodynamic studies in children at Red Cross War Memorial Children's Hospital, Cape town, South Africa. BMC Pediatr. 2022 Jul 8;22(1):401. doi: 10.1186/s12887-022-03462-4. PMID: 35804357; PMCID: PMC9263046.
Privilage Makanda-Charambira	Makanda-Charambira PD, Nourse P, Luyckx VA, Coetzee A, McCulloch MI. TB in paediatric kidney transplant recipients - A single-centre experience. Pediatr Transplant. 2022 Feb;26(1):e14141. doi: 10.1111/petr.14141. Epub 2021 Sep 16. PMID: 34528349.
Khadija Abugrain	Abugrain K, McCulloch MI, Muloiwa R, Luyckx VA, Buys H. A 6-year review of acute post-streptococcal glomerulonephritis at a public children's hospital in

	Cape Town, South Africa. Pediatr Nephrol. 2024 Jan 3. doi: 10.1007/s00467-023-06247-8. Epub ahead of print. PMID: 38170231
Patience Obiagwu	Obiagwu PN, Morrow B, McCulloch M, Argent A. Burden and severity of deranged electrolytes and kidney function in children seen in a tertiary hospital in Kano, northern Nigeria. PLoS One. 2023 Mar 17;18(3): e0283220. doi: 10.1371/journal.pone.0283220. PMID: 36930619; PMCID: PMC10022757.
Adewale Adetunji	Adetunji AE, Gajjar P, Luyckx V, Reddy D, Collison N, Abdo T, Pienaar T, Nourse P, Coetzee A, Morrow B, McCulloch M. Evaluation of the Implementation of a 'Paediatric Feasibility Assessment for Transplantation' (pFAT) Tool in Children and Adolescents at Red Cross War Memorial Children's Hospital, Cape Town, South Africa. *Accepted for publication in Ped Transplantation.*
Judith Caroline Aujo	Aujo JC. Drop-out of children with end stage kidney failure from chronic peritoneal dialysis and associated factors; a 10year review at Red Cross Children's Hospital, Cape Town, South Africa. 2023. *Submitted Ped Nephrology for publication pending revisions*

I also evaluated the return rate of these fellows (100%) to their home institutions and noted that for many they were the first paediatric nephrologists in their country.

The resources for paediatric kidney care are often not available in many countries so as part of this thesis, I performed a survey of our trainees to review their facilities and quality of service they are able to provide on return home. This feedback was very useful in allowing adaption and review of the training program which we had developed at RCWMCH/University of Cape Town (UCT) and in so doing preparing them for challenges on their return.

Despite the training of this significant number but there still remains a severe lack of paediatric nephrology trained specialists in sub-Saharan Africa, but this is a positive start, and these trainees can go on to train others. The training in research through this programme also allows trainees to understand the value of collecting accurate data, analysing this for programme improvement and the value of disseminating knowledge.

Chapter 3: Use of locally prepared peritoneal dialysis fluid for acute PD in children and infants in Africa (Paper 3)

Building block: Innovation to improve access to Essential Medicines and Technologies

The management of kidney disease and especially the management of dialysis generally relies on sophisticated dialysis equipment which requires highly trained and skilled personnel. We have focussed on the development of simple techniques, using basic equipment, which can be operated by trained clinicians and nursing staff at the bedside (without needing access to operating theatres). In the experience documented in both Paper 1 and 2, the majority of PD catheters have been safely inserted at the bedside - thus saving on theatre time and reducing delays to begin therapy - by paediatric nephrologists and trainees with surgeons only assisting in a small percentage of cases.

The success of this bedside PD catheter insertion has led to our improvisation of not only devices used as PD catheters, but also of improvised PD fluid using home-made sterile mixtures (sterile Ringer's lactate with dextrose) as PD fluid, with good effect and very low infection rates. These adaptations have been incorporated into international guidelines for acute peritoneal dialysis in low resource settings for adults and children and are being implemented in many places around the globe to save lives [45,51-52]. Anecdotally, during COVID-19 our combined South African experience was useful for colleagues in high income settings faced with having to perform acute PD in adults for the first time [53].

Chapter 4: Costing of dialysis modalities (Paper 4)

Building block: Collection data to inform sustainable financing

Advocacy for better access to dialysis inevitably must include cost considerations. I reviewed the costs associated with the various dialysis modalities – both peritoneal and haemodialysis - available for acute kidney injury in our program, which can inform service planning and advocacy for reduced prices to improve accessibility of dialysis in low resource settings.

Accurate costing of dialysis techniques is difficult in view of many hidden costs and the fact that children range in size from neonates to adolescents and costing depends on the patient's size.

CKRT is possible in our centre but is labour intensive and requires highly trained staff. The Carpe Diem® CKRT system for infants and neonates is the most expensive modality, in addition to being the most staff intensive.

Acute PD with improvised catheters and using manual locally produced dialysis fluid, was the least costly and therefore should be affordable even in very low resource settings.

This form of dialysis does save lives, specifically in facilities where acute dialysis was not previously available or affordable.

Chapter 5: Discussion and Conclusion

Building Block – Leadership and Governance issues

This final chapter is an overview of the work presented including putting this PhD into a Global Context. This chapter also addresses Advocacy and Leadership issues together with a view of strengthening teams that have been trained in low resource settings. Future research suggestions in the field of paediatric AKI include concentrating on availability of resources and leading to implementation research.

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1 Chapter 1: Dialysis for Paediatric Acute Kidney Injury in Cape Town, South Africa (Paper 1)

1.1 Overview

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1.2 Abstract

Introduction: Dialysis is life saving for acute kidney injury (AKI). Recent technological developments allow for dialysis even in small neonates, yet there is poor access in less resourced countries. Peritoneal dialysis (PD) first for AKI offers an accessible modality in such regions.

Aims: Describing acute PD as 'PD First for Paediatric AKI' for children with AKI requiring dialysis.

Method: Retrospective review of children dialysed acutely 1998–2020 at the Red Cross War Memorial Children's Hospital (RCWMCH), Cape Town.

Results: Of the 593 children with AKI who received dialysis, 463 (78.1%) received PD first. Median age was 9.0 (range 0.03–219.3; IQR 13.–69.6) months; 57.6% were <1 year old. Weights ranged from 0.9–62.0 kg (median 7.0 kg, IQR 3.0–16.0 kg); 38.6% were <5 kg. PD was used in younger children (median 6.4 months) and extracorporeal dialysis (ECD) in older children (median 71.7 months, p=0.001). PD was performed with Seldinger soft catheters (n=490/578, 84.8%), inserted predominantly by paediatricians at the bedside (n=412/490, 84.1%) rather than surgeons (78/490, 15.9%). Complications occurred in 127/560 (22.7%) children receiving PD. Overall, 314/542 (57.8%) children survived. Survival was significantly lower in neonates (<1 month old, 47.5%) and infants (<1 year old, 49.2%) compared to older children (>1 year old, 70.4%, p<0.0001). Survival was superior in the ECD (75.4%) vs the PD group (55.6%, p=0.002).

Conclusion: 'PD First for Paediatric AKI' remains a valuable modality for management of AKI in children, especially in less well-resourced regions where bedside Seldinger PD catheter technique using soft catheters can be safely taught. We demonstrate an acceptable survival rate in children with AKI requiring dialysis without which these children would not survive.

Keywords: *Acute Kidney Injury, Peritoneal Dialysis, Extracorporeal Dialysis Including Haemodialysis, Continuous Veno-Venohaemofiltration (CRRT)*

1.3 Introduction

There have been major recent advances in the diagnosis and management of acute kidney injury (AKI) including substantial development in kidney replacement technology globally, enabling even infants and small children to be dialysed [1]. However, most low and lower middle income countries (LLMIC) still have very limited paediatric nephrology services and even more limited access to effective dialysis,

particularly for acute dialysis, which may be lifesaving and cost effective even in the absence of chronic dialysis [1, 4–10].

An international survey of AKI treatment showed that peritoneal dialysis (PD) is widely available worldwide [11]. Peritonitis, a major concern with PD, can be minimized with strict aseptic techniques even with locally produced PD fluid in both adults and children [12–15].

The use of haemodialysis (HD) or continuous renal replacement therapy (CRRT), grouped together in this paper as extracorporeal dialysis (ECD), may be more challenging than PD due to lack of trained paediatric staff with expertise to place HD catheters which may be more difficult to place than PD catheters in small sick infants, reduced availability of appropriate paediatric sized equipment and consumables including both HD lines and HD catheters compared to PD catheters, and cost where PD(especially where improvised systems are used) should be cheaper than ECD.

The ‘PD First’ policy was first named in the adult literature in Hong Kong in 2007 for use in chronic kidney failure where PD was found to improve patient survival, retain kidney function, lower infection risk overall and increase patient satisfaction while reducing financial stress [16-18].

In adults, acute HD for AKI is preferentially used in high income countries (HIC) because HD is readily available, a lot easier and more efficient. In children, acute HD for AKI may be challenging particularly in small infants, in the absence of sophisticated dedicated neonatal dialysis lines and consumables, and so PD is frequently used in both HIC and as well as in LLMIC, where not only is it easier, cheaper, and more scalable but also realistically possible.

Thus, introducing the concept of ‘PD First in AKI’ in all cases of AKI requiring dialysis, i.e., using PD as the initial modality of dialysis in all cases unless there are specific contra-indications, allows for simple and effective dialysis at relatively low cost, with the potential of saving many lives. The ‘PD First in Paediatric AKI’ approach has the added benefit in small infants and children who may not otherwise have any access to dialysis [8, 9, 15]. In addition, applying the PD First in Paediatric AKI approach in situations where PD catheters are inserted at the bedside by medical staff, obviates the need for moving the patient to an operating theatre, dependence on a surgeon (who may not be available and may not be trained in laparoscopic techniques), and avoids delays in initiating dialysis. As an extension of this, the concept of Acute/Urgent-start dialysis, i.e., commencing dialysis immediately once the PD catheter has been inserted, instead of waiting a few days, as may occur in chronic PD, is also clinically valuable, especially where urgent dialysis is required [19,20].

A variety of PD catheters for bedside insertion have been described as alternatives to surgically inserted Tenckhoff catheters which are (usually inserted using open or

laparoscopic surgical technique) in both adults and children [21-23]. Previously, most catheters placed at the bedside were rigid ‘stick’ catheters (Romson® /Peritocat Braun®); these were used even in children [24]. More recently, the use of softer PD catheters using the safer Seldinger technique has been described [25]. Arising from the Seldinger technique, a peelaway sheath technology with a soft flexible PD catheter is also gaining popularity, especially in adult practice.

Failing availability of this technology, alternative devices such as chest drains, and nasogastric tubes have also been described for use in acute PD [23].

In clinical settings where protocols for bedside PD catheter insertion exist and clinicians feel comfortable inserting these catheters, training of nephrologists from less well-resourced centres globally has been scaled up and has been funded by organisations such as the International Pediatric Nephrology Association, the International Society of Peritoneal Dialysis, and the International Society of Nephrology [26].

Despite the PD First approach being well established in adult practice, there are very few studies examining its use in infants and children, particularly using soft catheters inserted by Seldinger technique [25].

Overall, access to dialysis for AKI treatment when needed is essential as, even in less well-resourced regions, children with AKI who received dialysis, have a 30–40% mortality compared with a 74% mortality among those who are not dialysed [8].

1.4 Background

1.4.1 Context

The South African health care system comprises government-funded and private medical insurance services. Private health care is funded through insurance or out of pocket. The government funds medical care for South Africans without medical insurance at government institutions, with varying degrees of cost-sharing depending on an individual’s income. This includes including acute and chronic dialysis and transplantation, if individuals meet eligibility criteria. In addition, health care for children under 6 years of age is free.

Red Cross War Memorial Children’s Hospital (RCWMCH) is a 300-bed, government-funded, tertiary-quaternary referral hospital that manages both government-funded patients and those with private medical insurance or private funding, as some highly specialised services are only available at RCWMCH and not in the private sector. The hospital primarily serves the needs of the greater Cape Town metropolitan region with roughly 1.1 million residents aged 0–14 years in 2021. The overall population increased by approximately 25% over the period of the study [27].

In addition, RCWMCH services a much bigger geographic region including the Western Cape province and the neighbouring Eastern and Northern Cape provinces (totalling 672 000km2, more than 50% of South Africa). Finally, a small number of children are referred from other parts of Southern Africa. In 2022, nearly 21 million, or 34% of South Africa's total population of 62 million people, were children younger than 18 years. Although RCWMCH has a government-imposed paediatric cut-off of 13 years, some older children in chronic services still undergo treatment at this institution.

The hospital has a 22-bed paediatric intensive care unit (PICU) with approximately 1400 admissions per annum across all disciplines, including medical and surgical cases; the latter includes cardiothoracic and neonatal surgery. In addition, the hospital has a paediatric nephrology service that provides acute- and long-term care for a wide variety of patients. Most patients will undergo acute dialysis within the PICU in keeping with their overall condition, but some patients may also undergo acute dialysis within the high care area of the paediatric nephrology unit. Staffing in the PICU is on a 1:1 nurse to patient ratio but may be a pair of senior and junior nurses per 2 beds as opposed to the high care unit where there is a 1:4 nurse to patient ratio. The full spectrum of dialysis modalities for both acute and chronic dialysis (including CRRT including the neonatal Carpe Diem® machine) and for the management of acute metabolic events, is available. Most of the nursing staff are trained in PD management (specifically manual PD) but this is not the case for ECD for which there is only a small team of trained staff; ECD requires both nephrology dialysis staff and paediatric nephrology backup. However, our overarching unit policy is the PD First in paediatric AKI approach, i.e., to consider PD (for acute and chronic dialysis) before other options, and to use an 'Acute/Urgent Start' approach, with PD catheters being inserted at the bedside by non-surgical nephrology or PICU staff [19-20, 28-29]. Note that for this study, we have excluded chronic dialysis as far as possible.

As stated earlier, RCWMCH manages both government-funded patients and those with private medical insurance or private funding; in the renal unit the ratio is 70:30, and all are treated equally. Hence, there is no selection bias in terms of children being turned down for treatment depending on parental affordability of treatment. This differs from some other low and middle-income countries (LMIC). Big geographic distances across a large country, however, may contribute to treatment bias for AKI depending on awareness and paediatric knowledge in district and local clinics.

1.4.2 Subject Eligibility

The inclusion criteria for this study were infants and children requiring acute dialysis who were assessed to have a reasonable chance of recovering kidney function without long-term chronic kidney failure or severe disability. In some cases, there may have been a suspicion of chronic kidney failure (KF), but if a child would have the option of transplantation, they were given a chance with acute PD and included in the analysis given that feasibility and complications of acute PD remain relevant.

Patients were excluded if deemed to have chronic kidney failure which would require long-term dialysis where transplantation was not deemed possibility. Such patients undergo a multidisciplinary team review process to assist in determining eligibility for further dialysis and transplantation or palliative care [30].

1.4.3 Clinical Processes

Dialysis consumables are purchased from the two main companies servicing our facilities, i.e., Fresenius and Adcock (Baxter). Specific supplies and equipment such as infant and neonatal lines may often require importation from Europe and North America, with a lengthy lead time for orders, although this has become easier in recent years. Dialysis machines used over the study period are listed in Supplementary Table 1.

Indications for dialysis included anuria/oliguria, acidosis, fluid overload, and hyperkalaemia and hyperphosphataemia not responding to medical therapy including trial of frusemide and aminophylline [31]. Inborn errors of metabolism, such as urea cycle defects with associated hyperammonaemia, are managed with PD as a temporising measure before moving to ECD, provided as either CRRT or HD (see Table 1.1).

Table 1.1: Methods of Insertion of Dialysis Catheters.

A. **Peritoneal Dialysis (PD) Catheter insertion**		
	Infants/Smaller children <10kg	**Bigger children >10kg**
Preparation of prior to PD catheter insertion	• Placed under strict aseptic technique. • Full theatre conditions including gowns and gloves. • Ensuring urinary catheter in bladder and patent by flushing to prevent bladder perforation. • Use of bedside ultrasound to assess bladder distension and increasingly identifying best PD catheter position. • Bowel perforation is prevented by initial instillation of 20 mL/kg fluid into the peritoneal cavity via a vascular cannula, thus creating artificial ascites, prior to placing a PD catheter	
Specific PD catheter used	• Seldinger technique	• Seldinger technique

	• Cook® PD (Straight 5Fr/ 8.5Fr) or Cook® Fuhrman drainage (pigtail 8.5Fr) • Uncuffed non tunnelling	• 'Peel-away' Tenckhoff catheters for bigger children • Uncuffed non tunnelling
Operator medical	• Paediatric nephrologists/Fellows/Neonatologists	
Operator Surgeon	• Rarely • Bedside in ICU in complicated cases • Small number of cases surgeons place cuffed PD catheters in operating theatre during cardiac or abdominal surgery	
At time of bedside PD catheter insertion	• Dose of vancomycin 10mg/kg (or Cefazolin 50mg/kg) intravenously stat over 1 hour slowly, unless already receiving antibiotics for their underlying condition • PD fluid is sent for microscopy and culture and, specifically, for a white cell count at the time of insertion and at any other time if concerns of peritonitis arise	
Infection surveillance	• Urine dipstick testing on the PD fluid is performed daily at the bedside to detect leucocytes. • In cases of suspected peritonitis, dialysis effluent is sent for microbiological examination and empiric intraperitoneal antibiotics (Ceftazidime and Vancomycin) are added as per local protocol until microbiological identification and sensitivities are available.	
Trouble shooting tricks	• Flushing is attempted for blocked or poorly draining catheters. • For leaking PD catheters, attempts are made to seal the leak with surgical glue or sutures. • Pleural effusions related to PD are diagnosed on chest x-ray or on ultrasound. If identified, pleural fluid is aspirated and tested for glucose to confirm the presence of dialysis fluid. Treatment includes placing the patient head up at 30 degrees, reducing the fill volume of each dialysis cycle, and inserting an intercostal chest drain in cases where respiratory embarrassment occurs. • In cases where PD fails or is not possible due to abdominal issues, it is changed to ECD either as HD or CRRT depending on stability of the patient.	

B. **Haemodialysis/Extracorporeal Dialysis Catheter insertion**

	Infants/Smaller children <10kg	**Bigger children >10kg**
Preparation of prior to PD catheter insertion	• Placed under strict aseptic technique. • Use of ultrasound guided Seldinger technique. • Dose of vancomycin 10mg/kg (or Cefazolin 50mg/kg) intravenously stat over 1 hour slowly, unless already receiving antibiotics for their underlying condition	
Access Vessel used	• Preferably neck vessels either internal jugular vein (avoid subclavian vein) • Femoral as second option	
Specific HD catheter used	• Gamcath® 6.5Fr. • Arrow® 5Fr (5cm double lumen 18G and 20G (not a custom-made HD catheter) • For small infants – have used in less than 2kg	Bigger children included sizes 7, 8 and 9 Fr (Medcomp® or Arrow®).
Operator medical	• Paediatric Intensivists/ Anaesthetists/ Nephrologists/ • Neonatologists	• Paediatric Intensivist/ Anaesthetists/ Nephrologists
Trouble shooting tricks	Heparin lock/other forms of locking e.g., TPA.	

1.4.4 Aims

Evaluation of outcomes of a 'PD First in Paediatric AKI' programme for children with AKI requiring acute dialysis at RCWMCH from 1998–2020.

1.4.5 Objectives

1. Describe the demographics of children receiving acute dialysis over the study period concentrating predominantly on the PD First in Paediatric AKI approach.
2. Describe conditions associated with AKI.
3. Document specifics of dialysis delivery including:
    a. Dialysis modalities
    b. Use of soft Seldinger placed PD catheters (as opposed to rigid PD catheters)
    c. Duration of dialysis
    d. Complications of PD
4. Patient outcomes

1.5 Methods

This is a retrospective descriptive review of a paper-based database of all children aged birth to 18 years who received acute dialysis between 1998 and 2020 at RCWMCH, predominantly in the PICU (a few children were dialysed acutely in the nephrology unit). The clinical team initiating dialysis were responsible for clinical data entry including age, weight, clinical indication for dialysis, type of dialysis used, type of dialysis catheter inserted including operator and location of insertion, duration of dialysis, complications, and patient outcomes. Paediatric-trained dialysis technologists recorded technical details of lines, dialysis times, and machine issues. This was cross referenced with the PICU electronic patient database that included dialysis information.

Data were extracted from these sources and were stratified into time quartiles according to dates: 1998–2003, 2004–2009, 2010–2015, and 2016–2020 to highlight changes that occurred over time particularly to having access to improved 'child-friendly' dialysis equipment including the acquisition of modern Fresenius machines (HD Fresenius 5008 Paeds 2014, Fresenius CRRT Multifiltrate machine 2012) and Carpe Diem® neonatal CRRT machine in 2019 as well as improved dialysis catheter technology. This information included in tables in a supplementary section.

Normally and non-normally distributed data were described and analysed using means and standard deviations or medians and interquartile ranges (IQR), respectively, with chi-squared, Wilcoxon sum rank, and Kruskal-Wallis tests used for comparisons, as appropriate. Missing data were not imputed. Analysis was performed using Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC and Microsoft Excel.

1.5.1 Ethics

This study complied with the ethical guidelines and principles of the Helsinki Declaration of 2008, South African Guidelines for Good Clinical Practice and the MRC Ethical Guidelines for Research and was approved by the Human Research Ethics committee of the University of Cape Town (Ethics approval UCT HREC Ref: 646/2015 [exp 28/2/2024]).

1.6 Results

The record keeping was paper based and retrospective with approximately 10% missing data.

1.6.1 Demographics of patients requiring dialysis for AKI

Over the study period, 593 children (55.0% male) with AKI received dialysis with 463(78.1%) receiving PD First for Paediatric AKI (Table 1.2). Their median age was 9.0 (range 0.03–219.3; IQR 1.3–69.6) months; most children (57.6%) were less than one year old. The median age for those who received PD only was 6.4 months vs. 73.9 months for those who received ECD only ($p<0.001$). Comparing modalities of dialysis, there was an even mix of neonates, infants and children receiving PD (27.6 – 36.1%) compared to ECD which was only done in 8% neonates, 16% in infants but 76% of bigger children. The weights of patients dialysed ranged from 0.9–62.0 kg (median 7.0 kg, IQR 3.0–16.0 kg). Almost 40% (38.6%) weighed <5kg, with 61.6% weighing <10kg, consistent with the age ranges. Importantly more than half (53.5%) of all patients dialysed, were under 1 year of age with a weight under 10 kg (58.6%). Overall, PD, 69.1% of patients receiving PD weighed less than 10kg whereas 52,3% of children receiving HD weighed over 20kg. From a clinical perspective, patients median weights remained relatively constant over the study period ranging from 6 to 10.8kg (Supplemental Table 2).

Table 1.2: Demographic and clinical details of patients requiring dialysis for acute kidney injury (AKI).

	N	Peritoneal dialysis	Extracorporeal dialysis	*p*-value
Male, n (%)	549	242 (55.3)	63 (56.8)	0.78
Age in months, median (IQR)	528	6.4 (0.92–30.4)	73.9 (17.5–133.9)	<0.001

Neonate, n (%)	134	126 (27.6)	8 (8.0)	<0.001
Infant, n (%)	182	166 (36.3)	16 (16.0)	
Child, n (%)	241	165 (36.1)	76 (76.0)	
Weight in kg, median (IQR)	502	6.0 (3.0–11.8)	20.0 (11.0–30.0)	<0.001
Weight <5 kg, n (%)	201	189 (46.0)	12 (11.0)	
Weight 5–9.9 kg, n (%)	106	95 (23.1)	11 (10.1)	
Weight 10–19.9 kg, n (%)	98	69 (16.8)	29 (26.6)	<0.001
Weight 20–29.9 kg, n (%)	52	31 (7.5)	21 (19.3)	
Weight 30–39.9 kg, n (%)	42	17 (4.1)	25 (22.9)	
Weight >40 kg, n (%)	21	10 (2.4)	11 (10.1)	
Underlying clinical condition resulting in acute kidney injury				
• Burns		6 (1.3)	1 (1.1)	0.98
• Cardiac medical [a] and surgical		137 (29.8)	5 (5.4)	0.23
• Encephalitis/meningitis		4 (0.9)	0	
• Necrotising enterocolitis		22 (4.8)	0	
• GIT medical		8 (1.7)	0	
• GIT surgical		10 (2.2)	5 (5.4)	0.74
• Liver/ Metabolic		28 (6.1)	11 (12.0)	0.53
• Haematology/Oncology		16 [b] (3.5)	21 [c] (22.8)	0.09
• Renal transplant		0	5 (5.5)	
• End stage kidney disease		24 (5.2)	17 (18.5)	0.17
• Haemolytic uraemic syndrome		36 (7.8)	2 (2.2)	0.77
• Other renal		22 (4.8)	13 (14.1)	0.33
• Respiratory		9 (2.0)	0	
• Sepsis/Shock [d]		122 (26.5)	6 (6.5)	0.27
• Trauma		5 (1.1)	5 (5.4)	0.70
• Miscellaneous		10 (2.2)	1 (1.1)	0.94
Survival	526	254 (55.6)	52 (75.4)	0.002

GIT, gastrointestinal tract

[a.] 9 had myocarditis, [b.] 2 had tumour lysis syndrome. [c.] 10 had tumour lysis syndrome
[d.] 9 had severe acute malnutrition with oedema

1.6.2 Conditions associated with dialysis-requiring AKI

The true prevalence of community vs. hospital acquired AKI cannot be ascertained from our data as these were all children admitted to PICU who required dialysis. The top five categories of conditions associated with AKI requiring dialysis in our study remained fairly constant over time (Supplemental Table 3). Medical and surgical cardiac conditions (n=145, 26.8%), primary kidney pathology (n=113, 20.9%), sepsis/septic shock requiring inotropic support (n=128, 24.4%), gastrointestinal conditions (n=59, 10.9%), and oncological disorders (n=30, 5.5%) (Table 1.2). Nine (1.6%) children had toxicity due to an administered toxin/traditional or other medication.

Children with burns or severe acute malnutrition with oedema had poor outcomes: 6 of 7 (85.7%) and 7 of 9 (77.0%) children with these respective conditions died. The most frequent indication for dialysis for kidney conditions was haemolytic uraemic syndrome (HUS) (n=38, 33.6%), while 41(36.3%) (had underlying chronic kidney failure (KF), and 9 (8.0%) had received a kidney transplant. Of those with a recorded Pediatric Index of Mortality (PIMS) score (n=327), the predicted mortality rates of around 10–12%.

1.6.3 Peritoneal dialysis modalities

The majority of children were commenced on dialysis in PICU although for 61(10%) children dialysis was initiated in the paediatric nephrology high care area while awaiting a bed in the PICU (Table 1.3).

Table 1.3: Mode of dialysis for paediatric AKI by study period, n (%).

Period	PD only			ECD only	PD and ECD	Total
	APD	MPD	APD+MPD			
1998–2003	46 (28.8)	110 (68.8)	0	2 (1.2)	3 (1.9)	161 (100)
2004–2009	62 (39.5)	72 (45.8)	2 (1.3)	18 (11.4)	3 (1.9)	157 (100)
2010–2015	28 (18/3)	82 (53.6)	4 (2.61)	37 (24.2)	1 (0.6)	153 (100)

2016–2020	18 (14.8)	38 (31.2)	1 (0.9)	57 (46.7)	8 (6.6)	122 (100)
Total	154 (26.0)	302 (50.9)	7 (1.2)	114 (19.2)	15 (2.5)	593 (100)

PD, peritoneal dialysis; ECD, extracorporeal dialysis; APD, automated peritoneal dialysis; MPD, manual peritoneal dialysis

PD consisted predominantly of manual PD, used more commonly in infants under 1 year, and automated cycling PD (requiring 5 kg weight in view of 100 mL fill volumes) used in older children. Overall, most children, 463 (78.1%) received only PD, with manual and automated PD being performed in 302 (65.2%) and 154 (33.3%) cases respectively, with a small number receiving both. Automated cycling PD machines were used in children over 5 kg in our setting for AKI which reduced the nursing workload related to manual PD.

1.6.4 Peritoneal dialysis catheter types and methods of insertion

Most PD catheters (n=480/578;83%) were inserted at the bedside using a Seldinger technique. These included 335/578 (60.9%) Cook® catheters (straight PD catheters and pigtail Fuhrman catheters), 145/578 (26.3%) peel-away PD catheters, and 45/578 (8.2%) surgical Tenckhoff PD catheters. Paediatric nephrologists/intensivists inserted 234 (47.8%) PD catheters and trainee nephrology fellows inserted 178 (36.3%) PD catheters under supervision as an essential part of their training. Surgeons inserted PD catheters in 78 (15.9%) cases either at the bedside or in the operating theatre.

1.6.5 Complications of peritoneal dialysis

The overall complication rate was 127/560 (22.7%) and included mainly technical problems including blockage or poor drainage (n=72, 56.7%), leakage (n=5, 3.9%), displacement of the PD catheter (n=6, 4.7%), pleural effusion secondary to PD (n=4, 3.2%), fungal peritonitis requiring discontinuation (n=3, 2.4%), and bladder perforation (n=2, 1.6%) not requiring surgical intervention.

There were no cases of bacterial peritonitis documented in this study. No bowel perforations were noted, but discoloured ascites on insertion alerted us to the presence of necrotic bowel or peritonitis requiring change in management in 7 (5.5%) cases. Where PD did not function adequately, ECD was used (n=17, 2.9%).

1.6.6 Extra-corporeal dialysis (including HD and CRRT) for AKI

For 113 (19.1%) children only ECD was used and for 17 (2.9%) both PD and ECD modalities were used as PD may not have been working optimally in terms of fluid removal; this occurred if one modality was unable to provide adequate dialysis (Table 1.3). There was a trend toward increasing use of ECD over time. Of the 130 children who received ECD with or without PD, the type of ECD used was recorded for 115, as follows: CRRT 47 (36.2%), Carpe Diem® CRRT Neonates 9 (6.9%), CRRT and HD 31 (23.8%), and HD only 28 (21.5%).

In the first 2 quartiles only 2 (1.2%, 1998–2003) and 18 (11.4%, 2004–2009) HD catheters used, compared to 37 (24.2%, 2010–2015) and 57 (46.7%, 2016–2020) HD catheters used in the last 2 quartiles studied.

1.6.7 Duration of dialysis

The AKI duration of dialysis was <5 days in 337 cases (56.8%), 5–7 days in 70 cases (11.8%), 8–14 days in 50 (8.4%) cases, >14 days in 47 cases (7.9%), and was not documented in 89 (15.1%) cases (Table 1.4).

Table 1.4: Survival proportions by dialysis modality and duration in paediatric patients with AKI.

	Survival proportions, n (%)		
Duration of dialysis	**Peritoneal dialysis**	**Extracorporeal dialysis**	***p*-value**
≤1 day	34 (28.8)	6 (50.0)	0.166
2–7 days	122 (60.4)	21 (72.4)	0.295
8–14 days	25 (67.6)	3 (60.0)	0.79
>14 days	13 (59.1)	15 (93.8)	0.028

Most children (n=407, 80.8%) were dialysed for 7 days or fewer. While a set lifespan for the use of acute PD catheters was not defined, we continued to use the inserted PD catheter for longer than 7 days in ~10% of children if the catheter remained functional while remaining vigilant for infection.

1.6.8 Survival of patients with AKI requiring dialysis

Overall, 314 (57.8%) children survived. The median age of those who survived was 11.2 (1.8–80.9) months; those who died had a median age of 4.8 (0.7–15.3) months (p<0.0001). Neonates and infants had poorer survival rates (47.5% and 49.2%, respectively) compared to older children (70.4%, p<0.0001). Similarly, survival was worse in the lowest weight category (<5kg, 47.6%) and higher in the patients over 40kg (70.0%, p<0.0001) (Table 1.5).

Table 1.5: Survival proportions by dialysis modality and patient weight in paediatric patients with AKI.

	Survival proportion, n (%)		
Weight	**Peritoneal dialysis**	**Extracorporeal dialysis**	***p*-value**
<5kg	88 (46.6)	7 (70.0)	0.23
5–9.9kg	48 (50.5)	4 (57.1)	0.80
10–19.9kg	43 (62.3)	10 (76.9)	0.38
20–29.9kg	20 (66.7)	10 (76.9)	0.56
30–39.9kg	15 (88.2)	13 (86.7)	0.90
>40kg	7 (70.0)	7 (77.8)	0.74
Total	221 (54.3)	51 (76.1)	0.003

Survival was significantly better in the group who received ECD only compared to those who received PD only (55.6% vs 75.4%, p=0.002). Survival remained relatively stable over time and by modality (Table 1.6). Five children with AKI developed chronic kidney disease.

Table 1.6: Survival of paediatric AKI patients per modality over time.

Period	Survival, n (%)				
	PD only	**ECD only**	**PD and ECD**	**p-value**	**Total**
1998–2003	89 (57.4)	-	1 (25.0)	0.17	90 (56.6)
2004–2009	74 (55.6)	1 (100)	2 (67.7)	0.63	77 (56.2)
2010–2015	61 (54.0)	14 (73.7)	1 (50.0)	0.27	76 (56.7)
2016–2020	30 (53.5)	37 (75.5)	4 (50.0)	0.05	71 (62.8)
Total	254 (55.6)	52 (75.4)	8 (47.0)		314 (57.8)
					p for trend = 0.73

PD, peritoneal dialysis; ECD, extracorporeal dialysis

1.6.9 Paediatric Index of Mortality (PIM) scoring in PICU

Most of the children in this study were critically ill with unfavourable PIM scores as an indicator of the severity of their illness and to calculate their standardized mortality ratio. In view of the long period of the study (1998–2020), comparing actual PIM scoring was difficult, as over this period there was an evolution of 3 PIM scoring systems. Of those with a recorded PIMS score (n=327), the predicted mortality rates of around 10–12%.

Nonetheless, despite most of the patients requiring dialysis were severely unwell with predicted mortality rates of around 10–12%; actual mortality was in the region of 5–7%.

1.7 Discussion

Substantial progress has been made over the past few years in kidney replacement technology to permit dialysis for even the smallest neonate. Unfortunately, access to dialysis facilities for children with AKI are absent in many LMIC's, leaving conservative management including diuretics as the only option, which may have deleterious outcomes [32].

A successful PD First policy in adult chronic dialysis has been well described with 3 important elements of a successful program including nephrologist experience and expertise, PD catheter access and psychosocial support [16-18].

In this study we present a large series of children with AKI managed predominantly with PD First for Paediatric AKI as the main form of dialysis over a 20-year period in a middle-income African country. This cumulative experience has allowed us to become trailblazers in this field, especially with paediatric nephrologists gaining experience in the bed-side insertion of soft PD catheters inserted using the Seldinger technique.

Elements identified as important in a successful PD-First program includes: nephrologist experience and expertise, PD Catheter access and psychosocial support for PD Patients (especially for those requiring chronic PD) [16].

Given that RCWMCH is a tertiary-quaternary hospital we have had increasing access over time to use of other dialysis modalities when PD was not clinically possible, including the Carpe Diem® Neonatal CRRT machine. We therefore also highlight our experiences with improved techniques of dialysis, showing that this transition may be possible in other lower resource settings in the coming years.

At RCWMCH, half of all 1400 annual PICU admissions are for infants <1 year of age. The dialysis numbers for AKI reflect this in that more than half of the patients who received dialysis were under 1 year of age with a weight <10 kg. PD was used predominantly in infants with median age of 6.4months and median weight of 6.0kg compared to ECD used in children with a median age of 73.9months and median weight of 20kg.

As a tertiary-quaternary hospital, around a quarter of patients requiring dialysis were children with cardiac conditions. This is different to other less well-resourced centres around the world [23] and mimics high income settings as reflected in the AWARE and AWAKEN studies [33-37].

The commonest conditions associated with AKI in our setting included cardiac causes followed by primary kidney pathology, predominantly HUS. The requirement for dialysis in sepsis/shock appears to have declined over time (Supplementary Table 3), which may be due to earlier recognition and appropriate treatment of sepsis/shock or in its reduction in part due to expanded immunisation schedule and/or improved socioeconomic conditions. Oncology patients still account for a number of dialysis cases as, despite the introduction of Rasburicase for tumour lysis syndrome with a resultant reduced AKI risk, there is an increasing stem cell transplant population with sepsis that requires dialysis. PIM scoring could not be included in the analysis due to the 3 different PIM scoring systems during the study period, but patients had a high predicted mortality scoring.

Peritoneal dialysis remains our first line dialysis therapy unless there are extreme surgical abdominal issues such as an open postoperative abdomen. As we employ a PD First in Paediatric AKI program that uses an 'Acute/Urgent start' approach, our nurses are PD trained in keeping with many centres in the world, where staff are more comfortable with providing PD than ECD [11, 23, 24].

The modalities of PD included manual PD predominantly for infants under 1 year, and automated cycling PD in older children. In manual PD, a group of infants received continuous flow PD with improved clearances, therefore future plans will include in this modality in training for LMIC's [38].

The use of automated cycling PD machines for children requiring dialysis for AKI (compared with chronic PD) is also a novel way of relieving staff pressures in a PICU setting. Locally produced PD fluid is a safe alternative to commercial PD fluid for regions where commercial fluid is unavailable [12–15].

PD is especially suited to neonates and infants where venous access is challenging, as well as for postoperative cardiac patients where surgeons may place PD catheters at the end of cardiac surgical procedures [39].

Catheters used for PD were mainly Seldinger Cook® or Peelaway catheters inserted at the bedside by the paediatric team (nephrologists/intensivists or fellows under supervision), with surgical backup needed in a minority of mainly complex cases. Custom made Cook® straight PD catheters have been discontinued and we have successfully used Fuhrman Cook® Pigtail catheters as an alternative. This is important in LMIC where surgeons may not readily be available, however in high income countries, this will also have an impact on expediating dialysis initiation, as well as freeing up surgical and operating theatre time for other non-renal conditions. Technical problems related to catheter leakage, blockage, or dislodgement were managed practically with surgical glue to leaking catheter sites and re-wiring/replacement of PD catheters at the bedside.

This study also highlights a training opportunity for paediatric nephrology fellows, teaching them to insert PD catheters under the supervision of paediatric nephrology consultants; relatively few complications were documented if the protocol was followed. This also allowed for catheter training in cases requiring continuous flow PD [38]. As seen in adult studies, there did not appear to be any safety concerns with non-surgical nephrologists placing PD catheters at the bedside, provided that existing protocols were followed specifically urethral catheter placement, prior to PD catheter insertion [15]. Use of bedside bladder ultrasound to ensure an empty bladder and visualise bowel on insertion of PD catheter and avoid bowel perforation is now our recommendation. Although no bowel perforation needing surgical intervention was reported, the presence of pre-existing discoloured ascitic fluid at time of catheter insertion, either infected (suggesting peritonitis) or discoloured fluid (suggesting pre-

existing bowel necrosis/perforation), resulted in change of management that included antibiotic administration or surgical referral.

Peritonitis rates were very low likely due to attention to detail in providing strict aseptic technique at the bedside – 'bringing theatre to the bedside'. In addition, many patients were already on systemic antibiotics for their underlying conditions leading to AKI. In rare cases where peritonitis was diagnosed, this was treated with intraperitoneal antibiotics without removal of the acute PD catheters, in the same way as endotracheal tubes are not removed in the diagnosis of ventilator-associated pneumonia. The exception was for fungal peritonitis episodes where acute catheters were removed, and systemic antifungal treatment initiated.

The use of PD declined over the duration of the study (p for trend = 0.08) from 96.9% in the first quartile to 46.7% in the last quartile. This likely reflects improved availability of access to ECD machines in our setting, especially for neonates through acquisition of the Carpe Diem® machine. Neonates being referred for dialysis may also have had more abdominal pathology precluding the use of PD [40]. These neonates would previously have died without the benefit of a trial of dialysis. Consequently, significant in-service training was required for the medical teams (doctors, technologists, and nurses) comfortable with PD but requiring upskilling in the provision of ECD, especially for smaller children. Additionally, HD catheters more suitable for infants are now available. Experience has grown but with resultant dialysis cost implications [41-43].

Overall, the mortality rate in our study for paediatric AKI patients requiring dialysis was 41% which is comparable to other LMIC centres such as reported in Thailand (41.5%) [44] and in India (36.8%) [45].

However, when comparing the mortality of our patients on dialysis, it is not that different from those patients with acute severe kidney injury requiring dialysis from the AWARE study, but to note that the populations are very different [46].

A systematic review from sub-Saharan Africa showed that mortality in children with AKI who received dialysis was 30% compared to 74% in those who did not receive dialysis [8]. Relevant here may be that children in LMIC often present much later for medical care and thus it is difficult to compare outcomes. Small infants may also not be dialysed or might only be dialysed for a limited time period, such as 5 days, if parents have to pay for this out-of-pocket [47].

In our study, lower survival was seen in neonates and infants under 1 year of age compared to older children (47.5% vs. 70.4%, $p<0.0001$; Supplemental table 5) as well as those in the lower weight categories (47.6% vs. patients over 40 kg (70.0%, $p<0.001$; Table 1.5).

These younger and smaller children were predominantly dialysed with acute PD, suggesting a higher mortality on PD. However, these findings taken together reflect that these younger and smaller patients were sicker, but also more difficult to dialyse historically due to lack of availability of all forms of dialysis equipment for small babies. The question remains whether PD is inferior to ECD, but this also depends on availability as PD, is more accessible and affordable. Future studies need to be designed to address outcomes of PD technique vs. patient selection.

In our centre, most children would have access to dialysis for AKI but not all qualify for chronic treatment (dialysis and transplant); some are offered a palliative care route after a multidisciplinary assessment. However, in this study, only a small proportion needed dialysis for more than 14 days and developed chronic kidney disease, suggesting that it is worthwhile to treat AKI in as many patients as possible even with limited resources, especially when there are no obvious features to suggest underlying chronic kidney disease, to give everyone a chance. Ideally all children who recover from AKI should be followed up in a nephrology clinic to assess completeness of recovery and/or the need for follow up of those who may develop chronic kidney disease.

In the last 5 years, there has been an overall trend towards improved survival (66.3%; Table 1.2). Multiple reasons may underlie this observation, including earlier referral and commencement of dialysis, as well as the availability of ECD for small infants that was not previously available. On review of the survival per modality, PD carried a 44.4% mortality compared with mortality of 24.6% on ECD (p=0.002). This may reflect better outcomes in the bigger patients for which CRRT was possible.

1.7.1 Limitations

Our study has several strengths and limitations including the paper-based record keeping with approximately 10% missing or incomplete data. In addition, despite our cohort being large by paediatric standards, it remains a single centre study from a less well-resourced region and thus has limited generalizability. PIM and AKI scoring such as the Kidney Disease: Improving Global Outcomes (KDIGO) score were not possible to determine retrospectively. Similarly, biomarkers such as urinary neutrophil gelatinase-associated lipocalin [37] were not available, thus we were unable to analyse the impact of severity of AKI on the outcomes of dialysis-treated AKI in our cohort. South Africa's dialysis registry does not capture children who were not deemed eligible for dialysis, therefore any assessment of incidence of AKI in our setting is not possible, and it is unknown whether this may have changed over time.

We do not currently have a PICU follow-up clinic but some of these patients do filter through to the renal clinic for follow-up. The long-term outcomes of the children reported here therefore remain unknown.

1.7.2 Strengths

This study does have significant strengths however, in that it has similar numbers to that of Abdelraheem from Sudan [24] and is one of the first of its kind to report a 20-year review of dialysis of children in Africa. The data collection was largely complete and included details on catheter types and dialysis techniques which are infrequently reported. Specifically, we analysed trends over time and found that the use of PD First for Paediatric AKI, with soft PD catheters inserted with Seldinger technique by nephrologists/trainees under supervision at the patient's bedside, is safe, feasible and successful and can be conducted with simple infrastructure. This should be encouraging to colleagues in similar settings who are beginning to scale up acute dialysis for children with AKI. When done carefully, PD does not need to be considered second best. Cost analyses of PD vs. ECD is beyond the scope of this study and will be reported on separately.

1.7.3 Recommendations

- Starting a 'PD First program for Paediatric AKI' is lifesaving even in the absence of commercially produced PD catheters fluids and formal surgical expertise.
- Acute PD can be applied in a wide size range of paediatric patients including small neonates.
- Perform Acute Start PD at the bedside using Seldinger inserted soft drainage catheters or peelaway Tenckhoff catheters with immediate commencement of PD.
- With custom made Cook® straight PD catheters being taken off the market, Cook® Pigtail (Fuhrman) catheters, although not officially licensed for PD, can been used safely and successfully.
- Perform bedside ultrasound at time of PD catheter insertions to ensure empty bladder and identify bowel.
- Non-surgically trained personnel including paediatric nephrologists/intensivists can insert PD catheters at the bedside in appropriate patients if trained correctly.
- The duration of PD with catheters inserted at the bedside can exceed 7 days provided sterile techniques are adhered to and there is infection surveillance.
- As PD programs develop, encourage advocacy for access to more advanced ECD dialysis facilities for patients where PD may not be possible.
- Establish an electronic data collection system for an PD First for Paediatric AKI program.

Evaluation of the economics of PD vs HD/CRRT is urgently required.

Long term follow-up clinics for these graduates of AKI therapy is also required but needs appropriate manpower.

In 2013, the International Society of Nephrology launched the “0 by 25” campaign with the goal that no patient should die from preventable or untreated AKI in low-resource areas by 2025 [48]. This paper aims to assist colleagues in other LMIC to achieve this goal, even in the absence of expensive equipment and consumables.

1.8 Conclusion

‘PD First for Paediatric AKI’ remains a valuable acute/urgent start modality for management of AKI in children, especially in less well-resourced regions where it is possible to safely teach the Seldinger technique of insertion of PD catheters at the bedside using pigtail catheters or peel away technology. Internationally, even in well-resourced countries, with the discontinuation of custom-made Cook® straight PD catheters, we have shown that Cook® Pigtail (Fuhrman) catheters, have been used successfully, this may solve the current shortage crisis.

As PICU and/or high care units become more established in less well-resourced regions and access to equipment for small children (including HD catheters and paediatric CRRT machines) become increasingly available, practice does change. However, this should not prevent those in regions who do not have access to this kind of equipment from using PD, as it has shown an acceptable survival rate in children with AKI.

Rather than attempting no intervention in children with AKI when ECD is not available, providing PD acutely using improvised equipment and PD fluid is both possible and lifesaving.

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1.10 Appendices

Supplemental Table 1: Dialysis machines used for AKI over the study period.

Peritoneal Dialysis		Extracorporeal Dialysis	
Manual	Automated	Haemodialysis	CRRT
Improvised Baxter products 1996–2010	PacXtra 1998–2002	Fresenius 4008B 2001–present Fresenius 4008S 2008–present	Gambro AK10 1999–2003 Baxter BM25 2004–2012
Fresenius PD Paeds system, 2010	Homechoice 2002–2018	Fresenius 5008 Paeds 2014–present	Fresenius Multifiltrate 2012–present
CFPD Automated BM25/manual 2008–2014	Claria 2018–present		Carpe Diem 2019–present

PD, peritoneal dialysis; CFPD, Continuous Flow Peritoneal Dialysis, CRRT, Continuous Renal Replacement Therapy

Supplemental Table 2: Demographic details of patients requiring dialysis for AKI, stratified by study period.

	N	**1998–2003**	**2004–2009**	**2010–2015**	**2016–2020**	**p-value**
Sex, male	522	83 (53.9)	70 (51.9)	79 (61.2)	54 (51.9)	0.387
Age in months, median (IQR)	502	6.6 (1.1–38.2)	9.1 (1.2–34.2)	5.3 (0.8–45.3)	13.1 (2.6–112.3)	0.009
Neonate, n (%)	140	37 (23.6)	35 (25.6)	44 (32.8)	24 (20.9)	0.080

Infant, n (%)	177	60 (38.2)	44 (32.1)	42 (31.3)	31 (26.9)	
Child, n (%)	226	60 (38.2)	58 (42.3)	48 (35.8)	60 (52.2)	
Weight in kg, median (IQR)	475	6.0 (2.6–12.0)	7.0 (3.3–12.8)	6.0 (3.0–13.0)	10.8 (4.0–28.0)	<0.001
<5kg, n (%)	195	57 (47.9)	47 (35.6)	60 (48.0)	31 (29.3)	
5–9.9kg, n (%)	102	20 (16.8)	42 (31.8)	23 (18.4)	17 (16.0)	
10–19.9kg, n (%)	85	23 (19.3)	23 (17.4)	19 (15.2)	20 (18.9)	0.001
20–29.9kg, n (%)	45	6 (5.0)	11 (8.3)	13 (10.4)	14 (13.2)	
30–39.9kg, n (%)	35	9 (7.6)	4 (3.8)	7 (5.6)	9 (13.9)	
>40kg, n (%)	20	4 (3.4)	4 (3.0)	3 (2.4)	9 (8.5)	

Supplemental Table 3: Underlying conditions of paediatric patients leading to AKI requiring dialysis, stratified by study period.

	1998-2003	2004-2009	2010-2015	2016-2020	Total
Burns	2 (1.3)	2 (1.5)	3 (2.3)	0	7 (1.3)
Cardiac	35 (22.0)	48 (33.6)	36 (25.7)	26 (23.3)	145 (26.2)
- medical	14 (40.0)	10 (20.8)	10 (27.7)	3 (11.5)	
- surgical	21 (60.0)	38 (70.2)	26 (72.2)	23 (88.5)	
Encephalitis/meningitis	2 (1.2)	2 (1.4)	0	0	4 (0.7)
GIT NEC	12 (7.5)	2 (1.4)	7 (4.9)	1 (0.9)	22 (4.1)
GIT medical	11 (6.9)	6 (4.4)	2 (1.5)	1 (0.9)	20 (3.7)
GIT surgical	5 (3.1)	2 (1.5)	3 (2.3)	7 (6.3)	17 (3.1)
Liver	2 (1.2)	5 (3.7)	3 (2.3)	3 (2.7)	13 (2.4)
Metabolic	7 (4.4)	10 (7.3)	6 (4.5)	5 (4.5)	28 (5.2)
Oncological	9 (5.6)	5 (3.5)	11 (7.6)	10 (8.6)	35 (6.2)
- tumour lysis syndrome	4 (44.5)	3 (60.0)	7 (63.6)	3 (30.0)	
Other	2 (1.2)	0	0	2 (1.7)	4 (0.7)
Renal	31 (19.2)	25 (17.5)	26 (18.1)	39 (33.6)	121 (21.5)
- renal transplant	0	1 (4.0)	2 (7.7)	6 (15.4)	
- ESKD	0	4 (16.0)	3 (11.5)	6 (15.4)	
- HUS	10 (32.2)	12 (48.0)	9 (36.0)	8 (20.5)	
Respiratory	1 (0.6)	2 (1.4)	5 (3.5)	1 (0.9)	9 (1.6)
Rheumatology	1 (0.6)	1 (0.7)	2 (1.4)	1 (0.9)	5 (0.9)
Sepsis	36 (22.6)	20 (14.0)	30 (20.8)	15 (12.9)	101 (17.9)
Shock	10 (6.2)	13 (9.1)	6 (4.2)	0	29 (5.1)
Trauma	4 (2.5)	1 (0.7)	3 (2.1)	2 (1.7)	10 (1.8)
Total	161 (100)	143 (100)	144 (100)	116 (100)	570 (100)

AKI, acute kidney injury; GIT, gastrointestinal tract; NEC necrotising enterocolitis; ESKD, end-stage kidney disease; HUS, haemolytic uraemic syndrome

Supplemental Table 4: Survival of paediatric AKI patients per modality over time.

	Survival, n (%)				
Period	**PD only**	**ECD only**	**PD and ECD**	**p-value**	**Total**
1998–2003	89 (57.4)	-	1 (25.0)	0.17	90 (56.6)
2004–2009	74 (55.6)	1 (100)	2 (67.7)	0.63	77 (56.2)
2010–2015	61 (54.0)	14 (73.7)	1 (50.0)	0.27	76 (56.7)
2016–2020	30 (53.5)	37 (75.5)	4 (50.0)	0.05	71 (62.8)
Total	254 (55.6)	52 (75.4)	8 (47.0)		314 (57.8)
					p for trend =0.73

PD, peritoneal dialysis; ECD, extracorporeal dialysis

Supplemental Table 5: Age of paediatric AKI patient receiving dialysis by survival (p<0.0001).

Age	Alive	Died	Total
Child (> 1 year)	157 (70.4)	66 (29.6)	223 (100)
Infant (<1 year)	88 (49.2)	89 (50.3)	177 (100)
Neonate (<1 month)	66 (47.5)	73 (52.5)	139 (100)
Total	311 (57.7)	228 42.3)	539 (100)

2 Chapter 2: Lessons learned from regional training of paediatric nephrology fellows in Africa

2.1 Overview

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2.2 Abstract

Background: Access to care for children with kidney disease is limited in less well-resourced regions of the world and paediatric nephrology (PN) workforce development with good practical skills is critical.

Method: Retrospective review of a PN training program and trainee feedback from 1999 to 2021, based at Red Cross War Memorial Children's Hospital (RCWMCH), University of Cape Town.

Results: A regionally appropriate 1–2-year training program enrolled 38 fellows with an initial 100% return rate to their country of origin. Program funding included fellowships from the International Pediatric Nephrology Association (IPNA), International Society of Nephrology (ISN), International Society of Peritoneal Dialysis (ISPD), and the African Paediatric Fellowship Program (APFP). Fellows were trained on both in- and out-patient management of infants and children with kidney disorders. "Hands-on skills" training included examination, diagnosis and management skills, practical insertion of peritoneal dialysis catheters for management of acute kidney injury and kidney biopsies. Of 16 trainees who completed > 1 year of training, 14 (88%) successfully completed subspecialty exams and 9 (56%) completed a master's degree with a research component. PN fellows reported that their training was appropriate and enabled them to make a difference in their respective communities.

Conclusion: This training program has successfully equipped African physicians with the requisite knowledge and skills to provide PN services in resource-constrained areas for children with kidney disease. The provision of funding from multiple organizations committed to paediatric kidney disease has contributed to the success of the program, along with the fellows' commitment to build PN healthcare capacity in Africa.

Keywords *Kidney disease; Pediatric nephrology fellows; Training; Hands-on; Acute kidney injury; Dialysis.*

2.3 Introduction

Access to care for adult patients with kidney disease is a challenge in less well-resourced communities [1] around the world and this situation is particularly bad for African children and adolescents with kidney disease, for whom even basic management resources for treatment of acute kidney injury (AKI) is often not available [2]. Regions in Sub-Saharan Africa, with an estimated population of 430 million children in 2015, face the same increases in demand for health services to address the "triple burden of disease" (communicable and non-communicable diseases and injury) along with extremely challenging social determinants of health (e.g., undernutrition; lack of access to education; problems related to globalization) [3].

A well-trained healthcare workforce is critical to optimize healthcare in less well-resourced countries and to achieve the sustainable development goals. In this context, training a paediatric specific nephrology workforce is critical to meet the increasing worldwide burden of kidney disease [4].

The availability of nephrologists who are able to provide care for individuals with kidney disorders is much higher in high income countries (HIC) compared to low income countries (LIC) [4]. Riaz et al. [5] reported a global nephrologist density of 10.0 per million population (pmp) and a nephrology trainee density of 1.4 pmp; however, the distribution of these human resources is highly variable, with LIC reporting nephrologist and nephrology trainee densities of 0.2 pmp and 0.1p mp compared to HIC densities of 23.2 pmp and 3.8 pmp, respectively. African and South Asian regions do not have a workforce that is sufficient to meet current clinical needs or one that is sustainable with the potential for population growth. A recent publication [6] has predicted an insufficient number of adult nephrologists globally by 2030, unless there is an increase in funded training posts and posts for qualified nephrologists in the public sector. The situation in paediatric nephrology is even more concerning [7]. The shortages in the nephrology workforce can be attributed to many factors, including limited physician training capacity [8] and migration of skilled workers across and between regions [9].

Various organizations have attempted to address some aspects of this problem by training nephrologists for adult practice. For instance, as part of its building capacity and outreach initiative, the International Society of Nephrology (ISN) has a fellowship program in which trainees travel to an advanced nephrology center to obtain skills and training and then return to their home country to practice [10–12]. In addition to enhanced patient care, positive impacts of the fellowships have included continuing medical education (CME), sister kidney centers (nephrology units in emerging economies teaming up with a supporting center), and clinical research educational ambassadors (receiving expert guidance and teaching) [10].

Physicians from low- and middle-income countries (LMIC) who undergo paediatric and adult nephrology training in high resource areas such as North America and Europe, however, often face many challenges upon returning to their countries of origin. These can include an inability to apply what they learned or experienced as a result of differences in disease patterns, poor availability of equipment, as well as a lack of support from management, administration, and even colleagues [10, 13, 14]. For example, there may be a lack of paediatric nephrology (PN) training in the management of endemic conditions such as AKI due to gastroenteritis and sepsis, and clinical skills are usually taught using highly specialized equipment and consumables that are not available in many African centers. In addition, due to regulations surrounding registration for clinical practice, many fellows training outside of Africa, cannot participate fully in “hands-on training” including performing kidney

biopsies and bedside insertion of acute peritoneal dialysis (PD) catheters and hemodialysis (HD) lines. Following training, many frustrated doctors may, in turn, not return to their countries of origin, further compromising the nephrology workforce.

Currently, South African regulations allow limited registration for fellowship trainees, which enables “hands-on” clinical practice under supervision in training institutions such as the Red Cross War Memorial Children’s Hospital (RCWMCH), situated in Cape Town. This center has developed a number of inexpensive and readily available improvisational interventions and devices that can be taught to African trainees to apply within their home settings [15, 16]. These include the use of multipurpose catheters, central lines, and chest drains, or nasogastric tubes for peritoneal dialysis (PD) access, in addition to locally made PD fluid [17, 18]. In the early 2000’s, the International Pediatric Nephrology Association (IPNA) approved Red Cross War Memorial Children’s Hospital (RCWMCH), University of Cape Town (UCT), as one of the first training centers for paediatric nephrology (PN) in a less well-resourced country and committed to funding a number of individual 6 to 24-month nephrology training fellowships. The ISN and the International Society for Peritoneal Dialysis (ISPD) have subsequently also assisted in providing pediatric nephrology fellowship funding, despite being predominantly adult programs. Very little has been published about paediatric nephrology fellowship training as a strategy to expand the nephrology workforce in LMIC. This paper aims to describe a paediatric nephrology training program within an African setting. Most of the fellows described in this paper originate from countries where AKI is common due to acute diarrhoeal diseases and infections including malaria.

Chronic kidney disease (CKD) is common in their countries as a result of undiagnosed congenital kidney pathology due to a lack of antenatal screening and the poor availability of genetic services. In addition, chronic dialysis and transplantation has only been an option for children in a few countries in Africa. Finally, with the exception of South Africa, most of the other Sub-Saharan African countries require self-funding by families for the care of patients with paediatric kidney diseases, but prior to our training program, almost no pediatric nephrology services were available in Sub-Saharan Africa.

2.4 Materials and Methods

This paper presents a descriptive audit of the development, curriculum, funding support, outputs, and experience of a paediatric nephrology (PN) fellowship training program between 1999 and 2021.

2.4.1 Study Site

The training program was initiated and largely conducted at the Red Cross War Memorial Children's Hospital (RCWMCH), Cape Town, South Africa. RCWMCH is a dedicated tertiary level, 300-bed paediatric hospital with a 12-bed paediatric nephrology and transplant unit providing care for 400 in-patients per year and 2000 outpatients. The hands-on training includes instruction on kidney biopsies, bedside insertion of acute PD catheters and all forms of acute and chronic kidney replacement therapy (KRT) for patients ranging from infants to adolescents in the nephrology unit, as well as in the 30-bed paediatric intensive care unit and neonatal high care. Senior nephrology staff consisted of 2–3 consultants over the study period, who provided all training. Whereas most of the training occurred at RCWMCH, training also occurred at the PN Unit at Tygerberg Hospital/University of Stellenbosch and in the adult tertiary center, Groote Schuur Hospital (GSH).

RCWMCH and GSH started an adolescent nephrology service in 2002, which was a relatively new concept and is still the only one of its kind in South Africa. Our fellows were also able to spend some time in this clinic learning how to manage adolescents with kidney problems and how to transition what they learned upon their return to their home institutions. We would hope that this would inspire paediatric and adult nephrologists to work more closely together (as occurs in ISN) and to set up similar programs with comparable content across Africa (context of training in paediatric nephrology training Supplemental Appendix 1). In addition, 5 adult nephrology trainees from the GSH Adult Nephrology Department spent 1 month in the pediatric training program at RCWMCH following the completion of their adult nephrology sub-speciality examinations. This was intended to provide them with skills to manage children with kidney diseases in addition to their adult patients upon return to their home institutions in regions where paediatric nephrology care was not available.

2.4.2 Participants

All individuals who participated in PN training were included in this review. For acceptance into the training program, fellows had to meet well-defined criteria including having completed training in general pediatrics; no prior formal training in pediatric nephrology; and approval of the application by the IPNA fellowship committee.

2.4.3 Data collection and analysis

Data obtained include details of all individuals who participated in PN training at the study site, including gender, country and institution of origin, period of training, and whether any PN tertiary qualifications were achieved. All African PN fellows from outside South Africa also completed a survey on completion of their training (Supplement Appendix 2).

The themes addressed included pre- and post-training work opportunities, and areas of training that were deemed particularly useful, including specific skills and exposure to multidisciplinary teams. Experiences with hands-on training opportunities were also explored.

2.4.4 Funding

Funding for the training program originated from three main sources: the IPNA and the ISN, both of which provided 1–2 years of funding per trainee, and the ISPD which provided funding for shorter durations of training (3 months).

Locally, the African Fellowship Program/Children's Hospital Trust (APFP/CHT) provided substantial administrative and moral support for all fellowship programs, as well as additional funding in cases where there was a shortfall.

2.4.5 Ethics

This study complied with the ethical guidelines and principles of the Helsinki Declaration of 2008, South African Guidelines for Good Clinical Practice, and the MRC Ethical Guidelines for Research and was approved by the Human Research Ethics Committee of the University of Cape Town (Ethics: 646/2015). Fellows completing the questionnaire consented to the publication of the information provided.

2.5 Results

2.5.1 Training Content

All fellows received comprehensive training in theoretical and clinical/practical aspects of paediatric nephrology, complemented by hands-on clinical training with prioritization of the management of AKI. A formal syllabus and weekly timetable were developed to address the educational content of the fellowship experience (Supplement Appendix 3). Fellows could attain paediatric nephrology levels 1 and 2 training competence based upon the training content (Supplement Appendix 4).

Ultimately, there is potential for the development of a common paediatric kidney training syllabus across the African continent.

2.5.2 Study population and demographics

A total of 38 paediatric nephrology fellows were trained at RCWMCH from 1999 to 2021. Eleven (28.9%; 5 male) fellows were from South Africa (SA), with all but one funded by local provincial funding. Eight of the SA fellows were from the Western Cape province and three were from other SA provinces. All completed 2 years of training and achieved their PN sub-specialty accreditation. All but three SA fellows returned to

their original centers, two of whom are working in private practice due to a shortage of public hospital posts, but remain as honorary lecturers for UCT/RCWMCH. Twenty-seven (71.1%; 14 male) fellows were from twelve anglophone African countries outside SA. The country of origin of the fellows is listed in Table 2.1.

The program has trained an average of 2 PN fellows per year overall, with the number increasing to 3 in the last 5 years. A total of 28 fellows from Africa have been trained (Supplement Appendix 5). The sources of funding for training are described in Table 2.2. The PN fellows from outside SA (African fellows) have had varied sources of funding, with IPNA and ISN supplying the majority of funds.

Table 2.1: Fellows country of origin.

Country of origin	Number of fellows
South Africa	11
Nigeria	11
Kenya	4
Ghana	2
Uganda	2
Zambia	2
Benin	1
Botswana	1
Libya	1
Sudan	1
Tanzania	1
Zimbabwe	1

Table 2.2: Funding sources for training

Funding source	Number of fellows*
IPNA (International Pediatric Nephrology Association)	24
ISN (International Society of Nephrology)	13
ISPD (International Society of Peritoneal Dialysis)	2
APFP (African Paediatric Fellowship Program)	8
Own funding	2 (Komfo Anokye Hospital, Ghana; Beit Fellowship Zambia)

* Some fellows were dual-funded

2.5.3 Impact of COVID

During the worldwide COVID-19 pandemic, the PN fellows continued their training at the RCWMCH uninterrupted. They were educated about the risks of COVID, provided with the required personal protective equipment (PPE) and afforded the same medical facilities as the local doctors, including access to COVID-19 testing and vaccines. The presence of COVID-19 did, however, preclude travel to their countries of origin for prolonged periods of time and compromise any short rotations to the adult hospitals, potentially impacting on the clinical experience gained in adult nephrology.

2.5.4 Duration of training

The duration of fellowship training for the African PN fellows varied, largely dependent on available funding. The training period was divided into two consecutive periods for analytical purposes: 2003–2012 (period 1) and 2013–2021 (period 2). Twelve African PN fellows were trained in the first period and 16 in the second period. During the first period, African PN fellows trained for a shorter duration with a mean of 11.9 (median 12) months; while training during the second period was longer with a mean and median training time of 18.4 and 23 months, respectively. The duration of training for the African Pediatric Nephrology fellows is documented in Table 2.3.

Table 2.3: Duration of PN training for African PN fellows.

Length of time (months)	Number of fellows	
3	1	12 months or less (n = 12)
6	5	
12	6	
15	3	15–24 months (n = 16)
18	5	
24	8	

2.5.5 Qualifications achieved

Qualifications obtained by PN fellows during training included a post-graduate diploma in PN (University of Cape Town 1-year program) or a sub-specialty certificate in pediatric nephrology (College of Paediatrics of South Africa – USA board certification equivalent), which required at least 18–24 months of supervised training at RCWMCH to be eligible to sit for the written, oral, and OSCE exam. Many of the African PN fellows now require a recognized qualification to return to their home institution for positions of leadership either at their universities or their hospitals. Of those fellows who completed ≤ 12 months training, only 3/12 (25%) completed a diploma in PN, whereas 14/16 (88%) fellows training for > 15 months graduated with a sub-specialty certificate in PN.

African PN fellows training at RCWMCH for more than 12 months can register with the University of Cape Town for a Master's in Philosophy degree, which uses the College of Paediatric Certificate as the clinical examination and requires an additional research component. Nine (56%) African PN fellows, all of whom trained for > 18 months, achieved this MPhil degree, re-affirming that 18 months was the minimum time required for optimal clinical and research training.

2.5.6 Research

Research is encouraged as part of the training, but has not always been possible for short fellowship training periods, as acquisition of hands-on clinical skills takes precedence.

Fellows who received more than 1 year of funded training were able to engage in research including topics such as patient audits of posterior urethral valves, pelvi-ureteric junction obstruction, crescentic nephritis, vitamin D status in CKD, drop out from chronic peritoneal dialysis, aminophylline affect on urine output, tuberculosis in paediatric kidney transplants, review of urodynamic studies, acute post-streptococcal glomerulonephritis, and severity of deranged electrolytes and kidney function.

2.5.7 Social factors

A majority of the fellows (n = 25; 92.6%) were unable to see their families for the full duration of training. Only three of the fellows were able to bring their families to Cape Town with them. This is evidence of the commitment and dedication the fellows had with respect to learning and the provision of service to children with paediatric nephrology disorders in their home countries.

2.5.8 Fellowship follow-up

All 27 (100%) of the African PN fellows initially returned to their countries of origin for at least 2 years, supporting the concept of training "in Africa for Africans." Subsequently, two PN fellows emigrated—one went to the Middle East in view of an unstable political situation in their home country, and the other moved to the UK as their partner was transferred there. Thus, 94.7% of trained African fellows remain in their home countries.

2.5.9 Post-training survey results

A voluntary survey was sent to all PN fellows coming from outside of South Africa following the completion of their training with a 100% (28/28) return rate (Supplement Appendix 2). Work positions changed in all cases to a more senior position once fellowship training was completed with a number becoming heads of departments in their hospitals (n = 4), lecturers in their universities (n = 18), and vice dean (n = 1).

2.5.10 Time dedicated to paediatric nephrology

Upon completion of fellowship training, the percentage of work effort dedicated to PN varied, with > 60% spending > 50% of their time in clinical PN (Table 2.4). More detailed information regarding daily workload on return to home institutions including clinical, teaching, and administrative commitments is available in Supplement Appendix 6.

Table 2.4: Time spent in clinical paediatric nephrology.

Number of fellows (%)	Percentage of total work time
4 (16%)	75–100%
12 (48%)	50–75%
4 (16%)	25–50%
3 (12%)	10–25%
2 (8%)	< 10%

2.5.11 Work facility

The majority of PN fellows worked in state or university hospitals following the completion of their training (Supplement Appendix 7).

2.5.12 Institutional support

Upon completion of their PN fellowships and return to their countries of origin, 12 (50% fellows who completed this part of the questionnaire) received excellent institutional support, 10 (42%) received some support, and 2 (8%) received no support. Paediatric kidney facilities available on return from training was variable (Table 2.5).

Table 2.5: Paediatric facilities available on return.

	Frequently available	Occasionally available	Rarely available
Equipment	Adult PD and HD catheters	Paediatric HD lines	Paediatric PD, HD, and consumables
Machines	Ultrasound machines Adult dialysis machines	Paediatric dialysis machines—HD	Paediatric cycling PD machines
Radiology	By day	At night or on weekends	Nuclear medicine and Urodynamics
Histology	By day Light microscopy	At night or on weekends	Electron microscopy/immunohistopathology
Surgeons and urologists	Mainly adult trained (65%)	Paediatric surgeons (30%)	Paediatric urologists

2.5.13 AKI management

PD remains a challenge in view of lack of dialysis solutions and standard PD catheters, resulting in the need to train fellows to have improvisation skills with homemade fluids and makeshift catheters (Figure 2.1).

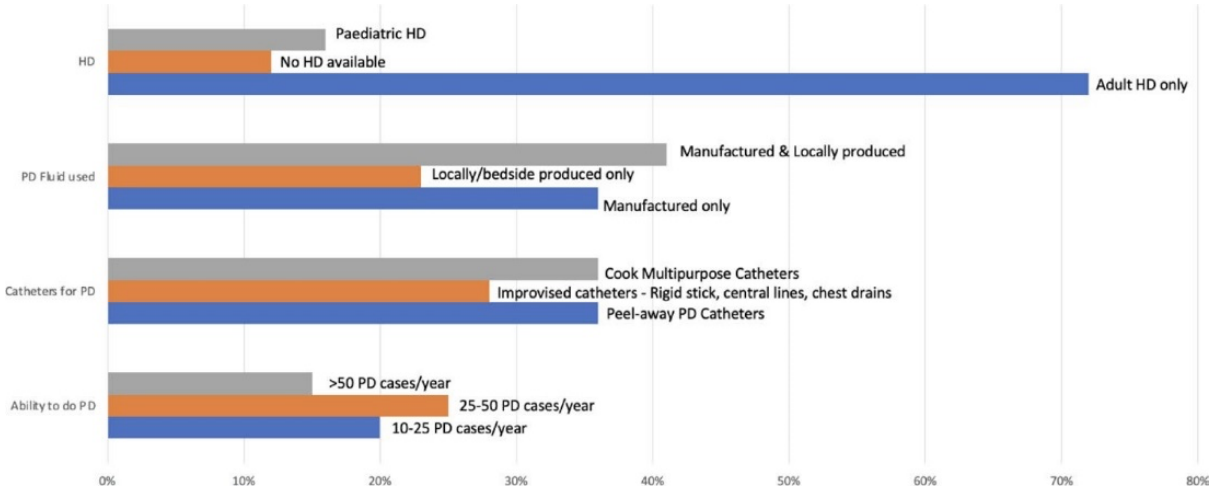

Figure 2.1: AKI management and resources in home institutions. The dialysis modalities used, the supplies available and the patient volumes were variable. HD, hemodialysis; PD, peritoneal dialysis.

2.5.14 Community health care

There was unanimous agreement that health care in the local community had been positively affected by PN training and the return of the trained fellow to their home institution. Qualitative comments pertaining to the impact of PN training were collected (Table 2.6).

Table 2.6: Impact of PN training on community health care.

Majority of patients are poor and can't afford investigations, lack of equipment
Accumulation large numbers of CKD patients with no dialysis or transplantation access
Set up lots of firsts/lots of acute PD, transplant, biopsies and fellowship training
Improved care for renal problems in children
My training has had a positive impact in my community, revised pediatric nephrology curriculum for medical school and post graduates; also our protocols, regularly talks on Ped Neph topics resulting in many difficult patients referred and phone consultation for difficult remote cases…also trained a team (doctor + nurse) from DRC on hands-on PD; who are doing very well
Yes. My unit has trained general medical officers in performing emergency PD for AKI. Regular consult from district
The training we pass on to our undergraduate and also during CME was significantly improved early diagnosis and referral of patient that require specialized care. Besides, understanding of preventable renal condition has significantly improved among doctors
Largely. One of two paediatric nephrologists in a city of about 20 million; median age is about 18 years
Improved identification of CKD, early intervention for acute kidney injury and better control for nephrotic children
Established enuresis clinic which serves a large population, contributed to establishing a charity for children with renal disease and contributed to HD unit and plasmapheresis

More nephrological problems are definitely being identified with better structure to patient management protocols and training doctors and nurses from different parts of the country in clinical skills
Yes - now have knowledge and capacity to do PD
Recognition of AKI with improved mortality and introduction of dialysis at the children's hospital and also improving picu capacity. Improved protocols of nephrotic syndrome
Established first paediatric nephro-urology collaboration in country to diagnose and integrate care. Established only paediatric chronic pd program in the country and train
Very much so, there has been an improvement in the care of children with kidney disorders in Tanzania, Telenephrology services for other cent- ers which are far from my center. Yes, management of children with kidney diseases have changed with my training, due to better and more organized care, e.g., paediatric NS not responding to steroid, now biopsied and receive immunosuppressants (CNI/MMF)
Identifying nephrological problems, YES. New approaches to management of renal issues, YES, training ongoing, long distance phone consults also happen. Clinical training, people skills, administrative and management issues have and continue to change
More healthcare professional have been educated on management of paediatric renal conditions and this has translated into better clinical outcomes
More nephrological problems identified—more recently lupus nephritis. Paediatric KRT for AKI done-though sometimes takes a lot of effort in terms of adaptations (a bit more difficult to teach others), as procedure done manually. Despite challenges we have seen some remarkable recoveries from AKI. Awareness and detection of pediatric AKI is high. Number of cases that are diagnostic challenges are also becoming less
We are picking more CAKUT, especially PUVs Some doctors are able to insert acute PD
Yes there has been a change as people are becoming more aware of Paediatric renal conditions and we are getting calls from across the country regarding management of various renal conditions and whether or not to refer to the unit

2.5.15 Teaching

All of the African PN fellows were required to provide teaching for both undergraduate and post-graduate students upon returning to their institutions. When asked if PN training prepared them for teaching, 12 (46%) felt they were well prepared to teach, 3 (12%) felt they were prepared to some extent, 2 (7%) felt they were not prepared, and 9 (35%) did not respond to this question. In general, fellows who stayed for a longer duration of training felt more confident with teaching.

2.5.16 Benefits of the training program

Overall, hands-on training was found to be very valuable and was deemed to be the most useful part of the training program on completion (Table 2.7).

Table 2.7: Feedback from fellows on completion of training program.

Hands-on training
Most useful part of the training given opportunities to gain appropriate skills
Allowing for practical management of common kidney diseases in Africa

Doing on-calls with mentor support
Procedures
Under close supervision giving confidence in kidney biopsies, placing bedside PD catheters, and setting up PD and forming the basis of what fellows do and giving an ability to train others
Doing procedures meant that you cannot forget what you saw and exercised (practiced) as to do a procedure oneself is more effective than just watching it being done
Where one makes mistakes, the person is immediately corrected by the trainer, and gets the opportunity to do it again, thus acquiring the skill. If it were only an observership, the trainee will not benefit from the knowledge inherent in practical errors
Acquiring Skills
Acquiring skills while, e.g., renal biopsy being careful watched which allowed for correction of technique as well as a safe space to practice while feeling assured that there was someone who “had your back”
The training was also felt to be appropriate for the setting that the fellows were returning to in Africa and teaching adapted or improvised tech- niques of managing AKI
Specific training
Spending time in the HD unit provided knowledge and confidence to establish HD for children
Confidence was also gained in making decisions in managing transplant patients
Visiting other units while training
Our combined sister platform Paediatric Nephrology Unit at Tygerberg Hospital/University of Stellenbosch (TBH/US) for varying periods of time as well as telephonic on-call support
Short periods (1 month) were also spent at our adult unit Groote Schuur Hospital (GSH), but this was curtailed during the Covid pandemic

2.5.17 Modifications to the training program

The majority (16/28) of the fellows who were able to spend more than 1 year in training managed to obtain enough experience in conducting kidney biopsies, acute PD, HD (lines and technique), KRT, and research time. Although the program was deemed to be comprehensive, the fellows reported that they required a longer duration of training to conduct research or learn teaching skills. Overall, a program lasting 18–24 months was seen as the ideal time period to learn all that was required. Additional recommendations for improved training are provided in Supplement Appendix 8.

2.5.18 Assessment of the training experience

All (100%) of the fellows felt that they would strongly recommend the program in terms of its hands-on approach and acquisition of skills. Subjective feedback from fellows on their training experience with subsequent recommendations has been collected (Supplement Appendix 9).

2.6 Discussion

The attractiveness of nephrology as a specialty has diminished over the past few decades leading to global concerns regarding the future of the specialty's workforce, even more so in LMIC [11]. There has been a call to boost recruitment of both adult and paediatric nephrologists by increasing exposure of medical students to nephrology, providing mentoring, improving the clinical experience, incorporating procedural skills, facilitating exchanges between trainees and senior nephrologists, adapting active approaches to identify dissatisfaction and burnout, increasing renumeration, and incentivizing advances in the field of nephrology [12].

Some high-income countries rely on foreign-trained doctors to cover shortages in nephrology staffing. For example, a study from Oman showed that the majority of practicing nephrologists were expatriate physicians, with local doctors representing only 14% of the workforce [13]. In the USA, a recent report showed that international medical graduates represented 47% of active nephrologists and 65% of nephrology trainees [14]. By comparison, our fellows had a 100% return rate to their home countries reversing the "brain drain" and providing PN knowledge to these countries.

The Paediatric Nephrology Department at RCWMCH/ UCT and the APFP/CHT have, with funding from international nephrology organizations, been able to assist in regional training of "African paediatric nephrology fellows in Africa for Africa" in 1 center. Invaluable experience was gained with "hands-on" patient examinations, diagnosis, and management, as well as procedures. Peritoneal dialysis for management of pediatric AKI using adapted techniques in the absence of the availability of a paediatric surgeon to place a Tenckhoff in a theater facility, has now become accepted as a safe and effective alternative, as recently published in the updated ISPD guidelines for management of children with AKI [19].

In the first decade of training, most of the fellows stayed for 1 year or less; however, the training duration of the fellows in the second decade increased to 2 years as home institutions requested that their fellows complete training with formal qualifications. As trainers, we also strongly supported this philosophy in keeping with international norms of 2–4 years of nephrology training [20] which often includes some clinical research training, the next logical step for our fellows following clinical training. In some cases, PN fellows have returned to their home institutions without completing their research training and then found it very difficult for them to complete it, as they have lacked clinical support to assist them in meeting the large workload of patients.

The measure of success of this program, in addition to the fellows acquiring sub-specialty exam/post-graduate qualifications or master's degrees, is the fact that there has been an initial "100% return rate" at 1 year to home institutions in Africa. The training program tried to ensure that the referring institution was prepared to support

trained fellows and offer them a position upon their return home. This is an area where human healthcare resource planning can become more involved in local countries.

More than two-thirds of the fellows returned to government/university positions, on occasion being part-time for those employed in private hospitals. As medical directors of kidney/dialysis units, communication skills, staff empowerment, allocation of resources, mentoring, team building, and strategic planning are all important skills [21, 22] and they learned these skills while training at RCWMCH. On return to their home centers, many of the fellows had their skills recognized which enabled them to take up more influential positions as heads of departments within their hospitals and universities.

In terms of daily workload, the majority of the fellows spent their time post-training in clinical work as opposed to teaching, with very little time dedicated to administration. Unfortunately, the survey did not specifically ask about dedicated research time or whether this was included in clinical or administration time.

Despite the recent publication of ISPD guidelines pertaining to the use of PD for management of AKI, overall there has been a decline in the use of PD in high-resource countries and this has resulted in the loss or absence of knowledge on PD leading to an unwarranted pessimistic view of this form of KRT [23, 24]. On review of the survey data pertaining to dialysis training for AKI and especially PD training with hands-on PD insertion techniques, the fellows generally felt it to be “extensively covered” and resulted in fellows being able to perform PD for the management of AKI in their own centers and characterizing it as a center strength. The benefits of PD in this setting have also been experienced by the “Saving Young Lives” initiative. Challenges pertaining to the provision of PD in LMICs include lack of PD catheters, consumables, and PD solutions [25]. PN working in these regions have highlighted their needs to focus on pragmatic pathways to provide kidney support therapy. This program has provided that particular focus and it has been recognized as a strength by the fellows.

In general, “hands-on training” was found to be the most useful part of the training, providing opportunities for fellows to acquire the skills necessary for practical management of common kidney diseases in Africa, as well as meeting on-call demands with mentor support. Supervised training for procedures such as kidney biopsies, placing bedside PD catheters, and setting up a PD system form the basis of what nephrologists do and promotes the training of others who often practice without the backup and support of interventional radiologists and surgeons specifically trained in pediatrics.

On return to their home institutions, 50% of fellows felt that they did receive some support from their institutions, but the remainder felt that they needed significantly more. The most useful equipment included dialysis (PD and HD) and biopsy consumables and ultrasound machines. Other departments thought to be essential,

but with limited time availability and resources included radiology (only office hour availability and absence of nuclear medicine and urodynamics), histology (office hours only and lack of EM and immunohistochemistry) and surgeons (shortage of paediatric trained surgeons and urologists, in particular). The role for training opportunities for allied and nursing healthcare workers (e.g., dialysis nurses, dialysis technicians, dietitians, and others) in their native languages also needs to be addressed because of their essential role in pediatric kidney care.

Despite the challenges in their institutions, the fellows felt unanimously that their training had enabled them to positively affect health care in their community with a summary statement illustrating this: *Yes, there has been a change as people are becoming more aware of paediatric kidney conditions and we are getting calls from across the country regarding management of various kidney conditions and whether or not to refer to the unit*.

An important part of their training was in the field of advocacy for children and adolescents with kidney disease.

Whereas data collection with identification of patient outcomes and a review of the impact of training and resources on outcomes in LMIC is difficult, registries of kidney disease in children need to be established in Africa, as occurs with other adult and pediatric kidney patients to determine the true extent of children's kidney disease and to facilitate the generation of successful diagnostic and treatment strategies [26–28].

Teaching of both under- and post-graduate students was an essential part of the fellows' responsibilities and in general, fellows who stayed for longer training, overall felt more confident with teaching. Whereas CME was also an essential part of training with many feeling it was adequate, suggestions have been made specifically to develop patient treatment pathways relevant to local conditions. In addition, the role of virtual webinars as a widely available avenue for CME education throughout LMICs requires close attention and evaluation.

Recommended modifications to the program include recommendations that the program duration be a minimum of 18–24 months to allow for sub-specialty exams in PN and to permit acquisition of skills in HD (iline access and chronic HD), KRT in PICU, teaching, and research methodologies, with time to complete any research projects once they have started.

Additional recommendations included development of different levels of training to allow for some local training followed by concentrated training in advanced nephrology once enough PN units have been established in the region, as well as post-graduate networking among fellows to promote the development of sister center programs. Many fellows are already on a WhatsApp group as a form of promoting a "PN Fellowship Network" in Africa and this support should be extended further (Table 2.8).

Table 2.8: Recommendations arising from this paper for a pediatric nephrology training program.

RCWMCH as a training center has been acknowledged as appropriate and excellent in terms of “hands-on training.” However, 6–12 months is too short and ideally need 18–24 months for “hands-on training,” teaching and research
Training to include case presentations on ward rounds as well as on-calls with senior backup
Also, Cape Town is expensive in terms of accommodation and travel and thus adequate funding is required to manage financially in this center and allow visits home
Extra time spent at this training center in addition to AKI and CKD management and dialysis as well as transplantation, would benefit in learn- ing advanced techniques of HD including line insertion and managing HD/CKRT in PICU settings. This is accommodated in a longer training program more than 12 months
Training in urodynamic studies and assessments
Training in developing registries—in less well-resourced countries, few adult units have registries but it is essential to start developing children’s registries too
Research training including “library” time to complete research would benefit in longer fellowships
Teaching methodology in preparation for returning to teaching/lecturing would similarly also benefit from longer fellowships
2 Training levels: Appendix 3
Basic competence level 1
This would involve basic concepts of PN including preventative PN and specifically AKI diagnosis and treatment using improvised techniques were not available. Ideally this could be done by previously graduated IPNA/ISN Fellows so that the “Trainee fellows become the teachers” and ensure adequate training in level 1 basic competence for 6–12 months
Advanced level 2
Fellows could then proceed to level 2 Advanced Skills training for a further 12–18 months to develop more advanced skills in not only AKI but also kidney biopsies and histology, CKD, dialysis, and transplantation (optional)
(Level 1 basic competence and 2 advanced clinical skills training syllabus for PN training—devised by Yap/McCulloch for IPNA.) IPNA website
Post training visits by mentors to PN fellows’ home institution for 2–4 weeks to offer support and advocacy, encourage nurses, multidisciplinary teams, and junior doctors to become enthusiastic about paediatric nephrology
Sister centers as developed by IPNA/ISN/IPTA—development of emerging and supportive centers following training of IPNA/ISN/ISPD fellows who then return to their home institution and are motivated to set up PN programs at these institutions where there may or not have been such programs
The aim is for these emerging centers to team with supportive centers (often from higher resourced regions) preferably from a similar geographic region to assist in educational development including teaching, development of protocols and services not previously well developed
Tension not to provide finances for drugs and service delivery as this may end up being a never-ending challenge

Adult nephrology fellows to spend some time in paediatric units to learn skills in managing children with kidney diseases especially in regions where this may not be available
Visa versa it also benefits PN fellows to spend time in adult units once the COVID pandemic abates
Advocacy in particular for management of children's kidney diseases including access for both acute and chronic dialysis not only at hospital level but also at local and national government levels
Learning about fundraising and meeting up with charities to promote access of paediatric patients to appropriate equipment and facilities for kidney disease
Continuing Medical Education (CME) by virtual teaching including Journal clubs
WhatsApp (or similar) to support groups of children's kidney specialists to manage difficult cases

2.6.1 Social factor consideration

The training of PN fellows funded by IPNA/ISN/ISPD and APFP has resulted in fellows not only becoming teachers and leaders in their own institutions/universities, but also leaders in IPNA, even as councilors.

All the PN Fellows who have trained at RCWMCH deserve significant accolades for the sacrifices of family time (many up to 24 months) they have made to gain knowledge and training to return to their home countries with skills to support paediatric nephrology. Funding to allow visits back home should be seen as being essential considering the sacrifice these fellows make. Without the commitment of these fellows, African PN would be a poorer specialty. Following the initiation of a PN training program at RCWMCH, PN units in the Gauteng region (Johannesburg and Pretoria) and more recently Durban have also expanded this training program for fellows from other parts of Africa with the same dedication of the participants that we have witnessed.

2.7 Conclusion

This paediatric nephrology fellowship "based in Africa for Africa" has made it possible for physicians to get comprehensive PN clinical training as a result of their commitment, the commitment of those at RCWMCH and the funding support from multiple organizations. The collaborative experience has contributed to substantial improvement in the availability of pediatric kidney care in LMICs.

2.7.1 Current IPNA fellows training situation

Since the IPNA Fellowship Program was initiated almost 20 years ago, more than 260 fellows have completed their training, coming from more than 56 countries, most of them low-income countries. Currently, 41 training centers participate in this initiative, aimed to disseminate pediatric nephrology expertise to under-served areas of the world. During the current year, 13 fellows are being trained in centers located in South Africa, China, Singapore, France, and Brazil, and 14 fellows are about to start their training, half of them coming from the African continent, highlightingthe relevance of this program for the region (personal communication Francisco Cano March 2023).

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3 Chapter 3: Use of locally prepared peritoneal dialysis (PD) fluid for acute PD in children and infants in Africa

3.1 Overview

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3.2 Abstract

Background: In less well-resourced countries, the high cost of commercially available peritoneal dialysis (PD) fluid limits its use. The major concerns regarding bedside-prepared PD fluid is peritonitis as well as electrolyte disorders. The aim of this study was to review our experience with the use of PD fluids prepared at the bedside using the intravenous infusion solution Balsol (Fresenius Kabi).

Method: This was a retrospective review of all patients who received PD for acute kidney injury (AKI) using a bedside-prepared PD solution adapted from the intravenous solution Balsol in our intensive care unit.

Results: In total, 49 cases of acute PD were performed. Of the 49 children, 21 (43%) were male. The ages of the patients ranged from newborn to 10.2 years (median 0.33 years). The weight of children ranged from 1.3 kg to 50 kg (median 4.1 kg). The type of PD catheters used: Cook catheters, 41 patients; Kimal peel-away, 10 patients; and surgical inserted Tenckhoff type of catheter, 2 patients. The duration of PD was 1–17 days (median 3 days) Complications included peritonitis in 2 of 49 patients and blocked catheter in 6 of 49 patients. There were no electrolyte disturbances as a result of the PD. Overall survival was 43% of patients.

Conclusion: Locally prepared PD solutions at the bedside adapted from intravenous solutions can be used safely and effectively. This has important relevance for centres in less well-resourced countries, where commercially produced PD fluid is not available for the management of AKI. Balsol, bedside-prepared PD fluid, bicarbonate-based fluid, intravenous solutions.

Keywords:*Acute kidney injury, glucose absorption, peritoneal dialysis, protein loss.*

3.3 Introduction

When dialysis is provided for children with acute kidney injury (AKI), mortality is significantly improved, as reviewed recently for AKI in sub-Saharan Africa [1]. Peritoneal dialysis (PD) is ideal for the treatment of paediatric AKI in low-income countries [2,3] but is usually performed with commercially manufactured PD fluid and surgically inserted PD catheters. The Saving Young Lives Programme has promoted the use of PD in AKI in low- and middle-income countries, but some centres have struggled with sustainability because of the high cost of commercially prepared PD fluid [4,5]. The role of locally prepared dialysis fluids using commercially available intravenous fluids is very relevant in these settings. Although recipes are available in the International Society for Peritoneal Dialysis (ISPD) guidelines [6] for the adaption of intravenous fluids to make PD solutions, very little is published in the modern era regarding the use of these types of fluids for dialysis.

Because of the bedside addition of glucose and extra manipulation of the bags, physicians are generally reticent to prepare these fluids because of the possible increased risk of infection. In a recent retrospective study in 68 children and adults from Cameroon, bedside-prepared solutions adapted from intravenous solutions were shown to be as effective as commercially made solutions in terms of patient survival and peritonitis rate [7]. Although Flynn et al. [8] and Santos et al. [9] described using hospital pharmacy prepared fluids (not adapted intravenous fluid), they do not report on the specific outcome of this subgroup of patients. The aim of our present work was to review our experience using beside-prepared PD fluids made from commercially available intravenous fluids to treat children with AKI in terms of safety and efficacy. This is important because these bedside mixed fluids if shown to be safe have the potential to save lives in areas where no commercially available PD fluids are available.

3.4 Materials and methods

This was a retrospective review of all patients who received PD using a bedside-prepared PD solution (Table 3.1), adapted from the intravenous solution Balsol (Fresenius Kabi). This bedside-prepared bicarbonate-based PD fluid was used during this time for those patients meeting the need for dialysis and in whom it was felt by the treating physician at the time that a bicarbonate-based fluid would be useful for severe acidosis. Initially, a 1.5% adapted Balsol solution was constituted by adding 30 ml of 50% dextrose to 1000 ml of Balsol. If a stronger solution was needed, either a 2.5% (50 ml of 50% dextrose) or 4.25% (85 ml of 50% dextrose) solution was constituted. Heparin 500 IU/L was routinely added to the PD solution. This fluid was made up in the intensive care unit (ICU) by the attending nephrologist under sterile conditions immediately prior to use. Patients were started on dialysis using 10–20 ml/kg fill volume as tolerated with a dwell time of 45–60 min and a drain time of 20 min. This was adapted according to specific needs of the individual patient. Exchanges were performed either manually by the nursing staff attending to the patient or by an automated PD machine (Homechoice, Paxtra, Deerfield, IL, USA). Manual PD was performed using PD fluid via a buretrol into a y-type connector attached to the PD catheter and then into a drainage bag. This system was not commercially available but was made up from available supplies at the time. The Balsol bags were connected to the automated PD machines in the same way as commercially produced PD fluids are attached, that is, via the spike that comes with the automated PD sets. Nurses performing manual PD in the ICU were regularly trained in this technique. Access for PD consisted of a temporary PD catheter which was inserted by Seldinger technique at the bedside by the attending nephrologist or by a surgically placed Tenckhoff catheter. The temporary bedside catheters used during this era were either Cook®.

(Cook Medical Inc., Bloomington, Indiana, USA) or Kimal insertion kits and catheters (UK). Bedside insertion was done using a sterile technique including sterile gowns, hat and gloves. It is our policy to give a stat dose of prophylactic Vancomycin at insertion of PD catheters. This, however, is not performed if the child is already on systemic antibiotics. Data were collected on patients from a dialysis database, which was kept throughout this period. Once cases were identified, folders were retrieved and the information (in de-identifiable format) recorded on a spreadsheet for analysis. Information recorded included gender, age, weight, underlying diagnosis, indication for dialysis, type of PD catheters (Cook, Kimal peel-away or surgical PD catheter), complications, outcomes and type of PD. The ISPD peritonitis definition was used to define peritonitis [10] This study was approved by the University of Cape Town's Faculty of Health Sciences Human Research Ethics Committee prior to commencement.

Table 3.1: Electrolyte content in mmol/L of Balsol IVI solution compared to other IVI solutions and commercially available PD solutions.

Type of fluid	Na þ	Kþ	Caþþ	Mg þþ	Cl-	HCO^{3-}	Lactate	pH	Osmolality
Balsol/plasmalyte B	130	4		1.5	110	27		7.4	273
Ringers lactate	131	4/5[a]	1.8		112		28	6.5	279
Dianeal 1.5%	132		2.5	0.25	95		35	5.2	344
Bicavera 1.5%	134		1.75	0.5	104.5	34		7.4	358

PD: peritoneal dialysis; IVI: intravenous infusion.

[a] Depending on the manufacturer, Ringers lactate may have 4 or 5 mmol/L of potassium.

3.4.1 Statistical Analysis

The data were captured on Excel for Microsoft Office version 10 (Redmond, Washington, USA). A descriptive statistical analysis of the data was conducted. Because the results are considerably skewed in terms of age, weight and time on PD, the data in this report are expressed as medians and a range or otherwise as a percentage. Because there were only two cases of peritonitis, further statistical analysis comparing different variables, for example, type of catheter, age and manual/ automated PD, was not performed as it was felt the results would not be meaningful.

3.5 Results

During this period, 49 patients were treated with bedside prepared PD solutions. Of the 49 children, 21(43%) were male. The ages ranged from newborn to 10.2 years (median 0.33 year). There were 17 neonates, 39 infants (<1 year including neonates) and 10 children (>1 year of age). The weight of children dialysed ranged from 1.3 kg to 50 kg (median 4.1 kg). The indications for dialysis are presented in Table 3.2. While Table 3.3 lists the underlying diagnoses of the patients. The type of PD catheters used depended on the size of the patients; the smaller infants (usually under 1 year or under 8 kg) received predominantly Cook catheters (predominantly size 8 Fr). Forty-one patients received Cook catheters ranging in age from newborn to 1.9 years (median age 0.3 years) and in weight from 1.3 kg to 14 kg (median weight 3.85 kg); Kimal peel-away insertion kits and Tenchkoff catheters were used in 10 patients ranging in age from 0.17 years to 10.2 years (median age 3.63 years) and in weight from 3 kg to 50 kg (median weight 13.35 kg). Surgically inserted Tenchkoff catheters were used in two patients (in a few patients both Cook and Tenckhoff catheters were used). The duration of PD was 1–17 days (median 3 days). No long-term or chronic dialysis resulted in this group as they either recovered completely or else died. The type of PD consisted of manual PD in 37 of 49 (75%) and automated PD in 12 of 49 (25%), of which the Paxtra machine was used in 1 patient and the Homechoice in 11 patients. At the time the Homechoice PRO, which has a smaller dead space, was not available and the prescribed fill volume needed to be at least 100 ml, thus automated PD was only used on bigger patients (7.6–50 kg). The overall survival rate was 21 of 49 (43%) cases.

Table 3.2: Indications for acute PD.

Indications for dialysis (more than one indication could be listed)	Number of Cases
Anuria/oliguria	36
Acidosis	49
Hyperkalaemia	17
Fluid overload	5
Hyperammonaemia	2

PD: Peritoneal Dialysis

Table 3.3: Underlying diagnoses.

Underlying diagnosis	Number of Cases
Cardiac – congenital post-operative or myocarditis	12 (25%)

Gastroenteritis (may be combined with sepsis)	9 (19%)
Sepsis	7 (14%)
Metabolic/liver/inborn error of metabolism	6 (12%)
Pneumonia	4 (8%)
Haemolytic uraemic syndrome	4 (8%)
Necrotising enterocolitis	2 (4%)
Other – acute lymphoblastic leukaemia, scalded skin (2), toxin ingestion and congenital abnormality affecting urinary tract.	5 (10%)

Complications included the following:

1. Blockage of catheter in 6 of the 49 cases. These were all in patients in which the small 5-Fr Cook catheters were used. This was managed by replacing the blocked catheter using a 'railroad technique' with another Cook catheter in five cases and by using a peel away Tenchkoff catheter in one case.
2. Insertion of Cook catheter into the bladder in one case. This was removed with no side effects and a second Cook catheter was placed in the correct peritoneal position.
3. Inadequate clearance in one patient. The patient was converted to continuous venovenous haemodialysis.
4. Peritonitis in 2 of the 49 patients. Microbiology Laboratory results were only available for 28 of the 49 patients as PD fluid was only sent for microbiology if the attending physician was concerned regarding peritonitis. Of the two cases, one patient had dialysis for less than 1 day having presented with ascites and the second had the acute PD catheter in for 12 days. This patient underwent a catheter change and survived long term. Most of the cases were on concomitant broad-spectrum antibiotics in view of their primary diagnosis at the time of starting PD. Because there were only two cases of peritonitis statistical analysis comparing different variables, for example, type of catheter, age and manual/ automated PD was not performed as it was thought it would not be meaningful.
5. Other complications included the following: one case died after only one cycle of PD had been performed. In one patient, the insertion of a peritoneal catheter demonstrated pus in the abdomen before initiation of PD. In one case, there was feculent material in the abdomen suggestive of a perforated bowel unrelated to the catheter insertion. No bleeding as a result of PD catheter insertion was noted. No electrolyte problems were noted in any of the cases as a result of the PD fluid.

3.6 Discussion

We have reported our experience with the use of a locally, bedside-prepared PD fluid made from the intravenous solution Balsol (Fresenius Kabi). This was adapted with 50% dextrose, as above, to produce a PD solution under sterile conditions by nephrologists in the ICU. This has relevance in view of the increasing interest in the treatment of AKI with PD in poorly resourced parts of the world including Africa. The principal concern when using locally bedside-prepared PD fluids is contamination because of the extra bag manipulations done when adding glucose at the bedside. Our peritonitis rate of 4% is well below many other paediatric studies using acute PD, although our results may not be a true reflection of the peritonitis rate as only 28 of the 49 patients had fluid sent for microbiology as this was done at the discretion of the attending physician. Nepfumbada et al. from Durban, South Africa, reported a peritonitis rate of 47.5% in children on acute PD using commercially manufactured fluids and bedside catheter placement [11]. They cited lack of ICU PD-trained nurses, high percentage of leaks and long dialysis periods as the possible cause for the high peritonitis rate. A similar peritonitis rate was reported from Pretoria also in South Africa using surgically place catheters [12]. From other parts of the world, with varying acute PD techniques, peritonitis rates in acute PD in children vary from 4%to 24% [13–17]. The only other reported study where bedside-prepared fluids using intravenous infusion (IVI) fluids were used was from Cameroon.1 This study included 32 children and a comparison was made to patients treated with commercially manufactured fluids. In both groups, a peritonitis rate of 16% was reported. Although many of our patients presented with sepsis, acidosis and deranged electrolytes, no cases of electrolyte imbalance occurred as a result of this adapted PD fluid. The resultant electrolyte concentrations in the bedside mixed fluids closely resemble commercially available PD fluids.

Thus, barring a mixing error, they would not be expected to cause additional electrolyte problems. The exception is that Balsol solution has a potassium concentration of 4 mmol/L, which could potentially have been a problem in hyperkalaemic patients; however, this was not found to be the case.

Most of this population were young with a median age of 3 months and with 80% (39 of 49) of cases under 1 year. They were also relatively small with a median weight of 4.1 kg showing that this technique can be used even in small infants. Our recommendation would be that this technique could be used in both adults and children. This may be relevant for neonatal units in high-income countries who have patients requiring PD as an emergency but where commercially produced dialysis fluids may not be available and prompt dialysis is required. The duration of PD was relatively short (median 3 days) and most cases were being managed by manual PD techniques (75% of cases). The short-time periods that patients were on PD could have contributed to the low peritonitis rate. This was a severely ill subgroup of patients and many patients did not survive very long which contributed to the overall short

median dialysis time. The survival rate of our patients of 43% is comparable to other series of acute PD throughout sub-Saharan Africa.1 It could be argued that a group of patients with AKI and severe acidosis may be at higher risk of dying than patients with uncomplicated AKI. In the ideal world, commercially manufactured PD fluid should be used after a surgeon has inserted a PD catheter surgically in an operating theatre environment. However, in many under-resourced regions of the world, commercially produced PD fluid as well as easily available surgeons are not available and thus alternative techniques using improvisation may be necessary [2,5,6]. Although the intravenous solution used in this study was Balsol, it was not the aim to specifically promote the use of this specific fluid as many other intravenous fluids can be used such as ringers lactate and other solutions, as stipulated in the ISPD acute PD guidelines [6]. Our aim was rather to show the safety of locally bedside-prepared solutions made from IVI solutions in general.

3.7 Conclusion

Bedside-prepared PD solutions have been made using intravenous fluid by adding appropriate volumes of 50% dextrose to a balanced electrolyte intravenous solution. We have reported on more than 40 children where this solution was used for acute PD without obvious complications. No cases of severe infection or electrolyte imbalance occurred as a result of this adapted PD fluid. This has important relevance for less well-resourced centres, where commercially produced PD fluid is not available for the management of AKI. It may also be relevant in neonatal units in high-income countries for emergency PD, where commercially produced PD fluid is also not immediately available.

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4 Chapter 4: Costing of dialysis modalities

4.1 Overview

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4.2 Abstract

Objectives:

Method:

Results:

Conclusion:

Keywords: *Dialysis modalities, children*

4.3 Introduction

One of the biggest challenges in the management of acute kidney injury(AKI) is the prohibitive cost of dialysis in low resource settings(LRS) and thus generation of evidence to support sustainable financing is crucial to addressing the 'know-do gap' in the real world setting [1]. There are not many publications looking specifically at the cost of dialysis in children across all spectrums of dialysis. This chapter reviews data on costing of dialysis for AKI and especially in children in sub-Saharan Africa and then compares this to the costing of dialysis for AKI in children at our centre. This includes both acute peritoneal dialysis as well as extracorporeal forms of dialysis (ECD) including Continuous Kidney Replacement Therapy (CKRT) and acute Haemodialysis (HD).

4.3.1 Background

A recent systematic review [2] examined access to care for AKI in Sub-Saharan Africa and highlighted the major systematic barriers as: reliance on out-of-pocket costs, erratic availability of hospital resources, late presentation, and female sex. In children needing dialysis for AKI, only 64% (666/1042) received dialysis with an overall mortality of 34%. The mortality for those who needed dialysis but did not receive it, was 73% . The prohibitive cost of dialysis for individuals and institutions was therefore a contributor to mortality in many children.

4.3.2 Comparison to other Low Resourced Settings

Comparison between the costs of peritoneal dialysis (PD) and haemodialysis (HD) was analyzed by Obiagwu et al. [3] for 20 children with AKI in Nigeria, of whom 60% received haemodialysis and 40% received PD. HD costs exceeded those of PD (USD 363.33.vs USD 311.66, p=0.313) with the difference mainly being driven by the mean cost of consumables (USD 248.49 vs USD 164.73, p=0.0009). Costs of nephrologist and nursing where not found to be significant. At the end of the day, all these costs came out of parents' pockets, and amounted to ten times the minimum monthly wage in Nigeria of 38 USD [4]. This cost for short-term dialysis for AKI is therefore clearly not achievable for most families.

More recently, Cullis et al. examined access to dialysis in LRS (not just in Africa) and included the burdens of funding [5]. Three themes of availability, affordability and acceptability were examined with respect to access to paediatric dialysis in low resource settings (as in Figure 4.1 below).

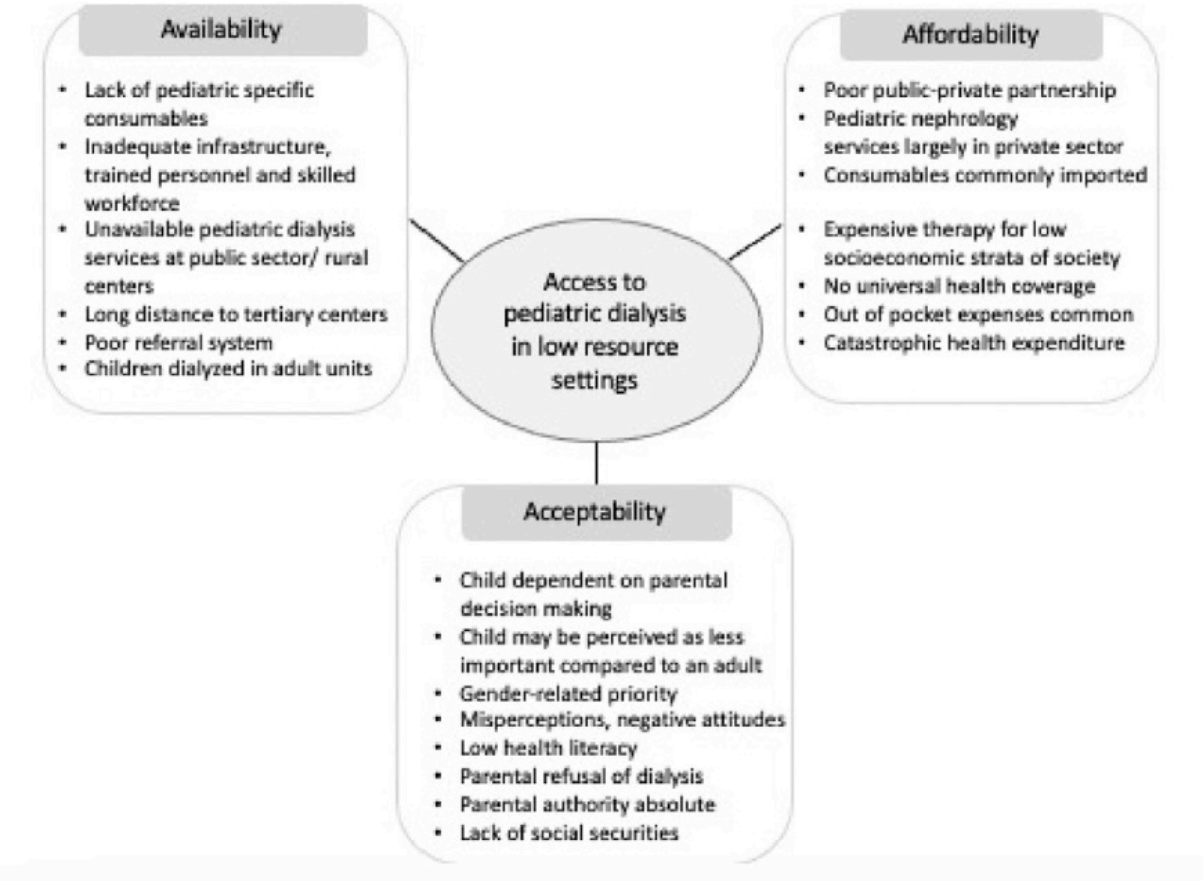

Figure 4.1: Factors affecting access to kidney replacement therapy in paediatrics. (Reproduced with permission from Cullis B, Calice da Silva V, McCulloch M, Ulasi I, Wijewickrama E, Iyengar A. Access to Dialysis for Acute Kidney Injury in Low-Resource Settings. Semin Nephrol. 2022 Sep;42(5):151313. doi: 10.1016/j.semnephrol.2023.151313. Epub 2023 Feb 22. PMID:36821914) [5].

The 'availability' theme concentrates on the availability of paediatric specific equipment (in terms of size of catheters and consumables) and paediatric 'friendly' personnel and facilities. These need to be both local and accessible.

The second theme of 'affordability' addresses the costs incurred in dialysis relative to the financial resources of families (usually without insurance or health cover, and required to pay out of pocket for any expenses). These may have a catastrophic impact on the financial welfare of entire families.

The last theme is that of acceptability of dialysis as a mode of treatment in the context of families and communities who may have limited experience of and insight into dialysis, or who may have more adult based priorities.

Table 4.1: Comparing costs of consumables for dialysis modalities in centres from 2 resourceconstrained countries demonstrating variability. (Reproduced with permission from Cullis B, Calice da Silva V, McCulloch M, Ulasi I, Wijewickrama E, Iyengar A. Access to Dialysis for Acute Kidney Injury in Low-Resource Settings. Semin Nephrol. 2022 Sep;42(5):151313. doi: 10.1016/j.semnephrol.2023.151313. Epub 2023 Feb 22. PMID:36821914) [5].

Table 1. Comparing Cost of Consumables for Dialysis Modalities in Centers From Two Resource-Constrained Countries Demonstrating Variability

Consumables for Pediatric Dialysis	Approximate Cost In India,* US$	Approximate Cost in South Africa,† US$
Acute PD		
Rigid catheter and tubing	20	–
Cook pigtail catheter (Seldinger)	–	105
Adapted central line as PD catheter	–	55
PD fluid, 1.5%, 1 L	2	5
APD–PD fluid, cassette, and consumables		25
Acute hemodialysis/SLED		
Catheter	20-90	40-80
Dialyzer	7-14	7-25
Circuits (tubing)	4	4
CRRT		
Hemofilter set	200-300	150-220
Fluid bag (2 L)	30	19

Abbreviations: APD, automated peritoneal dialysis; CRRT, continuous renal replacement therapy; PD, peritoneal dialysis; SLED, slow extended dialysis.
*Private academic (not-for-profit) institution.
†Public sector referral hospital for children but with a public–private partnership dialysis unit.

The same study also performed a costing comparison of dialysis consumables between India (more cost effective overall) and South Africa with improvised PD still being cost effective compared other forms of modalities as per Table 4.1.

We are fortunate at Red Cross War Memorial Hospital (RCWMH) in that we have all paediatric acute dialysis modalities available. In peritoneal dialysis (PD) the abdomen is filled with dialysis fluid through a catheter placed in the peritoneal cavity, which is allowed to dwell for a period and then drained out and the cycle starts again. This form of dialysis requires bedside nursing staff to perform this often hourly, which is quite labour intensive. An advantage however is that nursing staff can be rapidly trained in this form of dialysis, in both high income and lower resource settings [6]. The PD exchanges can also be performed using an automated cycler which can perform PD continuously for up to 24 hours without the need for staff to perform each cycle manually. The machine and consumables are however more costly than for manual PD and require a continuous electricity supply.

Other forms of dialysis include conventional acute Haemodialysis (HD) which requires a double lumen catheter to be placed into a large blood vessel and blood to be pumped outside the body through a blood filter for 3-4 hours every 1 – 2 days. This form of dialysis requires specific machines, filters, tubing and fluids and concentrates. It can be performed on wards where there is access to water and electricity but requires

experienced staff dedicated to monitor the patient for several hours during the dialysis session. Continuous Kidney Replacement Therapy (CKRT) is a form of less intense HD which runs over 24 hours. This requires a dedicated paediatric machine e.g. Fresenius Multifiltrate or for small Infants, a machine such as the Carpe Diem® machine. CKRT is a gentler form of HD (it probably causes fewer acute haemodynamic effects), and is usually reserved for unstable patients. It requires highly trained staff and is usually performed in an intensive care unit (ICU) with 1 to 1 nursing by highly trained staff.

4.4 Methods

The cost of all dialysis supplies(both PD and HD) in use in the paediatric ICU at RCWMH required for acute dialysis was determined per day:

1. An estimation of amounts of consumables including fluids, catheters, filters, etc. required for dialysis. (As children come in different sizes on average we used a 20kg child but this obviously varies significantly)
2. Use of the prices that had been paid by the hospital on the official procurement process (usually following a specific provincial tender process)

The costs of the dialysis machines (purchase, maintenance, repair etc) were not included as many of these machines were leased and under a service contract but this is obviously an additional cost to the daily rate. Costs of human resources (labour costs) pertaining to the performance of the dialysis process were estimated for CKRT and HD, but it was not possible to assess for PD both manual and automated as this was included in the daily nursing costs of the PICU. We did not include personnel costs for interventions such as insertion of lines / dialysis catheters, any surgical procedures or nursing services, or for PICU personnel costs. As acute dialysis tends to be performed in PICU in our setting, the PICU bedside nursing costs are likely not very different across the various forms of dialysis.

We did not include costs for operating theatre time for any of the procedures, nor did we include costs for surgical consumables and supplies.

The cost of improvised equipment for manual PD was also calculated in the event that this was needed as the only solution for managing AKI.

4.5 Results

The cost for components required for dialysis in children with AKI at RCWMH tabulated in Table 4.2.

Table 4.2: Costing of Dialysis for Children with AKI at Red Cross War Memorial Children's Hospital as a daily rate for a 20kg child

Cost Comparison between modalities # (Machine not included)	**KRT Carpe Diem**	**KRT Fresenius**	**Acute HD**	**Automated PD cycling**	**Manual PD Cook Catheter (Fresenius PD Paeds Set)**	**ManualPD Adult central venous catheter**
HD line	R 1500 (Arrow 5Fr, Gamca th 6.5Fr)	R1200 (Medcomp 7-9Fr)	R1200 (Medcom p7-9Fr)	-	-	
PD catheter Bedside inserted (children > 10kg)				Peel away sheath and Tenckhoff catheter R2 530	-	CVP Lineas PD Catheter R322
Cook pigtail catheter (Fuhrman) (smaller children <10kg)				-	R 1840	-
Fluid	R 370	R 1 110	R185	R 207	R 112	R112
Consumables	R 4 687	R 1 015	R 408	R 707		
Burettrol					R30	R30
Infusion set					R 473 manufact ured Fresenius PD Paeds set	R24 manual improvisedset
Sub total	R 6 557	R 3 325	R 1793	R 3 444	R 2479	R 488
PICU COST						
Labour	R 300	R 300	R 400	-	-	-
Total *	**R 6 857 (USD 370)**	**R 3 625 (USD 195)**	**R 2 193 (USD 120)**	**R 3 444 (USD 186)**	**R2 479 (USD 135)**	**R 488 (USD 26)**

* Conversion at the time of calculation USD = R 18.50

^ Labour for CKRT and Acute HD calculated at R100/hr(USD 5.50) (Rate at which overtime is paid by Contracted Supplier which is part of a Public Private partnership)

Many of our dialysis machines are leased to us or are part of a public private partnership – so having to purchase the machines would add significantly to the cost.

4.6 Discussion

Overall the bare minimum costing analysis of dialysis for acute kidney injury (AKI) in children, supported our 'PD First for paediatric AKI' (starting PD as first dialysis modality where possible in children with AKI) approach as being the most economical modality.

The costs of consumables for manual PD and Acute HD appear similar, but the size of patient range in children (from neonates to adolescents) may also require different volumes of fluid and costs of consumables. In low resourced settings (LRS), lines and consumables for small infants are often not easily available locally and require importation, at significantly higher costs than adult lines and consumables.

Further limitations include the infrastructural costs, which have not been considered here, including the need for non-interruptible power supplies, adequate water supplies and reverse osmosis purification systems. Other limitations include the fact that other 'hidden' costs include blood priming of HD lines in small children, anticoagulation costs and laboratory costs for monitoring. Medications may also be cleared by HD requiring higher dosing and associated higher costs.

In addition, costs are escalated for the replacement of lines and filters, if they should clot within the same day. In some of the CKRT machines, dialysis lines and filters can be used for 48 – 72hours continuously, saving costs compared to the Carpe Diem® system ,which is a closed system including the dialysis lines and filters, which requires changing every 24hours.

The neonatal CKRT dialysis systems (Carpe Diem®) are the only therapeutic option for performing CKRT in small and unstable infants/children, but these are by far the most expensive.

In addition, higher training skills are needed for HD and it is not always possible to perform HD on small infants (difficulty access due to small vessels, non-availability of small HD catheters and cardiovascular instability) or patients who are haemodynamically unstable. Important to mention, is the fact that if tubing providing dialysis in PD disconnects, the consequences are minor compared to those of HD/CKRT systems, where disconnection can be catastrophic.

Manual PD is more feasible for small infants (including neonates) and children both from an access as well as a haemodynamic stability point of view.

Automated PD using a cycler machine which in theory could run independently of staff input for 24hours, was more expensive than manual PD from a consumables point of view, but this could be offset against the nursing cost of manual dialysis for a 24 hour period. However if there are technical problems related to the cycler machine,

including drainage problems due to the PD catheter, trained staff who are familiar with the machine need to be available or on-call to trouble shoot these issues.

This can result in a heavy workload on nephrology staff (both nurses and doctors) compared to manual dialysis which is a lot less complicated. A consistent electrical supply – similar to that required for CKRT – is also necessary, which can be a challenge in less well-resourced, regions requiring invertors or generators in the event of power cuts which are often unpredictable.

The PD catheters inserted by bedside Seldinger technique used for either automated PD in bigger children (peelaway PD catheters in children over 5kg) or in smaller infants (Cook® catheters under 5kg) were costly.

In centres where soft Seldinger inserted PD catheters are not available, the use of any double lumen catheter can be adapted for PD. The use of adult based equipment such as central venous catheters can be easily used as PD catheters in children. Other forms of improvisation including chest drains and nasogastric tubes have also been successfully used [7]. This has been successful when used in conjunction with locally made dialysis fluid using Ringers Lactate and dextrose [8] or as in Chapter 3 in this PhD (Use of locally prepared peritoneal dialysis(PD) fluid for acute PD in children and infants in Africa). The safety profile compared to conventional PD has been similar at least in terms of infection rates.

Rigorous evaluation of the safety of these improvised techniques compared with acute PD performed with commercial supplies in a randomised control trial would be ideal, but this may be difficult to fund and to do, especially as the PD companies would not support such a study.

In the absence of rigorous data, the fact that improvised PD is the most affordable form of PD should encourage its use as a lifesaving therapy, but should not preclude paediatric nephrology teams from advocating for appropriate custom produced and size specific catheters and manufactured dialysis fluid and in the long term.

4.7 Conclusion of Costing

Accurate costing of dialysis techniques is difficult to quantify in view of many hidden costs and the fact that children range in size from neonates to adolescents and costing depends on the patient's size. CKRT is possible in our centre but is labour intensive and requires highly trained staff. The Carpe Diem® CKRT system for infants and neonates is the most expensive modality, in addition to being the most staff intensive. These costs must all be taken into consideration by hospital administrators and senior clinicians in our setting, as stewardship of resources at the facility level (without

compromising on quality of care for individual patients e.g. choosing PD over CKRT if the patient can tolerate it) may permit resources to be available for other needs. The juggling of patient and societal needs at the bedside, is a reality in settings such as ours where resources are limited, but the clinical need is large.

As described in previous chapters, our 'PD first for paediatric AKI' is a cheaper alternative to other forms of CKRT. In our setting automated cycling PD may be economically appropriate and staff sparing providing there are no complications.

Acute PD with improvised catheters and using manual locally produced dialysis fluid, was the least costly and therefore should be affordable even in very low resource settings.

This form of dialysis does save lives, specifically in facilities where acute dialysis was not previously available or unaffordable.

4.8 References

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5 Final Chapter: Discussion and Conclusion

Kidney disease has become an increasingly important health challenge world-wide. For the purposes of this thesis, I have only concentrated on acute kidney injury (AKI) in children, as this is a common under-recognized condition, and with appropriate and simple therapy, many lives can be saved, and most children will recover and be able to return to normal life.

This PhD aligns with the practice of implementation research, which although not utilizing highly novel techniques, is extremely important and practical as it addresses the challenges of the 'know-do' gaps in real world settings by linking research, practice and the application of knowledge to improve the implementation of health programmes, policies and practices [1]. I have used the WHO Building Blocks framework as a baseline structure within which to place the research findings into context, and to highlight the important contribution of this work to health systems strengthening for kidney care services in low resource settings [2]. Studying paediatric AKI in the South African context, where resources are simultaneously present but restricted, provides a unique and strategic opportunity to learn lessons which may be generalizable across diverse lower resource regions. In the concluding chapter of this PhD I summarize the main findings of my work and consider some future directions for further research.

5.1 Global Context of this PhD

In view of the current poor outcomes of AKI (both mortality and risk of long-term chronic kidney disease), which has been equated to a silent killer, there has been a global drive to raise awareness of AKI [3,4].

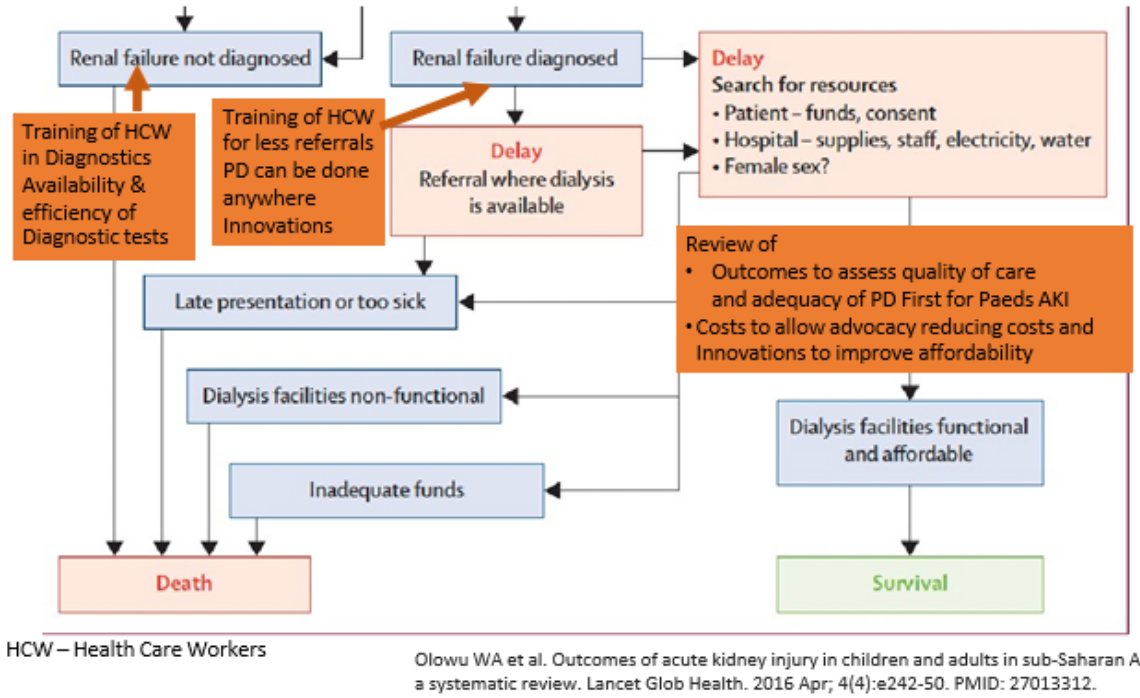

Figure 5.1: Action points of this PhD in approaching paediatric AKI (blocks in dark orange) (Reproduced with permission Olowu WA et al. Outcomes of acute kidney injury in children and adults in sub-Saharan Africa: a systematic review. Lancet Glob Health. 2016 Apr;4(4):e242-50. PMID: 27013312 [4].

To summarise the actions in response to the systematic review, in the course of this PhD, we looked at increasing training of health care workers to increase diagnosis of AKI as in Figure 5.1. By enabling easy PD for AKI locally in the community, we would also hope less referrals for treatment. Finally, we would also hope to reduce costs of dialysis as well as innovative means to provide PD where none existed previously.

The International Society of Nephrology (ISN) performed a 'Global Snapshot' to try to estimate the size of the AKI problem and challenges in access to care around the world. They then developed the 0 by 25 initiative to strengthen diagnostic capacity for those at high risk of AKI by using point of care testing (serum creatinine and urine dipstix) and implementing protocol-based management of AKI to limit kidney injury and optimize chance of recovery, aiming at zero preventable deaths from AKI by 2025, calling this a human rights case for nephrology [5-8].

Short term training programs have also been developed in the 'Saving Young Lives' (SYL) program, which was initially a collaboration of the International Society of Nephrology (ISN), International Pediatric Nephrology Association (IPNA) and the International Society of Peritoneal Dialysis (ISPD) focused on supporting capacity

building and trying to develop sustainable acute PD for AKI in low-resource settings(LRS). The focus is on providing training and educational activities in the community to improve awareness and equip local health practitioners to prevent AKI, identify cases needing hospital care, and to provide basic dialysis when required.

The Red Cross War Memorial Children's Hospital SYL course was initially the pilot of the 'Saving Young Lives' program which has developed all over the world now. This training was developed to included teams of health care workers with Doctor and Nurse teams attending together to learn. These teams were from various parts of Africa where there were little resources and so the training was aimed at improvised techniques and bedside PD to save lives [9-13]. I have been a core member of these initiatives and the SYL program originated at Red Cross War Memorial Children's Hospital and was piloted in Africa and with a 'hands-on' training course aimed at the management of AKI with a particular focus on training 'teams of doctors and nurses together' in the use of PD, using bedside placed PD catheters [3,14-16].

Such vertical programmes driven by external funders and organizations do have value during their implementation, but unless integrated within the health system, these programmes may not be sustainable or scalable. Countries must become independent, and must over time develop sustainable kidney care services that include the spectrum of kidney care, ranging from early diagnosis and intervention to dialysis. Dialysis may be expensive and consumes disproportionate proportions of the healthcare budgets, and therefore has not been prioritized in most lower resource settings [17].

Countries are slowly recognizing that given the numbers of patients affected, dialysis services must be expanded, and patients must be protected from catastrophic out of pocket expenses.

In South Africa access to chronic dialysis is rationed, but acute dialysis is theoretically accessible to all under the state health system, although not available in all settings. In many other countries in Africa, patients must pay for some or all of the costs, which severely limit access [17,18].

The current lack of accurate data on costs and burden of disease is a major hindrance to governments including kidney disease as a priority for financing. It is clear that chronic dialysis cannot rapidly be scaled up to meet all the need in African countries, however it is possible that dialysis for AKI, and especially in children could be cost-effective (as it could restore the child back to their baseline health level), and would score high among interventions that would improve equity given the current lack of access. Indeed, dialysis for pediatric AKI has been listed as a potentially high priority intervention, but thus far cannot be recommended because of lack of robust data [19].

Prevention of AKI, as discussed above should be prioritized in any country that is considering provision of dialysis for AKI as this is likely to be the most cost-effective option and if associated with improvements in public health and the social determinates of disease would have far more benefits in addition preventing AKI. A holistic approach to AKI is therefore required.

Overall, when reviewing AKI diagnosis and management, it is evident that there are significant inequities in access to care for AKI in Sub-Saharan Africa, given limited access to the systems, processes, and personnel required to diagnose AKI, and to resources necessary to provide appropriate treatment including dialysis if needed [3]. This presents a real challenge for quality improvement and advocacy especially when related to children [4]. Given that AKI is in general short-lived and there is a good chance of recovery with appropriate and time-limited therapy, strengthening health systems to deliver high quality AKI care is a good place to start building kidney care programmes and developing robust procurement and delivery systems to support dialysis.

5.2 Dialysis for Paediatric Acute Kidney Injury in Cape Town, South Africa

In Chapter 1, analysis of the AKI dialysis database at RCWMH revealed that a large number of paediatric cases of AKI (just under 600) have been managed with dialysis over a 22year period. Over this period variable dialysis techniques were available including Peritoneal dialysis (manual and automated) and Extracorporeal dialysis (Haemodialysis (HD), continuous kidney replacement therapy (CKRT) including the Carpe Diem for infant dialysis). The children dialysed ranged in age from neonates to adolescents, but the majority were smaller children (median age of 9.0 months; 60% under 1 year of age; 40% under 5 kg). The majority of children also received PD (78.1%) as the first form of dialysis showing that ‘PD First’ for paediatric AKI is a real and practical possibility. The PD catheters were inserted by Seldinger technique at the bedside in the majority of cases (84.4%) by paediatric nephrologists or fellows (as described in the next paper) and surgeons with theatre facilities were not required. This makes access to this form of dialysis much easier than having to wait for a theatre or surgical expertise. Complications were mainly technical and related to blockage or leakage of these catheters with no significant adverse events when the protocol was followed correctly. Extracorporeal dialysis was used in the older children (median 71.7 months) as opposed to PD. The overall survival in a very sick cohort of children, with AKI mainly due to cardiac conditions/surgery, sepsis/shock, renal and oncological conditions, was just under 60%. When further stratified, the survival of PD patients was 55% compared to 75% receiving ECD. Although the smaller children

predominantly received PD and had a poorer survival, many of these children were unlikely to have survived without dialysis and so we feel that the survival is acceptable.

Our overall conclusions following this study, was that PD First for Paediatric AKI' remains a valuable modality for management of AKI in children, especially in less well-resourced regions where bedside Seldinger PD catheter technique using soft catheters can be safely taught and implemented. We demonstrated an acceptable survival rate in children with AKI requiring dialysis without which these children would not survive.

As a bedside clinician and researcher, my purview here combines the goals of strengthening Service Delivery and utilizing Health Information Systems within the WHO health systems framework, to evaluate the use of scalable, effective and affordable interventions for management of paediatric AKI [2]. Since we began the SYL programme, we have demonstrated that basic PD provides a useful modality of treatment of AKI; that making this available would not involve particularly high costs, but could potentially save many lives. As a result, other centers around Africa have been implementing acute PD for AKI in children and we are currently collecting the data as to how many children thus far dialyzed and the survival rate [15]. The results from this study will provide further support that this form of PD is acceptable, especially when there is no alternative, and can save the lives of many children in Africa. This in turn aligns strongly with targets of SDG 3 (Introduction Chapter Table 2) to reduce infant and child mortality and reduce mortality from NCDs by 1/3 by 2030. The provision of access to basic PD could contribute significantly to the achievement of the SDG3 goal.

5.3 Regional training of paediatric nephrology in Africa

A shortage of the nephrology workforce has been described globally[20 - 23]. In particular we know that access to care for children with kidney disease is limited in less well-resourced regions of the world. Paediatric nephrology(PN) workforce development with good practical skills is critical. As described in Chapter 2 we performed a retrospective review of our PN training program and trainee feedback from 1999 to 2021, based at Red Cross War Memorial Children's Hospital (RCWMCH), University of Cape Town. This included 38 fellows who passed through the program for 1-2 years with an initial return rate to their home institutions of 100%.

Funding was obtained from multiple international nephrology societies as shown in Table 2.2 of Chapter 2. A follow-up survey was performed among the fellows to understand their impressions of their training. One of the most important parts of their training reported by the fellows was the provision 'hands-on' training with clinical examinations to assess diagnostic and management skills. In addition, they also reported that the practical skills of PD catheter insertion and kidney biopsies were very valuable (Table 2.7 of Chapter 2).

Fellows who stayed for a 2 year period were able to complete sub-specialty exams as well as completing master's degrees with research components achieving publications in peer reviewed paediatric nephrology journals as demonstrated in Table 6 of the Introduction Chapter of this PhD. These extra qualifications enabled them to take up positions of leadership in their own government and university institutions.

Fellows reported that challenges faced upon returning home were frequent and included lack of facilities, equipment, drugs and access to laboratory service as documented in Table 2.5 of Chapter 2. There remains a lot of advocacy to be done in this field.

Overall, this study revealed that the training program has successfully equipped African physicians with the requisite knowledge and skills to provide services for children with kidney disease in resource-constrained areas. The provision of funding from multiple organizations committed to paediatric kidney disease has contributed to the success of the program, along with the fellows' commitment to building PN healthcare capacity in Africa.

Strengthening of the pediatric nephrology health workforce in SSA is crucial if AKI is to be diagnosed and treated early and appropriately. This again aligns with the WHO framework of Health Systems building blocks in that it builds capacity of the health care workforce. Importantly in this survey the retention of these trained PN specialists was high in their home countries and therefore this programme does not appear to exacerbate brain drain which has been an important concern especially when training occurred in the Global North outside of Africa. As they continue to gain experience and benefit from an extended network of PN graduates and trainees across Africa, these individuals will in turn contribute to the training of others, making this a scalable and sustainable activity to strengthen delivery of kidney care for children in Africa.

5.4 Use of locally prepared peritoneal dialysis(PD) fluid for acute PD in children and infants in Africa

Access to dialysis especially in children is a challenge in low resource settings . The high costs of commercially available PD fluid and HD supplies limit their use, especially when patients have to pay for this out of pocket. In addition to this, due to logistics, challenges in availability of appropriately sized PD supplies, and political problems, there are also frequent shortages of dialysis consumables and fluids.

Improvisation in terms of locally made PD fluid as well as use of alternative dialysis catheters for acute PD have made dialysis possible in places where it had previously been impossible [24,25]. As described in Chapter 1 analysis of the data from the RCWMH AKI dialysis database revealed that pigtail catheters inserted using the

Seldinger technique, which are not custom made for dialysis (Table 1.1) can be safely placed at the bedside by paediatric nephrologists without the need for surgical support. Locally prepared PD solutions at the bedside adapted from intravenous solutions. Analysis of outcomes with the use of such locally made dialysis solutions Chapter 3, showed that this was safe, with a low rate of peritonitis. These findings have relevance for low resource settings across the world where regular PD solutions may be unavailable and therefore would preclude dialysis in children unless other solutions can be constituted. These two innovations can be implemented by trained personel where dialysis facilities are not available.

The two innovations described here therefore permit the use of dialysis technologies in environments with minimal resources and therefore again aligns with the WHO Health Systems building blocks to improve access to essential medications and technologies to improve care delivery. The SYL program aimed to help establish and maintain hospital services for the care of AKI, including facilities for acute PD. To date SYL trained doctors and nurses have treated more than 500 patients with AKI using acute PD with a 65% survival rate [15,16]. In several settings acute PD using these 2 innovations has been successfully implemented, and infection rates have been reported to be comparable to those seen with commercially prepared PD fluids. Importantly however it is important to acknowledge that these innovations represent “compromise” solutions that are acceptable when commercially produced PD catheters and fluids are not available, but these should not preclude advocacy for better facilities and resources and indeed should provide evidence to the health system decision-makers that PD is safely possible and scalable should be integrated into acute care services for children everywhere.

5.5 Cost of dialysis modalities for paediatric AKI

Absence of costing data related to dialysis provision is one of the major stumbling blocks in advocating for improved access to care [26]. At RCWMH we are fortunate in that we have a wide variety of dialysis systems available, which presented the opportunity to calculate and compare the cost of each dialysis modality as shown in Table 2 of Chapter 4. Analysis of the relative costs of PD and HD in our unit show that it is possible to provide PD for paediatric AKI for as little as R 500 (USD 25) using improvised material which can still be a significant in a low resource setting.

Neonatal hemodialysis machines (e.g. Carpe Diem ®) are by far the most expensive form of dialysis. This form of dialysis would therefore not be available or affordable in most centres where parents have to cover costs in low resource regions. In addition, manufacturers often do not want to produce small quantities of paediatric appropriate sized lines and consumables with resultant non-availability of paediatric sized products even in high income settings [27]. All of these factors emphasise the importance of

strengthening acute PD as the first dialysis modality of choice for children in lower resource settings.

Sustainable financing is core to Health Systems building block, therefore these data should be useful to inform policy makers and hospital administrators in developing budgets to support acute dialysis care for children with AKI.

5.6 Advocating for quality care for children with AKI

Ultimately the information generated through this PhD should be useful to develop strategic advocacy to support policy-making regarding dialysis. Innovative approaches have led to the development of techniques involving locally made dialysis fluid, improvised catheters and dialysis systems and training programmes have upskilled health care workers to provide acute PD in settings where dialysis had previously not been possible [24-25]. These strategies are aimed especially at supporting provision of affordable dialysis for children with AKI in low resource settings. If dialysis is available for children with AKI, there is the potential to save many young lives.

Our studies have demonstrated that:

1) it is possible to provide acute PD at very low cost to children of all ages with AKI
2) that simple consumables and processes can be used if more complex ones are not available
3) that potentially this could save lives.

What now need to happen are trials in multiple regions to optimise the processes, the indications, and the policies. Following on from this it is important to then demonstrate what the actual outcomes are in low resource settings and what the cost-effectiveness of implementation of ‘PD first for Paediatric AKI’ could be as a result.

Local studies are important to prove the that quality care for AKI is possible with appropriate and affordable treatment, and that staff training at both local and national level can scale up these practices in places where there previously were none. Government departments often come to local kidney organisations for input on policy.

Advocacy must also include linking with policy makers with international kidney organisations such as IPNA(the International Pediatric Nephrology Association) and ISN(the International Society of Nephrology) to access expertise when needed and to progress towards equitable care opportunities children with AKI (often forgotten) everywhere. As such, this PhD also aligns with the ISN World Kidney Day14 March 2024 in Kidney Health For All – Advancing equitable access to care and optimal medication practice globally – including for the children of Africa with AKI.

5.7 Future research suggestions based in the findings of this PhD

The concept of implementation research is highly relevant in our setting as it tests the impact of real practices in real settings, and does not always need vast amounts of additional resources. It has been important to evaluate the approaches to acute dialysis care that we have developed and implemented over the past 2 decades, as well as to evaluate the training of a new pediatric nephrology workforce after training a critical number of fellows who largely remained in their home countries. The studies outlined in this PhD have provided useful information that will feed into improvements in dialysis delivery and in training of the health workforce for pediatric AKI care. Through international societies and collaborations these findings may support expansion of dialysis access and advocacy for better kidney care for children across lower resource settings.

This PhD is a form of situational analysis of what is currently possible, acceptable, and affordable in term of optimizing dialysis care for children with AKI in a resource limited environment. Much more work is needed to refine current practices, develop more robust databases and to understand how to improve quality of care across the spectrum of AKI. These studies would include:

- Early diagnosis with ready access to basic testing (electrolytes and creatinine, using dipstick), as well as early management of AKI (including fluid management, diuretics and basic renal replacement therapy) are key to reduce the need for dialysis and enhance the chances of renal recovery in children with AKI. Studies in children analysing suitability and cost of point of care Creatinine measurement may be a faster alternative than relying on formal laboratory testing to make the diagnosis of AKI. The use of biomarkers such as NGAL which has been adapted to urine dipstix testing may work as a early marker of kidney injury [28]. Ongoing studies of these novel diagnostics should include children in lower resource settings to determine utility and cos- effectiveness
- Follow-up (short, medium and long-term) after AKI is required given the risk of CKD. This far these studies have almost exclusively been performed in high resource settings. Strategies to integrate long term monitoring for any child who has had AKI using good paediatric nephrology screening techniques (growth, blood pressure, urine dipstix) into routine pediatric care must be developed and tested in multiple contexts to identify and overcome barriers.
- It is important to capture data to inform clinical management, service improvement and planning as well as to track the burden of disease and potential targets for prevention. An electronic database is definitely needed. Registries for chronic kidney failure are slowly developing in Africa but there is not a lot of activity yet in paediatrics [29,30]. Paediatric kidney registries (both acute and chronic) ideally online and electronic, must be established to allow

audit and research of understand the true epidemiology and outcomes of AKI in children across the world.

- If we are to understand the implications of AKI (with and without some dialysis support), it is essential to develop databases across the world, and to integrate the data. This faces many challenges (need for electronic health systems, challenges with sharing of data between institutions and countries. But we do need to agree on the data to be collected, the definition of terms within databases. We also need to develop collaborations in order to collate and disseminate the data.
- Research related to workforce training is required, e.g. longitudinal follow up of fellows trained in paediatric nephrology over a longer time period e.g. 3-5 years after return to their home countries, to assess how they have managed to navigate their paediatric nephrology services around their local challenges.
- Trainees becoming trainers is an exciting concept and it would be good to plan and then review any teaching programs that are occurring locally following our fellows returning to their home institution. This could also expand to other less well-resourced regions where trained paediatric nephrologists can develop central teaching hubs for countries in the same region.
- In terms of short-term training programs in acute dialysis techniques, research is needed not only immediately post attendance of a teaching course but also longer-term follow-up to assess if skills taught are retained, and assessment of clinical impact would be important, e.g. numbers of patients who received acute dialysis and their outcomes.
- Documentation of processes and outcomes is important when acute dialysis is performed using improvised systems e.g. nasogastric tubes are being used as PD catheters by kidney team in Zambia. Such data may strengthen calls for local companies producing intravenous fluids to expand to also manufacture dialysis fluid which could then be included in follow-up studies for safety and affordability.
- It is also important to review the ethics around acute dialysis as it pertains to patients who may not recover and would require long term dialysis in settings where this may be restricted [17,26, 31]. One needs to think of when to start dialysis; how one withdraws if there is no chance of chronic dialysis. One would need to see how the implementation of dialysis potentially impacts on the care of other children with other treatable conditions and health priorities.
- Formal research to determine the cost-effectiveness of dialysis including both acute and chronic is required for planning of services at both local and governmental level. The impact and value of public-private partnerships such as the Fresenius – Red Cross War Memorial Children's Hospital(RCWMCH) dialysis facility which has been successful for providing service both for private as well as state patients' needs to be evaluated more rigorously.

- Climate change and ‘Green’ nephrology are relevant for paediatric nephrology as dialysis is a major contributor to carbon emissions, which is important to consider for advocacy and planning, as well as research and innovation to reduce this impact.

5.8 My journey and learnings through this PhD

During the course of this thesis, I have learned multiple research techniques related to data management (data collection and extraction), statistical techniques (survey and analysis), as well as writing culminating in the publication process. At the same time, I have mentored multiple fellows in their research for their Masters’ theses (see Table 6 of Introduction Chapter).

It has been a difficult process at times as I have been supporting a very busy paediatric renal service based at Red Cross War Memorial Children’s Hospital (RCWMCH) which includes dialysis and transplantation. This service is run with a small consultant faculty staff of only 3 paediatric nephrologists. In addition to this, we are responsible for student (under-and post graduate training) as part of our University of Cape Town (UCT) commitment. Research as part of our Senior lecturer component is also required as part of the university requirements.

In the last 5 years, I have also taken over the leadership of the Paediatric Solid Organ Transplant service – the biggest for children in the country – and in addition to paediatric kidney and liver transplantation, we have recently added heart and lung transplantation to this service.

As a senior clinician I also support the Paediatric Intensive Care Unit at RCWMCH – the largest in Africa - which has not left me much time for writing and reflection. All of this clinical practice has been an integral part of my journey in the PhD, which has grown out of the challenges faced at the bedside and the desire to find sustainable and acceptable solutions today and for the future, to improve access to and quality of dialysis for SAKI in children in Africa and elsewhere.

The line between clinical practice and research is therefore relatively thin, but each chapter reflects a research study which utilized different research techniques and arrived at answers which all for part of the bigger jigsaw puzzle that I am building, with my colleagues and our international networks.

I am currently also the only Full Professor in Paediatric Nephrology in the country something of which I am really proud of in addition to be the only female in this position.

In addition, I have held several national and international positions of leadership including President of the South African Paediatric Association (SAPA) during the COVID pandemic, and still remain on the executive as the advocacy voice to the media.

I am currently the President of the South African Transplantation Society – the first non-surgeon and paediatrician in this role – playing an important role in promoting transplantation in South Africa.

In addition, I currently serve on the Ministerial Advisory Board for Organ Transplantation (MACOT) for the government as an advocate for children.

I have also just stepped down as the President of the International Paediatric Transplantation Association (IPTA) as the first African president which gave me a lot of opportunity to promote transplantation in LMIC while in that position.

Currently I am very excited to be the Congress Chair for the International Paediatric Nephrology Association 2025 and hosting this in Cape Town as the first time on the African continent.

All this has only been possibly due to the amazing team of medical, nursing, allied health and cleaning staff that make up our services at RCWMCH not only in the renal and PICU but also throughout the whole hospital and the University of Cape Town at large.

5.9 Ongoing activities to keep strengthen capacity building for AKI management

All these experiences have provided me a great opportunity for teaching and mentoring gaining insights to be innovative in teaching and service provision. In addition, I have been dedicated to excellence in paediatric patient care and to advocacy for better care. Despite showing here what one can achieve with paper-based databases and improvised catheters and PD fluid in low resource settings, these are not really ideal long-term solutions. Advocacy must continue for improved health information systems, better quality service delivery and equitable access to medicine and technologies to improve care for children of all ages with AKI everywhere in the world.

For me this thesis truly embodies African solutions for African patients, where innovation has really been essential in aiming towards the goal that ‘no-one should die of AKI without at least an attempt of acute peritoneal dialysis’.

Thank you for taking the time to read and review this manuscript. I hope to make my long-suffering supervisors proud.

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Lessons learned from regional training of paediatric nephrology (PN) fellows in Africa

Graphical Abstract

HYPOTHESIS: Access to care for children with kidney disease is limited in less well-resourced regions of the world and development of a paediatric nephrology (PN) clinical workforce to fill the gap in care is possible

DESIGN & OUTCOMES: Review of PN training 1999 – 2021 Red Cross War Memorial Children's Hospital, Cape Town

Trainees 38 total

Country of Origin	Number of Fellows
South Africa	11
Nigeria	11
Kenya	4
Ghana, Uganda, Zambia	2 each
Benin, Botswana, Libya, Sudan, Tanzania, Zimbabwe	1 each

Funding Source (Some combined)	Number of Fellows
IPNA(International Pediatric Nephrology Assoc)	24
ISN(International Society of Nephrology)	13
ISPD(International Society of Peritoneal Dialysis)	2
APFP(African Paediatric Fellowship Program)	8
Own funding – home institutions	2

Clinical Impact of Fellowship
Hands-On training is the most useful training in practical management of African kidney diseases
Acquisition of procedural skills with direct mentorship from faculty
Regular supervision of kidney biopsy procedure facilitating PN fellow confidence in performing and teaching kidney biopsy on return to home centre
Specific training in improvised techniques for management of AKI including bedside PD catheter placement
Acquired skills and confidence gained in kidney transplant management

Conclusion: Training successfully equipped African PN fellows with knowledge and skills for children with kidney disease. Funding from organisations committed to paediatric kidney disease contributed to the success, together with fellows' commitment to build PN healthcare capacity in Africa.

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