Department of Paediatrics & Child Health

ANNUAL RESEARCH DAYS 2023

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Programme and Abstract Book

Tuesday, 31st October and Wednesday, 01st November 2023

Venue: D3 Lecture Theatre, Red Cross War Memorial Children's Hospital (with livestreaming via Zoom)

CPD Points for Tuesday, 31st October and Wednesday, 01st November 2023

Please sign attendance registers on both days to claim your CPD points.

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Wednesday, 01st November 2023

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Title: **DIALYSIS FOR PAEDIATRIC ACUTE KIDNEY INJURY IN CAPE TOWN, SOUTH AFRICA**

Authors: McCulloch MI[1], Luyckx VA[2], Morrow B[2], Nourse P[1], Coetzee A[1], Reddy D[1], Du Buisson C[3], Buckley J[1], Webber I[2], Numanoglu A[2], Sinclair G[1], Nelson C[1], Salie S[1], Reichmuth K[2], Argent A[2]

Affiliation: [1] Red Cross War Memorial Children's Hospital(RCWMCH) & University of Cape Town; [2]University of Cape Town; [3]Tygerberg Children's Hospital, University of Stellenbosch

Introduction:
Substantial developments have been made over the last few years in kidney replacement therapy (KRT) technology across the world with equipment being developed for even the smallest neonate. Unfortunately, many lower and middle-income countries(LMIC) have not had access to these facilities, and we wanted to review the results of KRT in paediatric acute kidney injury (AKI) in our centre.

Objective:
To describe:
1. Profile of AKI for which KRT was offered over the last 20 years
2. Methods of delivering KRT over the study period
3. Outcomes and complications of children receiving acute KRT over the study period

Methods:
Retrospective descriptive case review of the acute dialysis database, including children aged birth to 18 years who received acute dialysis in the Paediatric Intensive care Unit (PICU), from 1998 to 2020 in 4 consecutive time quartiles.

Results:
Overall, 593 children with AKI received dialysis. Their median age was 8.0 (range 0.03 to 219.3; IQR1.0–58.3) months; the biggest group (57.6%) were <1 year old. Patients' weights ranged from 0.9–62.0 kg (median 7.0 kg, IQR 3.0–16.0 kg); again the biggest group (38.6%) were <5 kg.
Underlying conditions requiring dialysis for AKI included cardiac disease (26.2%), underlying kidney pathology (21.5%), sepsis (17.9%)/shock (5.1%) and oncology (6.2%) as the main causes.

Peritoneal dialysis(PD) was more common than extracorporeal dialysis (ECD) (76.97% compared to 20.41%) with (PD) used in younger children (median 6.4 months) and ECD in older children (median 71.7 months, p=0.001). Bed-side PD catheter insertions (n=490/578, 83%) were predominantly by paediatric nephrologists/intensivists and nephrology fellows (n=412/490, 84.1%) under supervision, as an essential part of their training, rather than surgeons (78/490, 15.9%), who were most likely to do the difficult or complicated cases. Catheter types inserted; included 335/578 (60.9%) Cook® catheters, 145/578 (26.3%) peel-away PD and only 45/578 (8.2%) surgically inserted PD catheters .

Complications occurred in 127/560 (22.7%) children receiving PD including: blockage or poor drainage in 72 (56.7%) with only a small number leaking 5(3.9%); displacement of the PD catheter 6 (4.7%); pleural effusion secondary to PD in 4(3.2%); fungal peritonitis requiring discontinuation 3(2.4%); bladder perforation 2(1.6%%). No bowel perforations were noted, but discoloured ascites on insertion suggesting peritonitis or bowel necrosis required change in management 7(5.5%) and changing of PD to ECD in 28 (22.7%).
Overall, 314/542 (57.8%) children survived. Survival was better in the ECD (75.4%) than in the PD group (55.6%, p=0.002). 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).

Conclusions:
We demonstrate an acceptable survival in children with AKI who required dialysis throughout the study period. Outcomes were poorer in smaller children. Acute PD, with bed-side catheter placement placed by non-surgeons, is a feasible, practical and acceptable dialysis modality in our setting.

HREC REF: 646/2015

Title: **INTRA-ABDOMINAL PRESSURE MEASUREMENT IN CHILDREN WITH ACUTE KIDNEY INJURY ON PERITONEAL DIALYSIS**

Authors: Peter Nourse[1], Mignon McCulloch[1], Ashton Coetzee[1], Tim Bunchman[2], Stefano Picca[3], Jody Rusch[4], Andre Brooks[5], Hilton Heydenrych[6], Brenda Morrow[7]

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Objective
Critically ill Children on peritoneal dialysis are at increased risk of raised intrabdominal pressure (IAP). There is no data on the pressure generated with a standard peritoneal dialysis (PD) prescription fill volume in children with AKI. The aim of this study was to determine the IAP after filling the abdomen with a standard PD fill volume in children, and to compare the two different techniques of measuring IAP.

Method:
This study was a secondary analysis of a previously published crossover randomised controlled trial. We analysed IAP in 15 children with AKI after a standard PD fill volume. We also compared direct vs vs intravesical pressure measurements. Additionally, differences in pressure depending on dialysis technique i.e conventional PD vs continuous flow peritoneal dialysis (CFPD)and correlation to baseline characteristics were also analysed.

Results:
Median (range) age and weight of participants were 6.0 (0.2-14) months and 5.8 (2.3-14.0) kg respectively. Nine out of fifteen patients had raised IAP after filling . No children developed compartment syndrome. Mean ± SD IAP on convention PD was 9.35 ±2.97and 11.5±2.96 when measure directly and indirectly respectively. Mean IAP on CFPD was 9.33±.35 and 11.2±3.62. when measure directly and indirectly respectively. IAP was significantly lower when measured by the direct method compared to intra-vesically. (p=0.002). There was however good correlation and moderate agreement between the methods. There were no differences when comparing PD to CFPD. There was no correlation with baseline characteristics.

Conclusion:
Increased IAP was common in patients with AKI on PD and although not associated with compartment syndrome, this warrants IAP monitoring in these patients. There was only moderate agreement between direct and intravesical measurements calling for more studies to define IAH in children on acute PD.

This study was approved by the University of Cape Town's Human Research Ethics Committee (HREC REF: 363/2017)

Title: **REVIEW OF THE RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL PAEDIATRIC KIDNEY TRANSPLANT PROGRAM OVER THE LAST 20 YEARS**

Authors: Pienaar T[1], Coetzee A[1], Nourse P[1], Abdo T,[1] Reddy D[1], Buckley J[1], Du Buisson C[3], Sinclair P[1], Gajjar P[1], Siyotula T[1], Du Toit T[2], Thomson D[2], McCurdie F[2], Gili B[1], Ndamase B[1], Wilson G[1], Salie S[1], McCulloch M[1].

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Introduction:
RCWMCH is one of only a few centres in South Africa performing paediatric kidney transplants(KTx). Dialysis is challenging in children and ideally we aim for an early pre-emptive transplant from a living related donor.
The first paediatric KTx in South Africa was performed at Karl Bremmer Hospital, Cape Town in 1967 and up until 2022 a total of 284 KTx have been performed in our centre. Paediatric KTx requires a multidisciplinary team approach for a successful program

Method:
Review of RCWMCH paediatric KTx database between 2003 and 2022 and highlights the demographics, donor complications and survival rates.

Results:
169 of the total 284 paediatric KTx were performed during the study period of which 95(56.2%) male and 74(43.7%)female.
The patient ages ranged from 1year 11months to 20year 7months; with age groups divided into 10-15year old patients 76/169(44.9%), 5-10year olds 35/169(20.7%), 15years and older 33/169(19.5%) and finally 0-5year olds 25/169(14.7%).
Commonest causes of Kidney Failure were nephrotic syndrome 58/169(34.3%), posterior urethral valves and kidney dysplasia each 17/169(10%).
The donor kidney type included 91/169(53.8%) donation after brain death(DBD), 65/169(38.4%) living related donation(LRD), 3/169(1.7%) living non related donation(LNRD)needing ministerial permission, and 2/169(1.1%) donation after circulatory death(DCD).
Thirteen(8.2%) kidneys were re-do kidney transplants.
Eight(4.7%) patients had combined liver and kidney transplants.

Overall survival; 1yr and 5yr patient survival 158/168(94%) and 140/163(85.8%); 1yr and 5yr graft survival 141/169(84.4%) and 77/169(62.6%) which included a cohort of teenagers(20%) over 15years.

Conclusions:
We report a paediatric KTx program with a wide age range of recipients including teenagers. Our donor kidneys come from living related donors in more than a third of cases and we have also used kidneys from DCD donors. Our patient and graft survival at 5 years are acceptable for a paediatric KTx program in a less well-resourced region.

HREC REF: 675/2023

Title: **REVIEW OF THE RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL PAEDIATRIC LIVER TRANSPLANT PROGRAM OVER THE LAST 20 YEARS**

Authors: Abdo T[1], De Lacy R[1], Pienaar T[1], Radebe L[1], Mokoto T[1], Spearman CWN[2], Siyotula T[1], Du Toit T[2], Thomson D[2], McCurdie F[2], Gili B, Ndamase B[1], Wilson G[1], Salie S[1], McCulloch M[1].

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Introduction:
RCWMCH is one of only 2 centres in South Africa performing paediatric liver transplants. The first paediatric liver transplant (LTx) in South Africa was performed at RCWMCH in 1987 and up until 2022 a total of 141 LTx have been performed in our centre. A successful paediatric LTx program requires a multidisciplinary team. It is important to review the results of these LTx patients both in terms of their complications and outcomes in order to assess the success of this program.

Method:
Review of the RCWMCH paediatric LTx database between 2003 and 2022 and highlights the demographics, complications and survival rates.

Results:
Seventy one of the total 141 paediatric LTx were performed during this study period. 8 of 11 total combined liver kidney transplants were performed in study period.
There were 25 males and 46 females with a mean age at transplant of 4.6 years. 50/71 (70%) were transplanted for extrahepatic biliary atresia. All transplants during this period were deceased donors and the most common graft type was the Left Lateral Segment of the liver(25/71; 35%).
The 1 and 5 year survival rates were 83.8% and 72.5% respectively. A total of 6/71 (8.4%) patients died within 1 month post-transplant of which 3 were due to Hepatic Artery thrombosis (HAT). Other post-transplant complications included post-transplant lymphoproliferative disease (9), HAT (6), portal vein thrombosis (6) and bile duct pathology (11).
In terms of facilitating the program there was a requirement not only for appropriately trained paediatric transplant coordinators, paediatric surgeons, hepatologists and interventional radiologists but also paediatric anaesthetists and intensivists with a robust paediatric intensive care unit supported by well-trained nursing staff, physiotherapists, dietitians, social workers, laboratory services, blood bank and hospital managers.

Conclusion:
Paediatric LTx requires a multidisciplinary team of health care workers dedicated to transplantation. This study demonstrates that a paediatric liver transplant program is possible in a South African dedicated children's state hospital and highlights challenges that must be addressed to further improve outcomes in paediatric liver transplantation.

HREC REF: 657/2023

Title: **CRITICAL PERTUSSIS INFECTION IN THE PAEDIATRIC INTENSIVE CARE UNIT OF RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL: *A CASE SERIES IN AN OUTBREAK***

Authors: Nnedima Nkado[1], Helen Crichton[2], Brenda Morrow[3], Shamiel Salie[2], Claire Procter[2]

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Background:
Bordetella Pertussis is a highly infectious disease associated with increased mortality in young infants. Critical pertussis is defined as pertussis disease resulting in Paediatric intensive Care Unit admission or death.

Objective:
Our study aims to describe the clinical profile, morbidity, mortality and management of children with critical pertussis admitted to Red Cross War Memorial Childrens Hospital Paediatric Intensive Care unit (RCWMCH PICU).

Study design:
A retrospective analysis of children with critical pertussis admitted to RCWMCH PICU over 1 year, January 2022-December 2022.

Results:
There were 1273 admissions to RCWMCH PICU during 2022, 19 patients tested positive for Bordetella pertussis and of those, 7/19 patients (36.8%) demised. One patient did not receive azithromycin prior to demising. There were 13/19 (68.4%) patients that were completely unimmunized, with 9 being too young to be vaccinated.
The median (IQR) total duration of ventilation was 7.0 (3.0 – 21.0) days, with a maximum of 35 days. Mortality rates were significantly higher in patients that were HIV exposed (n=3/7,42.9% vs n=3/12, 25%; p <0.001), preterm (n=4/7,57.1% vs n=4/12, 33.3%; p <0.001); had septic shock (n=7/7, 100% vs n=4/7, 33.3%; p = 0.02) or acute kidney injury (n=6/7,85.7% vs. n=2/12, 16.7%; p<0.001) on univariate analysis. The maximum WCC was significantly lower in those patients that survived vs those that demised (27.75 vs 76.32; p <0.001). There was no significant association between hospital acquired blood stream infections and mortality. On multivariate regression, none of the variables were independently associated with mortality.

Conclusion:
Further research is required in patients with critical pertussis to establish morbidity and mortality in South Africa as well as other low- and middle-income countries. Further research is also needed to establish the best management protocols to optimize survival rates. We advocate for vaccination against pertussis in the third trimester of pregnancy and to strengthen current vaccination campaigns.

Key words: Bordetella pertussis, critical pertussis, outcomes

HREC REF: 082/2023

Title: **CARBAPENEM RESISTANT ENTEROBACTERALES INFECTION AND COLONIZATION IN A PAEDIATRIC INTENSIVE CARE UNIT IN A MIDDLE INCOME COUNTRY**

Authors: Claire Procter[1], Brenda Morrow[2], Nnedima Nkado[3], Shamiel Salie[1]

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Background:
The number of patients with multi-drug resistant bacterial infection and/or colonization has been increasing worldwide in recent years and is resulting in an important public health proble. Options for treating infections due to these organisms are extremely limited and they are associated with high mortality rates. Previous studies have shown that active surveillance and appropriate isolation reduced the incidence of CRE infection and risk-factors for CRE have been identified. There is a paucity of data describing the burden of CRE in children admitted to paediatric intensive care units (PICUs) in Southern Africa. This data is needed to inform management protocols.

Objective:
To describe and compare the number, clinical spectrum and outcomes of CRE-infected and colonized patients identified in the PICU at Red Cross War Memorial Children's Hospital (RCWMCH) over a 1 year period.

Methods:
This was a single-centre, retrospective descriptive study. Data was extracted from the clinical records of all patients admitted to PICU in 2021. Patients were screened for CRE according to the Western Cape Provincial Policy of 2019.

Results:
There were 1062 patients admitted to PICU during the study period with 1232 admissions. 350 patients were screened for CRE with 61/350 (17.4%) testing positive. Patients with positive cultures i.e. CRE infection had a significantly longer duration of PICU stay (median 22 days) compared to those who were only CRE colonised on rectal swabs (median 3 days; $p<0.001$). The overall mortality rate in PICU was 10.1% (107 patients), 19 (18%) of whom were CRE infected or colonised. Of those screened for CRE (n=350) mortality was significantly higher in CRE positive (n=19;31%) compared to CRE negative patients (n-28;9.7%; $p<0.001$). There was no difference in mortality rates between patients infected vs. colonised with CRE ($p=0.2$). On multivariate analysis, no independent factors associated with CRE infection or colonisation could be identified.

Conclusion:
CRE infection or colonisation was associated with significantly increased mortality, whilst CRE infection was associated with significant morbidity with increased duration of PICU stay compared to colonised patients. Considering the significant associated mortality and morbidity, active surveillance screening for CRE is recommended in the PICU.

HREC REF: 794/2022

Title: **CHILDREN ADMITTED TO PAEDIATRIC INTENSIVE CARE AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL WITH NON-ACCIDENTAL INJURIES (2012-2020): A RETROSPECTIVE DESCRIPTIVE STUDY**

Authors: Lynelle Bowes[1]; Carla Brown[2]; Beyra Rossouw[1]; Dirk von Delft[3]; Brenda Morrow[1]

Affiliation: [1]Department of Paediatrics and Child Health, University of Cape Town; [2]Social Work Department, Red Cross War Memorial Children's Hospital; [3]Paediatric Trauma Department; Red Cross War Memorial Children's Hospital

Objectives:
South Africa has a high burden of paediatric non-accidental injury (NAI), defined as the deliberate infliction of injury or harm to infants and children, with considerable associated morbidity and mortality. There is a paucity of evidence on the prevalence or outcomes of children with severe NAI requiring paediatric intensive care unit (PICU) admission in South Africa. This study therefore aimed to describe the characteristics and outcomes of patients admitted to the PICU at Red Cross War Memorial Children's Hospital with suspected NAI, to inform advocacy initiatives and create clinical awareness.

Methods:
This was a retrospective descriptive study of routinely collected data from all infants and children admitted to the PICU with suspected NAI, as documented by a medical practitioner, between 1 January 2012 to 31 December 2020. Patients admitted following accidental or self-inflicted injury were excluded. Patient characteristics were compared between PICU survivors and non-survivors using Mann Whitney U or Chi^2 tests, as appropriate. Statistically significant and clinically relevant factors identified on univariate analysis were entered into a multivariable binary regression analysis to identify any independent predictive or modifiable factors for mortality. A significance level of $p < 0.05$ was chosen.

Results:
A total of 11345 children were admitted to PICU over the study period, of which 119 patients (1.0%) were screened for inclusion after reviewing PICU and Social Work databases for all documented cases of suspected NAI. Fifty-five (46.2%) of these children were admitted with gunshot wounds (GSW). After determining that the injuries sustained were accidental, 69 patients (including 47 with GSW) were subsequently excluded. A total of 42 children (median (interquartile range, IQR) 20.3 (7.9 – 62.6) months; 61.9% male) were included in data analysis.

Most patients sustained physical injury (n=31; 73.8%) from assaults (n=19; 45.2%), with head injury (n=24; 57.1%) the most common site, followed by skin (n=23; 54.8%), polytrauma (n=17; 40.5%) and chest (n=15; 35.7%) injury. In most cases (n=24;57.1%) the perpetrator, where known, was a family member and the incident occurred in the home (n=35; 83.3%).

During their PICU stay, most patients (n=37; 88.1%) received invasive mechanical ventilation for median (IQR) duration 2.0 (1.0 – 3.8) days. Inotropic support was required by 11 (26.2) patients; 18 (42.9%) received blood products and 23 (54.8%) underwent surgery during their PICU admission.

PICU mortality was 28.6% (n=12), with a risk adjusted mortality (observed/mean predicted mortality) of 1.2. Ten of these children (83.3%) died following withdrawal of life-sustaining therapy. Of the 30 PICU survivors, 7 (23.3%) were discharged with long-term disability, whilst the functional outcome of 16 (53.3%) survivors is not known.

On univariate analysis, PICU mortality was associated with having a head (91.7% vs 43.3%; $p = 0.004$), skin (83.3% vs. 43.3%; $p = 0.02$), or eye injury (50.0% vs 10.0%; $p = 0.004$); having sustained a combination of physical abuse and neglect (33.3% vs 0%; $p = 0.006$); and receipt of inotropes (50.0% vs 16.7%; $p = 0.03$). No independent predictors of mortality could be identified on multivariable analysis.

Conclusions:
Children who have sustained NAI represent a small proportion of PICU admissions, with higher-than-expected mortality and considerable morbidity. Gunshot wounds are relatively common, and although not all met NAI criteria, these results support advocacy efforts to create a gun-free South Africa. Early recognition of children who may have sustained severe NAI, based on presenting signs and injury patterns, is important to facilitate prompt referral and management. Standardised follow-up of survivors of severe NAI is recommended to determine and optimise long-term functional and psychosocial outcomes. Urgent action and policy change is needed to achieve the Sustainable Development Goal of eliminating violence against children by 2030.

HREC REF: 493/2021

Title: **INVESTIGATING THE GENETICS OF CONGENITAL HEART DISEASE IN SOUTH AFRICA BY EXOME SEQUENCING**

Authors: Timothy F Spracklen,[1,2,3] Thomas Aldersley,[2] John Lawrenson,[2] Blanche Cupido,[4] George AM Comitis,[2] Rik De Decker,[2] Lenise Swanson,[2] Alexia Joachim,[2] Barend Fourie,[5] Andre Brooks,[6] Raj Ramesar,[7] Bernard D Keavney,[8] Liesl J Zühlke[1,2,3,4]*

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Objective: Congenital heart disease (CHD) is the most common birth defect and a leading cause of paediatric morbidity and mortality worldwide. The burden of disease, however, falls heavily on low- and middle-income countries. In other populations, a role for genetic factors has been demonstrated, where they can have implications on diagnosis and management. Here, we sought to investigate genetic causes of CHD in South African patients.

Methods: Exome sequencing was used to screen 255 patients with various cardiac phenotypes for pathogenic variants in established CHD genes. The cohort included 228 patients with isolated CHD and 27 with extracardiac anomalies. Patients with known genetic syndromes were excluded.

Results: We identified a total of 45 pathogenic or likely pathogenic variants in 43 patients (variant yield: 16.9%). Fewer genetic results were observed in patients with extracardiac anomalies ($p=0.00626$). Patients with conotruncal defects were slightly more likely to generate a positive genetic finding, and those with isolated septal defects slightly less likely; all other phenotypes were equally likely to generate a genetic result. There was a high rate of uncertain genetic findings, with 65.9% of the cohort having variants of uncertain clinical significance as a final genetic result. In addition, we observed many novel genotype-phenotype correlations in our dataset. These included several pathogenic variants in syndromic CHD genes in patients with isolated cardiac lesions. We also identified ten new genes for conotruncal defects, mainly Tetralogy of Fallot, in our cohort.

Conclusions: We show that a genetic cause of disease can be identified in a subset of South African CHD patients. This is in accordance with findings in international CHD studies, although we report several novel genotype-phenotype correlations which may affect variant interpretation in other population groups. Unexpectedly, a lower mutation yield was observed in patients with extracardiac anomalies. Avenues for future research will include re-examining the high burden of variants of uncertain significance, interrogation of these data for novel candidate CHD genes, and determining any associations between identified variants and patient outcomes, so genetic data can be used to improve management of CHD patients in Africa.

Ethics approval number: R016/2014
Previous presentations of this work: none (pending – World Congress of Paediatric Cardiology and Cardiac Surgery, 27 August – 01 September 2023)

Title: **A Systematic Scoping Review of the Use of Surfactant Replacement Therapy for Respiratory Distress Syndrome in Preterm Neonates in Resource Limited Settings**

Authors: Dr Caris Price, Professor Lloyd Tooke, Professor Heather Zar, Professor Brenda Morrow

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Objectives:
Approximately 45% of prematurity-related deaths in low and middle income countries **(**LMICs) are attributable to respiratory distress syndrome (RDS), a consequence of lung immaturity and surfactant deficiency. The availability and use of surfactant replacement therapy (SRT) in LMICs is variable and limited by resource constraints, with unclear impact on patient outcome.

This systematic scoping review aimed to synthesize the published evidence on SRT in the management of preterm neonates with or at risk of RDS in LMICs (as defined by the World Bank), with regard to surfactant type, method and timing of administration and cost implications.

Methods:
A systematic scoping review of seven databases was conducted, following the Preferred Items for Systematic Reviews and Meta-Analysis guidelines extension for Scoping Reviews (PRISMA- ScR. English language systematic reviews, observational and experimental studies, published between January 2010 - October 2023, which investigated the use of SRT in preterm neonates with or at-risk of RDS, in LMICs were eligible for inclusion. Case reports, small case series and qualitative studies were excluded.

Titles and abstracts were screened by one reviewer, and full text by two independent researchers. Data from included studies were extracted in a standardised manner. Sufficiently homogeneous randomised controlled trials (RCTs) were synthesised using random effects meta- analyses, whilst other results were synthesised narratively. Primary outcomes for meta-analyses were 1) progression to invasive mechanical ventilation; 2) development of bronchopulmonary dysplasia (BPD) and 3) mortality.

Results:
After screening 483 titles/abstracts and 266 full texts, 123 articles were included in the final review (including 50 RCTs, 48 observational studies and 2 cost-effectiveness/cost-utility studies).

Studies reported both INtubation-SURfactant-Extubation (INSURE) and Less/Minimal Invasive Surfactant Administration/Treatment (LISA/MIST) methods of SRT, with different threshold criteria for implementation, frequently related to resource limitations.

There was moderate certainty evidence that using LISA/MIST reduced the need for mechanical ventilation (RD 0.10 (0.04 – 0.17); p = 0.001) compared to INSURE, with no significant effect on BPD (RD 0.04 (0.00 – 0.08); p = 0.05) or mortality (RD 0.01 (-0.02 – 0.04; p = 0.5).

There was low certainty evidence that Poractant alfa (200mg/kg) was associated with a reduced need for mechanical ventilation compared to Beractant (100mg/kg) (risk difference (RD) (95%CI) 0.10 (0.02 – 0.18); p = 0.01), with a similar reduction in mortality (RD 0.07 (0.01 – 0.13); p = 0.02), but lack of effect on BPD (RD 0.02 (-0.03 – 0.07); p = 0.4). Reduced morbidity and mortality may offset the increased expense of Poractant alfa compared to Beractant, but no such cost- effectiveness studies could be identified from LMICs.

Conclusion:
In LMICs, where invasive mechanical ventilation is a scarce resource, we recommend that LISA/MIST be used in preference to INSURE. Poractant alfa (200mg/kg) is also conditionally recommended in preference to Beractant (100mg/kg) for SRT where available. Regionally relevant cost-effectiveness studies are recommended to inform clinical recommendations for implementation in resource limited settings.

Title: **INCIDENCE, AETIOLOGY AND SHORT TERM OUTCOMES OF EXTREME HYPERBILIRUBINAEMIA IN TERM INFANTS IN THE WEST METRO AREA OF CAPE TOWN**

Authors: Carin Coraizin, MBCHB (Stell)[1]; Heleen Vreede, MBCHB, FCPathSA (Chem Path) [2]; Cara Van Niekerk, MBCHB (UCT), [3] Yaseen Joolay, MBCHB(Stell),FCPaedSA, Cert. Neonatology SA, MPhil Neonatology (UCT) [4]

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Introduction:
Extreme levels of bilirubin in the newborn is a major cause of lifelong neurodevelopmental impairment, which places a financial burden on healthcare resources and caregivers.

Objective:
To determine the incidence, aetiology and short term outcomes of extreme hyperbilirubinaemia in term infants born in a resource limited setting.

Methods:
This is a retrospective observational study looking at term neonates with a birth weight ≥ 2500g, born in the West Metro referral area of Cape Town, South Africa, between 1 January 2019 and 31 December 2020, who were exposed to a serum bilirubin level of ≥ 430 μmol/L in the first week of life and received care in the public health system.

Results:
Extreme hyperbilirubinaemia occurred in 59 term infants. The incidence was 74 cases per 100 000 live births equating to 1 case in every 1345 live births. The cause of hyperbilirubinaemia was identified in 51 of the cases (86%), the most common being ABO incompatibility (31/51, 61%), followed by glucose-6-phosphate dehydrogenase deficiency (11/51, 22%). Twelve infants (20 %) underwent an exchange transfusion and 6 infants (10%) were treated with intravenous immune globulin. Six infants had abnormal neurological signs and symptoms. Forty-seven infants (80%) were readmitted after initial post-natal discharge, with a mean age of readmission of 113 hours old (SD 31 hours). Five out of the 6 infants who had abnormal neurology were readmitted to hospital. All 59 infants survived to be discharged home.

Conclusion:
The incidence of extreme hyperbilirubinaemia in the Western Cape in South Africa is higher than in high income settings. Further work should focus on early detection of significant hyperbilirubinaemia to prevent neurological complications caused by bilirubin toxicity.

HREC REF: 210/2021

Title: **A DESCRIPTIVE STUDY OF THE COMMUNITY-BASED FOLLOW-UP AND OUTCOMES OF VERY LOW BIRTH WEIGHT BABIES DISCHARGED FROM A REGIONAL HOSPITAL**

Authors: De Wit TMG, Hendricks Prof M

Affiliation: Department of Paediatrics and Child Health, University of Cape Town

Background and Objectives:
Neonatal mortality continues to be a significant global health concern, especially in low/middle income countries. In South Africa, neonatal deaths contribute to 32% of the under-five mortality rate, with 48% of these deaths attributed to prematurity. One of the components aimed at reducing neonatal deaths in the Western Cape, is the Home and Community-Based Services (HCBS) for very low birth weight (VLBW) babies. This intervention could reduce neonatal deaths by 25%. This study aimed to describe the Home and Community-Based Services (HCBS) referral pathway and follow-up of very low birth weight (VLBW) babies discharged from a regional hospital in Cape Town during 2018. The objectives were to describe the cohort of VLBW babies and those referred to HCBS in terms of their co-morbidities and social demographics; the referral process and adherence to the protocols; their follow up by the community health workers (CHWs); their outcomes as well as some caregivers' perceptions of the service.

Methods:
This was a retrospective descriptive mixed methods study. Quantitative data from an accredited database were used to describe the VLBW cohort. Meetings with stakeholders and referral form analyses were used to assess the referral pathway and follow-up. Telephonic interviews were held with VLBW babies' caregivers to obtain further quantitative and qualitative data about the HCBS programme. Simple descriptive analyses were used for the quantitative data using STATA 2015 ©. The qualitative data was categorised into themes using qualitative content analysis.

Results:
During 2018, 169 VLBW babies were included in the population with a mean (SD) gestational age of 30 (±2.21) weeks and median (IQR) birthweight of 1210g (1045-1390g). At delivery, 84.6% had respiratory distress with 60% requiring continuous positive airway pressure; 64% had presumed and 15.3% had suspected or proven nosocomial sepsis. Caregiver characteristics included unbooked pregnancies (10%), primigravida deliveries (15%), smoking (11%), maternal alcohol use (9%), teenage pregnancy (5%), drug addiction (3%) and babies born before hospital arrival (4%) with 14% being referred to a social worker. Folder review showed plans for HCBS referral in only 49 (43.4%) of the cohort, however only 20 (17.7%) referral forms were received by HCBS. Learning about the VLBW HCBS programme identified several challenges relating to the referral process from both the hospital and HCBS side. Overall, the caregivers interviewed had positive perceptions of the HCBS. Those not visited by HCBS felt they would have benefitted from a visit.

Conclusion:
The burden of this medically and socially vulnerable VLBW cohort, who are at high risk of neonatal mortality and morbidity, remains large at this regional hospital - constituting nearly 15% of all their neonatal discharges. Despite the identified challenges, the caregivers' interviewed remained positive about the HCBS. HCBS can play an essential role in providing education, counselling and support following hospital discharge. However, for the HCBS to be fully effective, further promotion, strengthening and monitoring of the referral system is required.

HREC REF: 582/2019

Title: **A RETROSPECTIVE DESCRIPTIVE REVIEW OF CHILDREN DIAGNOSED WITH HENOCH SCHÖNLEIN PURPURA AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL OVER A 5-YEAR PERIOD (2015-2019)**

Authors: Mpho Makhwarene, Heloise Buys, Mignon Mc Culloch

Affiliation: Department of Paediatrics and Child Health, University of Cape Town

Objectives:
To document the number, presentation features and special investigations of all children with Henoch Schoenlein purpura at RCWMCH over a 5-year period.

Methods:
A retrospective folder review of all children with a discharge diagnosis of IgA vasculitis at (RCWMCH) a tertiary children's hospital between January 2015 and December 2019 was performed. Patient demographics, clinical characteristics, laboratory findings, management and short-term outcomes were summarised; conventional descriptive and inferential statistical methods were used to analyse the dataset.

Results:
Forty-nine children were eligible for inclusion in the analysis, mean age was 6 years and 5 months, male-to-female ratio was 1:1. Rash was the presenting symptom in 48 (97%) children; arthralgia 41 (84%), abdominal pain 18 (37%); oedema manifested as scrotal oedema in 1 (2%) and angioedema in three (6%) children. Kidney involvement was evident in twenty-five (51%) children with proteinuria and or haematuria, while isolated microscopic haematuria occurred in six (12%). Complications were infrequent, five (10%) patients had IgA nephritis on biopsy and one (2%) had a gastrointestinal bleed. The mean length of hospital stay was 1.6 (SD 2) days. At one year of follow-up, two (4%) children had persistent proteinuria and only one patient (2%) still had haematuria.

Conclusion:
The clinical course of IgA vasculitis in this cohort of South African children was mostly self-limiting, consistent with international literature. However, patients with persistent haematuria or proteinuria require longer-term follow-up. Collaborative studies within South Africa and sub-Saharan Africa may provide a more accurate picture of the epidemiology of childhood HSP and its complication rates.

HREC REF: 652/2021

Title: **BREASTFEEDING EXPERIENCE AND PRACTICE DURING THE COVID-19 PANDEMIC – A QUALITATIVE STUDY**

Presenting Author: Yolanda Nkanuka-Makangala; Supervisors: Dr NR Rhoda and Dr Max Kroon

Affiliation: Department of Paediatrics and Child Health, University of Cape Town

Background:
Breastfeeding is the simplest, safest and most affordable type of infant feeding and critical to child health and survival particularly in countries with a high burden of infectious diseases. The COVID-19 pandemic and its associated restrictions limited access to health care, breastfeeding information and support, and may have impacted the lived experience of mothers and their knowledge, perceptions and practice of infant feeding.

Objective:
To explore the knowledge, perceptions and attitudes of mothers' breastfeeding experience and breastfeeding practice in Cape Town, South Africa, during the COVID-19 pandemic and how it affected their breastfeeding practices.

Methods:
A qualitative study was conducted. Ten mothers, who breastfed their infants during the pandemic, were purposively selected from the short stay ward at a large children's hospital to participate. Data was collected and recorded from face-to-face semi-structured interviews. Thematic data analysis was conducted using Nvivo10 from translated and transcribed interviews and interpreted to obtain a better understanding of the breastfeeding narrative of the participants.

Results/findings:
The research was carried out over 5 weeks between April 2021 – June 2021, just over a year after the announcement of the hard lockdown in South Africa. Six themes were identified: 1. Experience of health care services, 2. Experience of the pregnancy, 3. Breastfeeding Experience, 4. Employment and source of income, 5. Breastfeeding knowledge, 6. Psychosocial support. These themes highlighted the factors that impacted breastfeeding understanding, experience and practices of the mothers.

Conclusion:
The COVID-19 pandemic affected breastfeeding mothers differently, influenced by their preceding breastfeeding experience, exposure to infant feeding practices and support or lack thereof. While many mothers struggled with breastfeeding in the face of stressors like isolation, lack of support, conflict with/ loss of loved ones as well as food insecurity, others saw the shutdown restrictions and social distancing as a welcome opportunity to bond with their infants. These mothers used their "unemployment" to increase breastfeeding time with their infants. The study exposed the urgency and importance of strengthening breastfeeding support systems, including protected time for infant care. The lockdown inadvertently had a positive impact, as it protected and promoted breastfeeding while also showcasing the potential of social media platforms for virtual health promotion and breastfeeding support.

HREC REF: 760/2020

Title: **OUTCOMES OF ACUTE LYMPHOBLASTIC LEUKAEMIA AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL FROM 2007 TO 2017**

Authors: Beatrice Chikaphonya Phiri[1], Alan Davidson[1]

Affiliation: [1]Haematology-Oncology Service, Red Cross War Memorial Children's Hospital, University of Cape Town

Objective:
This study describes clinical features and outcomes of patients diagnosed with Acute Lymphoblastic Leukaemia (ALL) at Red Cross War Memorial Children's Hospital (RCWMCH) from 2007 to 2017. It compares them to historical data of a cohort of ALL patients at RCWMCH from 1995 to 2004 with a 5 year Event free survical (EFS) of 72% which was presented at the South Africa Children's Cancer Study Group (SACCSG) conference in 2006.

Methods:
A retrospective folder review of 160 children diagnosed with acute lymphoblastic leukaemia (ALL) from 2007 to 2017 was conducted in the paediatric oncology unit of the Red Cross War Memorial Children's Hospital (RCWMCH). Those under the age of 1 year and those who were transferred out to other facilities were excluded. Data on demographics, clinical characteristics, treatment provided and outcomes of all the patients was collected. Descriptive analyses were performed, and Kaplan-Meier curves were used for survival analysis. P-values less than 5% were considered significant.

Results:
160 children were diagnosed with ALL, 60% were male with a median age of 6 years. Eight one percent (129) were aged between 1 and 10 years of age whereas 19 % were older than 10 years old. Seventy three percent presented with white cell count more than 50,000 cells/µl. Seventy eight percent had B cell phenotype ALL (B-ALL), 21% had T cell phenotype -ALL (T-ALL) and 2% had central nervous system (CNS) disease.
The majority (68%) of those with B-ALL had favourable karyotypes but overall, 82% were risk stratified to be high risk when all the prognostic factors were considered whereas all T-ALL were treated on high-risk protocols. Eighty one percent of the patients were alive and disease free at the time of last follow up with estimated 5- and 10-year EFS of 81% and 77% respectively. Those with T-ALL had 5- and 10-year EFS of 83% and 79% respectively compared to 80 % and 77% for those with B-ALL (Log rank P value 0.9894). Standard risk B-ALL patients had 5- and 10-year EFS of 93% and 89% compared to 74 and 69% (Log rank P value 0.0198) in those with high risk disease.
The relapse rate was 19% (30), the majority (25) had B-ALL while 5 had T-ALL. Eighteen percent (29) of the patients died in this period, 22 had B-ALL and 7 had T-ALL. Seventy six percent (22) of the deaths were attributed to relapse, all 5 patients with relapse T-ALL died while 16 of the 25 B-ALL relapse patients died, 15 of whom were high risk patients.

Conclusion:
The improved survival of children with ALL is encouraging**.** It demonstrates the efforts made over time to improve treatment and supportive care at RCWMCH. There is still room to optimise the treatment of high-risk patients to maximise survival and limit cranial radiotherapy to patients with frank CNS disease.

HREC REF: 181/2023, New research

Title: **RISK FACTORS FOR SEVERE COVID-19 AMONG CHILDREN AND ADOLESCENTS ENROLLED IN ACUTE RESPIRATORY INFECTION SENTINEL SURVEILLANCE IN SOUTH AFRICA, 2020-2022**

Authors: *Kate Bishop[1], Susan Meiring[1], Sibongile Walaza[2,3], Stefano Tempia[2,4,5,6], Anne von Gottberg[2,7], Nicole Wolter[2,7], Jackie Kleynhans[2,4], Fahima Moosa[2], Mignon du Plessis[2], Jocelyn Moyes[2], Mvuyo Makhasi[2], Boitumelo Chuene[2], Aaron M. Samuels[6,8], Halima Dawood[9], Gary Reubenson[10], Heather J. Zar[11], Vanessa Quan[1], Cheryl Cohen[2,4]

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Background:
Identifying children at risk for severe disease from Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) may guide future mitigation interventions. We evaluated risk factors for hospitalisation for respiratory coronavirus disease 2019 (COVID-19) among patients aged ≤18 years.

Methods:
From April 2020 through March 2022, patients meeting study case definitions were systematically enrolled at four outpatient influenza-like illness (ILI) and five inpatient severe respiratory infection (SRI) surveillance sites and tested for SARS-CoV-2 infection using polymerase chain reaction (PCR). Each ILI clinic site shared a catchment area with its corresponding SRI hospital sites. Factors associated with inpatient versus outpatient disease were assessed using univariable and multivariable random effects logistic regression.

Results:
Of 4,688 participants aged ≤18 years, 4,556 (97%) with complete PCR and HIV data were included in the analysis. Among patients with ILI and SRI, 92/1,145 (8%) and 154/3,411 (5%) tested SARS-CoV-2 positive, respectively. Compared to outpatient cases, SARS-CoV-2 SRI cases were associated with age <6 months [adjusted odds ratio (aOR) 6.0, 95% confidence interval (CI) 2.1-17.4] versus 1-4 years; underlying medical condition other than HIV [aOR 4.4, 95% CI 1.8-10.6]; laboratory-confirmed Omicron BA.1/BA.2 variant [aOR 4.5, 95% CI 1.6-12.7] compared to ancestral SARS-CoV-2; and respiratory syncytial virus (RSV) co-infection [aOR 5.1, 95% CI 1.0-26.5]. No significant associations were observed between HIV status and an increased risk of hospitalisation.

Conclusion:
We corroborate previous research that identified age <6 months or having an underlying condition as risk factors for SARS-CoV-2-associated SRI. Sentinel surveillance programmes are useful to monitor the epidemiology of COVID-19 in children.

HREC REF: 836/2014 and HREC REF: 573/2018

Title: VALIDATING THE WHO INTEGRATED TREATMENT DECISION ALGORITHMS FOR PULMONARY TB IN HIGH-RISK CHILDREN FROM THREE AFRICAN COUNTRIES

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Background: The World Health Organisation (WHO) endorsed integrated treatment decision algorithms for childhood tuberculosis (TB), including two new algorithms with and without chest x-ray (CXR). However, these have not been externally validated, especially among high-risk children (<2 years old, children living with HIV [CLHIV], or with severe acute malnutrition [SAM]).

Methods: We included data on children under 2 years, CLHIV, or with SAM enrolled in prospective pulmonary TB (PTB) diagnostic cohorts in South Africa, Uganda and The Gambia. Clinical data were collected, and CXR, HIV and TB microbiological testing (Xpert MTB/RIF Ultra and culture) performed. Children were classified according to NIH consensus definitions, and a TB treatment decision score calculated based on Algorithm A (with CXR) and B (without CXR). A score >10 was defined as PTB; we determined diagnostic accuracy according to composite (CRS) and microbiological reference standards (MRS).

Results: We included 385 children with presumptive TB: 87.3% were <2 years, 23.7% were CLHIV, and 22.7% had SAM. 17.4% had Confirmed TB, 53.0% Unconfirmed TB and 29.6% Unlikely TB. 42.1% had a known TB exposure, where the algorithms recommend treating for PTB without requiring a clinical/radiological score. Of these children, 15.4% were classified as Unlikely TB. Compared to the CRS, sensitivities of Algorithms A and B were 92.6% and 94.8% respectively, and specificities 24.6% and 11.4%. Diagnostic accuracy was similar among children <2 years old, CLHIV, and children with SAM. By following the algorithm and excluding children with TB exposure, sensitivity decreased and specificity improved, albeit minimally for Algorithm B (Table 1), with a further reduction in sensitivities when Xpert was disregarded (representing settings where Xpert is unavailable).

Conclusion: WHO integrated treatment decision algorithms have high sensitivity but very low specificity for PTB, likely leading to over-treatment if consistently applied. Further study of algorithm implementation and modifications to increase diagnostic accuracy is required.

	Composite Reference Standard[a]				Microbiological Reference Standard[b]			
	Algorithm A (with CXR)		Algorithm B (without CXR)		Algorithm A (with CXR)		Algorithm B (without CXR)	
	Sensitivity % (95% CI)	Specificity % (95% CI)	Sensitivity % (95% CI)	Specificity % (95% CI)	Sensitivity % (95% CI)	Specificity % (95% CI)	Sensitivity % (95% CI)	Specificity % (95% CI)
Overall (n=385)	92.6 (88.8- 95.4)	24.6 (17.0-33.5)	94.8 (91.5-97.1)	11.4 (6.2-18.7)	98.5 (92.0-99.9)	14.8 (11.1-19.2)	98.5 (92.0-99.9)	8.2 (5.4-11.8)
Children under 2 years (336/385)	93.6 (89.7-96.4)	24.8 (16.7-34.3)	95.3 (91.8-97.6)	10.9 (5.6-18.7)	98.3 (90.9-99.9)	14.1 (10.2-18.7)	98.3 (90.9-99.9)	7.6 (4.8-11.4)
Children living with HIV (89/385)	89.4 (79.4-95.6)	21.7 (7.4-43.7)	95.5 (87.3-99.1)	13.0 (2.8-33.6)	91.7 (61.5-99.8)	14.3 (7.4-24.1)	100.0 (73.5-100.0)	7.8 (29-16.2)
Severe Acute Malnutrition (82/385)	90.0 (79.5-96.2)	22.7 (7.8-45.4)	96.7 (88.5-99.6)	13.6 (2.9-34.9)	93.3 (68.1-99.8)	14.9 (7.4-25.7)	100.0 (78.2-100.0)	7.5 (2.5-16.6)
Excluding children with TB exposure (n=221)	85.7 (78.6-91.2)	31.8 (22.3-42.6)	90.2 (83.9-94.7)	14.8 (8.1-23.9)	97.0 (84.2-99.9)	24.5 (18.5-31.3)	97.0 (84.2-99.9)	13.3 (8.8-19.0)
Excluding children with TB exposure, disregarding Xpert result (n=221)	78.9 (71.0-85.5)	32.9 (23.3-43.8)	87.2 (80.3-92.4)	15.9 (9.0-25.2)	75.8 (57.7-88.9)	26.1 (19.9-33.0)	93.9 (79.8-99.3)	15.4 (10.6-21.4)

[a] Accuracy based on a composite reference standard of Confirmed or Unconfirmed TB vs. Unlikely TB according to NIH consensus definitions

[b] Accuracy based on a microbiological reference standard

Table 1. Diagnostic Accuracy of the World Health Organization Integrated Treatment Decision Algorithms among High-Risk Children from South Africa, Uganda, and the Gambia.

HREC REF: 045/2008

Title: **AETIOLOGY OF PLEURAL EFFUSIONS DIAGNOSED BY ROUTINE CULTURE AND MOLECULAR TECHNIQUES IN CHILDREN LIVING IN A HIGH TUBERCULOSIS (TB) ENDEMIC SETTING: A PROSPECTIVE STUDY**

Authors: Seyram Wordui,[1] Adelaide Masu,[1] Lauren Golden,[1] Shakira Chaya,[1] Kirsten Reichmuth,[1] Ane Visagie,[1] Ada Ayuk,[1] Sandra Kwarteng Owusu,[1] Diana Marangu,[1] Noor Affendi,[1] Aruna Lakhan,[1] Diane Gray,[1] Aneesa Vanker,[1] Heather Zar,[1] Marco Zampoli[1]

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Aim:
1. To describe the diagnostic value of polymerase chain reaction (PCR)-based molecular tests in determining the aetiology of pleural effusions (PE) among children in a setting with high rates of tuberculosis (TB) and HIV.
2. To determine the clinical and laboratory features that distinguish bacterial versus other causes of PE as a strategy to guide antimicrobial treatment.

Method:
We reanalysed data on PE among children enrolled in a prospective study in Cape Town, South Africa, from December 2016 to December 2019, adding data from PCR testing. Routine investigations included culture of blood and pleural fluid (PF); PF biochemistry; blood white cell count (WCC), C-reactive protein (CRP); and procalcitonin (PCT). TB investigations were Mantoux, Xpert MTB/RIF® or Xpert-Ultra® and TB culture of sputum and PF. Stored PF was analysed using quantitative 33-multiplex real-time PCR (FastTrack®). Aetiological category of PE was defined by microbiological confirmation.

Results:
Ninety-one children were enrolled [median age 31 months (IQR 12-102); 61.5% males]. Fourteen (15%) were HIV-exposed; 4 (4%) HIV infected and 39 (43%) received at least one dose of pneumococcal conjugate vaccination. Aetiology of PE was bacteria (n=36, 40%), TB (n=10, 11%), viruses (n=3) and polymicrobial (11%; bacteria-virus n=7; bacteria-TB n=2; bacteria-bacteria n=1). Thirty-two (35%) had no pathogen identified. The commonest pathogen was *S. aureus* with similar yield on culture (n=24, 26 %) and PCR (n=21, 23 %). 11 cases had discordant culture and PCR results. Second commonest pathogen was *S. pneumoniae,* detected more commonly by PCR (n=12, 13%) than culture (n=3, 3%); $p < 0.0001$, with all culture-positive cases detected by PCR. Adding FastTrack® to routine culture and TB investigations increased the yield of individual pathogens from 45 to 75 in this cohort. Compared to TB and no pathogen groups, children with bacterial and polymicrobial PE were younger, had significantly higher WCC, CRP, PCT, PF lactate dehydrogenase and adenosine deaminase, and lower PF glucose. The biomarker that best predicted bacterial PE on receiver operator characteristic analysis was pleural fluid LDH > 1716 U/L, with a sensitivity of 85% and a specificity of 95%. The no pathogen group was most similar to children with TB in terms of age, Mantoux positivity (67%) and other blood and PF biomarkers.

Conclusion:
In children with PE, adding FastTrack® to routine culture and TB investigations improved the diagnostic yield. Molecular testing of PF should be employed to complement routine diagnostic techniques. Pleural fluid LDH >1716 U/L best predicts bacterial PE and may guide antimicrobial decision-making in the absence of microbiological confirmation. The role of viruses and polymicrobial PE in children is highlighted in this study.

Acknowledgments: We thank Prof Mark Nicol and the staff at the UCT microbiology laboratory for their assistance. This work and the investigators are supported by the University of Cape Town and the African Paediatric Fellowship Programme.

HREC REF: 607/2022

Title: **RISK AND RATES OF HOSPITALISATION IN YOUNG CHILDREN: A PROSPECTIVE STUDY OF A SOUTH AFRICAN BIRTH COHORT**

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Objective:
Children in sub-Saharan Africa (SSA) are disproportionately affected by morbidity and mortality; there is also a growing vulnerable population of children who are HIV-exposed uninfected (HEU). Understanding reasons and risk factors for early-life child hospitalisation will help optimise interventions to improve health outcomes. We investigated hospitalisations from birth to two years in a South African birth cohort.

Methods:
Pregnant women were enrolled into the Drakenstein Child Health Study (DCHS) between 5 March 2012 and 31 March 2015. Mother-child pairs in the DCHS were followed from birth to two years with active surveillance for hospital admission and investigation of aetiology and outcome. Incidence rates, duration, cause, and factors associated with child hospitalisation were investigated, and compared between HEU and HIV-unexposed uninfected (HUU) children. Cox Proportional Hazards models were conducted to assess HIV exposure differences in hospitalisations. Crude incidence rate ratios (IRR) were reported for unadjusted analyses, whilst adjusted hazard ratios (HR) were reported for multivariable analyses and assessing other risk and protective factors.

Results:
Of 1136 children (247 HEU; 889 HUU), 314 (28%) children were hospitalised in 430 episodes despite >98% childhood vaccination coverage. The highest hospitalisation rate was from 0-6 months, decreasing thereafter; 20% (84/430) of hospitalisations occurred in neonates at birth. Amongst hospitalisations subsequent to discharge after birth, 83% (288/346) had an infectious cause; lower respiratory tract infection (LRTI) was the most common cause (49%;169/346) with respiratory syncytial virus (RSV) responsible for 31% of LRTIs; from 0-6 months, RSV-LRTI accounted for 22% (36/164) of all-cause hospitalisations. HIV exposure was a risk factor for hospitalisation in infants (IRR 1.63 [95% confidence interval [CI] 1.29-2.05]) and longer hospital admission (p=0.004). Prematurity (HR 2.82 [95% CI 2.28-3.49]), delayed infant vaccinations (HR 1.43 [95% CI 1.12-1.82]), or raised maternal HIV viral load in HEU infants were risk factors; breastfeeding was protective (HR 0.69 [95% CI 0.53-0.90]).

Conclusion:
Children in SSA continue to experience high rates of hospitalisation in early life. Infectious causes, especially RSV-LRTI, underly most hospital admissions. HEU children are at particular risk in infancy. Available strategies such as promoting breastfeeding, timely vaccination, and optimising antenatal maternal HIV care should be strengthened. New interventions to prevent RSV may have a large additional impact in reducing hospitalisation.

HREC REF: 401/2009

Title: **BUILDING CAPACITY IN SOUTH AFRICA FOR THE DIAGNOSIS OF PRIMARY CILIARY DYSKINESIA**

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Introduction:
Primary ciliary dyskinesia (PCD) is a rare autosomal recessive disorder which causes abnormal motility of cilia. PCD presents with chronic upper respiratory tract symptoms, chronic wet cough, bronchiectasis and infertility; and may be associated with situs inversus and heterotaxy syndromes. There is currently limited capacity to diagnose PCD in sub-Saharan Africa and the incidence of PCD in Africa is unknown. We report the early findings of study employing a variety of PCD diagnostic methods which were previously not available in South Africa (SA).

Methods:
Children and adults with suspected PCD were prospectively recruited in this observational study at Red Cross War Memorial Children's Hospital (RCWMCH), Cape Town, SA, in partnership with University of Münster, Germany. Diagnostic tests performed included: nasal nitric oxide (nNO), nasal brushings for video microscopy of ciliary beat patterns, immunofluorescence (IF) of ciliary proteins, electron microscopy (EM), and genotyping for variants of PCD-related genes. Clinical characteristics of participants were documented from the routine medical records. The study was approved by the University of Cape Town Research Ethics Committee (HREC 762/2020).

Results:
Diagnostic testing facility for PCD was established de novo within the RCWMCH laboratory with the technical support from co-investigators from the laboratory. This initially involved training one of the co-investigators, Dr. Joy Eze, in skills for obtaining nasal specimens, and conducting high-speed video-microscopy. The training was anchored at the University of Cape Town by Prof. Heymut Omran of the Department of General Pediatrics, University Children's Hospital, Münster, Germany. Participants were enrolled within a period of one year from July 2023 to July 2023. Preliminary results of the first 33 participants (31 children and 2 adults) are presented: median (IQR) age was of 5.6 years (3.8, 8.2), and 16 males (49%). Participant ancestry was mixed (45%, n=15), Caucasian (33.3%, n=11), Black African (18%, n=6), and Other (3%, n=1). The most frequent clinical characteristics were chronic rhinitis (82%, n=27), chronic wet cough (73%, n=24), chronic sinusitis (63%, n=21), chronic otitis media (52%, n=17), neonatal respiratory distress (48%, n=16), bronchiectasis (36%, n=12), situs inversus (36%, n=12) and hearing impairment (21%, n=7). Microbiological cultures of respiratory tract samples were positive in 39% (n=13), including *Pseudomonas s*pecies in three (9%). Median FEV_1 z-score was -1.9 (min -5.1, max 1.1). The median nNO was 104.9 (range 5.9 - 232) nl/min; 7/17 (41%) participants recorded <77nl/min suggesting possible PCD diagnosis. Ciliary beat microscopy was considered abnormal in 55% of the participants (n=18). Of the 24 participants with completed genotyping and IF, PCD was confirmed genetically in 5/24 (21%) by identification of known pathogenic variants, of which two had abnormal localisation by IF. Further analyses are planned to compare clinical characteristics and other diagnostic test performances, including EM, in those with and without confirmed PCD.

Conclusion:
Using a range of diagnostic modalities previously not available in SA, preliminary results in the study have identified a significant number of PCD cases who would otherwise not have been diagnosed correctly. This study will further assist in developing locally relevant protocols to improve diagnostic capacity of PCD in SA and care of people with PCD in the region.

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HREC REF: 762/2020

Title: **HEALTH RELATED QUALITY OF LIFE IN CHILDREN DEPENDANT ON TECHNOLOGY FOR BREATHING**

Authors: Janine Verstraete[1], Christopher Booth[1], Jane Booth[2], Shazia Peer[3,4], Jessica McGuire[3,4], Fiona Kritzinger[1], Taryn Gray[2], Noluthando Zibi[4], Primrose Shabangu[4] and Marco Zampoli[1,4]

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Background:
Advances in medical technology have enabled children to survive congenital airway anomalies and critical illnesses including technologies such as tracheostomies and long-term ventilation at home. Measuring Health Related Quality of Life (HRQoL) in these children can provide valuable feedback for routine clinical care and can assist with decision making for funding new technology or medication. This study aimed to assess the Health Related Quality of Life (HRQoL) of the EQ-TIPS and EQ-5D-Y-3L in children dependent on technology and the impact of caring for these children using the Paediatric Tracheostomy Health Status Instrument (PTHSI) and CarerQoL.

Methods:
Caregivers of children aged 1 month to 18 years were recruited between January and December 2022. Consenting caregivers completed the EQ-TIPS or EQ-5D-Y-3L and PTHSI to reflect the child's health. In addition caregivers self-completed the PTHSI, EQ-5D-5L and CarerQoL. Report of problems on EQ dimensions were compared across known groups with the Fisher Exact test. Spearman and Pearson's correlation coefficients, and Kruskal–Wallis H-test were used to explore the association between caregiver and child scores and known-groups.

Results:
Responses from 144 caregivers were collected, 66 for children aged 1 month - 4 years completing EQ-TIPS and 78 for children aged 5-18 years completing EQ-5D-Y-3L. The sample included those dependent on a tracheostomy only (n=99, 68.8%), invasive ventilation (n=19, 13.2%) and non-invasive ventilation (n=26, 18.1%). The indication for assisted-breathing technology were upper airway obstruction (n=85, 59.0%), neuromuscular disease (n=24, 17.0%) and long term ventilation (n=14, 10.0%). The majority of proxy respondents were mothers (n=128, 88.9%) who had completed either high school (n=84, 58.3%) or tertiary education (n=40, 27.8%). The EQ-TIPS had the lowest report of problems for pain (n=14, 22%) and the highest problems reported for communication (n=22, 33%). Children aged 1-12 months had a significantly lower reporting of problems with social interaction than older children. Children aged 5-18 years had higher reports of problems most notably for the physical dimensions of looking after myself (n=39, 50.6%), mobility (n=38, 49.4%) and pain (n=35, 45.5%), with higher reports of problems in older children ($p<0.05$). There was notably very low report of being worried, sad or unhappy (n=21, 27.3%). The EQ-5D-Y-3L can discriminate between breathing technology, where those with only a tracheostomy reported better HRQoL compared to those with invasive or non-invasive ventilation ($H=8.92$, $p=0.012$). The EQ-5D-Y-3L could further discriminate between children with mild and moderate clinical severity ($H=19.42$, $p<0.001$), no children were classified as severe. Caregiver and child HRQoL scores showed moderate to strong associations. The burden of care, measured on the CarerQoL, was significantly higher for children with moderate clinical severity. Caregivers of children dependent on invasive ventilation reported significantly lower HRQoL on the PTHSI than those on non-invasive ventilation or a tracheostomy only ($p=0.003$). Similarly, caregivers of the youngest (1-24 months) and oldest children (13-18 years) reported significantly lower HRQoL than the other age groups ($p<0.05$).

Conclusion:
Despite the heterogeneity and complexity of underlying conditions, the EQ-TIPS and EQ-5D-Y-3L showed good validity in children dependent on technology for breathing and can be recommended as an outcome measure in this group for routine monitoring or in clinical trials. There is a high burden of care associated with caring for these children particularly in those on invasive ventilation. This highlights the importance of supporting the caregivers and families of children dependent on technology for breathing.

HREC REF: 740/2021

Title: **A DESCRIPTIVE STUDY OF VANCOMYCIN USE AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL, CAPE TOWN**

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Objective:
To document the use, prescribing practices and monitoring of intravenous vancomycin and the spectrum of bacteria isolated on microbiological culture in children treated with intravenous vancomycin during a 12-month period at Red Cross War Memorial Children's Hospital (RCWMCH).

Methods:
A retrospective audit was conducted on the use of intravenous vancomycin in children who were admitted to RCWMCH during 2019. The collected data was summarised using proportions, median, and interquartile range (IQR). To compare the daily doses of vancomycin between different treatment groups, the Wilcoxon rank sum test was employed.
In order to assess whether participants who tested positive for Gram-positive bacteria in cultures were more likely to be prescribed vancomycin for a duration exceeding 14 days compared to those with negative culture results, odds ratios were calculated using the immediate command in STATA. A significance level of $p < 0.05$ was used to determine statistical significance.

Results:
All 158 vancomycin prescription episodes for 143 children were included. Overall usage of intravenous vancomycin was 63 days of therapy/1000 patient days (IQR 38–72). The median starting dose was 15 mg/kg/dose (IQR 14–15) and median daily dose was 45 mg/kg/day (IQR 43–60). Vancomycin was prescribed as empiric (127/158, 80%) and directed (31/158, 20%) treatment. The median duration of treatment for the directed group (seven days) was longer than the empiric group (four days) (p=0.001). Vancomycin serum trough concentrations were performed in 65/98 (66%) episodes where vancomycin treatment exceeded three days, with only 16/65 (25%) of these samples obtained before the fourth dose. Prolonged antibiotic treatment of 14 days or more was not associated with Gram-positive bacteria on culture (OR 1.02, 95% CI 0.17–4.2).

Conclusion:
Dosing errors, prolonged empiric treatment and inappropriate vancomycin monitoring were problems associated with vancomycin prescriptions.

HREC REF: 498/2020

Title: **DIFFERENTIAL CYTOKINE EXPRESSION IN MIS-C AS COMPARED TO OTHER INFLAMMATORY CONDITIONS IN A COHORT STUDY IN CAPE TOWN, SOUTH AFRICA**

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Background:
Multisystem inflammatory syndrome in children (MIS-C) is a hyperinflammatory disease that presents in children after exposure to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is unclear whether MIS-C has a distinct cytokine expression compared to similar, severe inflammatory diseases in children.

Objectives:
To compare and contrast the expression of seven cytokines in the serum of children with MIS-C, children with similar severe diseases and healthy children.

Methods:
From 26 June 2020 to 9 February 2022, children with suspected MIS-C were recruited at the Red Cross War Memorial Children's Hospital in Cape Town. Those who met the World Health Organisation criteria were diagnosed with MIS-C and those who had alternate diagnoses were included as inflammatory controls (e.g. sepsis, dysentery etc.). Serum samples were taken throughout admission. In the same time period, healthy children undergoing non-inflammatory elective surgeries were recruited with consent. Serum samples were analysed using a Luminex panel of seven cytokines. C-reactive protein (CRP) was clinically performed at the local clinical laboratory.

Results:
Twenty-three children with MIS-C, 13 inflammatory controls and 41 healthy participants were recruited. Before treatment, children with MIS-C had elevated serum concentrations of interleukin (IL)-10 ($p=0.033$), CRP ($p=0.002$) and IL1 receptor antagonist (RA) ($p=0.054$) compared to children with other inflammatory conditions. Compared to healthy children, patients with MIS-C had elevated serum concentrations of IL-1RA ($p<0.001$), IL-1B ($p=0.024$), IL-10 ($p<0.001$), IL-6 ($p<0.001$), monocyte chemoattractant protein (MCP)-1 ($p<0.001$), tumour necrosis factor (TNF) a ($p=0.002$) and IL-27 ($p<0.001$). In children with MIS-C, the concentrations of all eight inflammatory markers rapidly decreased after treatment with intravenous immunoglobulins and/or steroids.

Conclusion:
These data show that MIS-C is a markedly hyperinflammatory condition, with a distinct profile of inflammatory marker expression as compared to clinically similar inflammatory diseases in children.

HREC REF: 599/2020

Title: **POST-GRADUATE PUBLIC HEALTH TEACHING IN THE DEPARTMENT OF PAEDIATRICS AND CHILD HEALTH AT THE UNIVERSITY OF CAPE TOWN: A QUALITATIVE OBSERVATIONAL STUDY**

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Objective:
The discipline of Maternal, Neonatal, Child and Adolescent Public Health (MNCAPH) concerns the health and wellbeing of these groups in their social and economic contexts. Globally MNCAPH has been foregrounded as a key priority area. Higher education institutions play a significant role in equipping health professionals to be responsive to the dynamic and complex health care needs within MNCAPH. This study explored the postgraduate (PG) educational response to the burden of disease in MNCAPH from the perspective of the Department of Paediatrics and Child Health (DPCH) at the University of Cape Town.

Methods:
The study adopted a qualitative case study methodology. Conveners of all the PG programmes were invited to participate in online semi-structured interviews. They were also invited to share curricular documents. Using an inductive approach, three interviewers analysed themes from anonymised transcripts and the documentation. Consensus on the themes was reached iteratively.

Results:
Between March and August 2021, 28 of the 33 programmes participated. Eleven were sub-speciality training programmes; two programmes only taught public health. All except two of the clinical programmes only trained doctors.
MNCAPH was included in all programmes. It was largely taught with the aim of equipping graduates to be agents of change who would strengthen health systems. This was especially true for fellows from Africa. A broad range of public health topics were taught though emphasis and content varied across the programmes. Many interviewees aspired to expose their students to more MNCAPH teaching than they received and, for sub-speciality programmes, more than was required from the Colleges of Medicine of South Africa curricula. Most of the teaching in clinical disciplines was via an apprenticeship model. The public health programmes taught all the MNCAPH topics identified by the clinical programmes.

Conclusion:
MNCAPH education was integral to PG programmes in the DPCH. Teachers felt that most students required more than they currently receive in order to achieve the outcomes they envisage for trainees. Educational resources exist within the DPCH to meet many of these needs and could be integrated into PG programmes across the DPCH.

HREC REF: 767/2020

Title: **SIGNIFICANCE OF RETURNING INDIVIDUAL GENETIC RESEARCH FINDINGS FROM NEURODEV STUDY: IMPACT ON CLINICAL MANAGEMENT, FAMILIAL IMPLICATIONS AND RECURRENCE RISKS**

Authors: Zandré Bruwer[1], Emma Eastman[1], Brigitte Melly[1], Emily O'Heir[2], Christina Austin Tse[2,3], Victoria de Menil[2,4], Alice Galvin[2], Celia van der Merwe[2], Anne O'Donnell-Luria[2,5], Elise Robinson[2,3], Kirsten A. Donald[1,6] on behalf of the NeuroDev study

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Objective:
Whole exome sequencing (WES) was performed for 224 South-African families from the Western Cape, with a child with a neurodevelopmental disorder (NDD), as part of the NeuroDev study. Causal variants, illustrating evidence for pathogenicity according to the American College of Medical Genetics and Genomics and Association for Molecular Pathology guidelines, were identified in 37 of the 224 cases (diagnostic rate of 16.5%). These research results, once clinically confirmed, are returned to interested families and have the potential to facilitate accurate genetic counselling and patient management. This work considers the significance of returning the study results by considering the impact that the information has on the patient's management recommendations and implications for recurrence risk to the nuclear and extended family.

Methods:
Study participants were recruited from August 2018 – March 2020. Either DuoWES or TrioWES was performed. A retrospective review of all medical records of the 37 diagnosed cases from the NeuroDev study was then undertaken. Cases were individually evaluated with regards to 1) defining the NDD and mode of inheritance 2) determining if accurate recurrence risk and familial implications could be determined from the result and 3) assessing if the diagnosis impacted on the patient's management recommendations.

Results:
Genetically diagnosed cases included 20 single nucleotide variants or indels (54%) and seventeen copy number variants (CNV) (46%). For the CNV's, microdeletions (76%; 13/17) were more common than microduplications (24%; 4/17). These cases included 29 males and eight females, ranging in age from six to 20 years. Syndromic neurodevelopmental disorders were identified in 65% of patients (24/37), neurodevelopmental disorders in 27% (10/37) and inborn errors of metabolism in 8% (3/37). Pathogenic variants causing autosomal dominant genetic disorders were found in 84% of cases (31/37), followed by X-linked in 11% of cases (4/37) and autosomal recessive in 5% (2/37). Fourteen percent (5/37) of these variants were inherited, 35% (13/37) were de novo in origin, 51% (19/37) required additional parental testing to assess. The recurrence risk was classified as low (<1-2%) for 20 families and associated with high recurrence (between 25-50% risk) for five families with potential implications for extended family members. For the remaining 12, recurrence risk could not be excluded as clarification required additional testing. For 81% of cases (30/37), the molecular diagnosis was associated with additional surveillance and or management recommendations.

Conclusion:
Most diagnoses from the NeuroDev study yielded additional medical interventions, typically due to the identification of a syndromic neurodevelopmental disorder or an underlying CNV. Significant recurrence risks were also identified for a subset of families. These findings underscore the importance of returning study results to research participants, to inform management and provide appropriate genetic counselling.

HREC REF: 810/2016

Title: **CHARACTERISTICS OF EPILEPSY IN CHILDREN WITH CEREBRAL PALSY SEEN AT A TERTIARY PAEDIATRIC HOSPITAL IN CAPE TOWN SOUTH AFRICA**

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Objective:
To describe patterns of epilepsies in children with Cerebral Palsy (CP) seen at tertiary paediatric hospital in Cape Town, South Africa.

Methods:
This study was a retrospective review. All children who attended the CP clinic at the Red Cross Memorial War Children's Hospital (RCWMCH) in the year 2021 (according to the Surveillance of Cerebral Palsy in Europe (SCPE), clinical classification) were eligible for inclusion. Epilepsy clinical phenotype, electroencephalogram (EEG) semiology and management were reported. Data was captured into REDCap and analyzed for descriptive statistics.

Results:
Three hundred and seventy-four children were included in this analysis. Mean age was 10.2 years with 50.2% being males. Seventy eight percent had bilateral CP with 70.2 % having spasticity as the motor disorder. In terms of Gross Motor Function Classification System (GMFCS), 44.7% and 10.9% were classified as V and IV respectively. Of the total sample, 51.9 % had a seizure outside the neonatal period with 93.3% of these children being diagnosed with epilepsy. Generalized epilepsies were reported in 76% of those with epilepsy, with 80% having a defined structural aetiology and 99% abnormal EEG. In respect to impact of epilepsy on cognitive functioning 84.7% had Developmental Encephalopathy (DE). Drug resistant epilepsy was noted in 13.9%.

Conclusion:
Epilepsy is a common comorbidity in children with CP. Increased awareness of drug resistant and DE categorization of epilepsy for purposes of anti-seizure medication rationalization to improving quality of life and minimizing/avoidance of drug related side effects is needed, in the management of these children.

HREC REF: 563/2022

Title: **DISTINCT T CELL FUNCTIONAL PROFILES IN UNVACCINATED SARS-COV-2 SEROPOSITIVE AND SERONEGATIVE CHILDREN ASSOCIATED WITH ENDEMIC HUMAN CORONAVIRUS HKU1 CROSS-REACTIVITY**

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Background:
Children infected with SARS-CoV-2 are more likely to exhibit mild or even asymptomatic disease compared to adults. Moreover, severe COVID-19 is uncommon in children and often associated with underling co-morbidity. The immune mechanisms for the differences in disease progression between children and adults is not fully understood and studies assessing SARS-CoV-2 immune responses of paediatric populations in Africa is still scarce.

Objective:
We investigated the frequency and functional profile of SARS-CoV-2-specific T cells in unvaccinated South African children who were seropositive or seronegative for SARS-CoV-2. We also compare the magnitude of the T cell response between SARS-CoV-2 seropositive children and COVID-19 convalescent adults.

Methods:
Our study included 71 unvaccinated children with median age of 7 years (IQR 2.8-9 years) recruited from 1 February 2021 – 20 May 2021 at Red Cross War Memorial Children's Hospital (n=50) or from the Drakenstein Child Health Study (n=21). Additionally, COVID-19 convalescent unvaccinated adults (n=30) with median age of 38 years (IQR 32-45 years) were recruited from Groote Schuur Hospital from 22 January 2021 – 23 February 2021. Indirect ELISA was used to measure SARS-CoV-2 spike and nucleocapsid-specific IgG antibodies which were used to characterise the cohort serologically. SARS-CoV-2-specific CD4+ and CD8+ T cell responses were measured using flow cytometry.

Results:
58% of children were seropositive for SARS-CoV-2, indicating past infection. As expected, 83% (34/41) of seropositive and interestingly 60% (18/30) of seronegative children had detectable SARS-CoV-2-specific CD4+ T cell responses. Morover, SARS-CoV-2-specific CD8+ T cell responses were detectable in both seropositive (49%) and seronegative (47%) children. Although the magnitude of the CD4+ T cell response did not differ significantly between the seropositive and seronegative children, their functional profiles were distinct. SARS-CoV-2 seropositive children exhibited a higher proportion of polyfunctional cells compared to their seronegative counterparts. Of note, the frequency of SARS-CoV-2-specific CD4+ T cells in SARS-CoV-2 seronegative children was moderately associated with the magnitude of HCoV-HKU1 spike-specific IgG. Finally, SARS-CoV-2 seropositive children had a significantly lower magnitude T cell response compared to convalescent adults.

Conclusion:
Despite having no serological evidence of SARS-CoV-2 infection, more than half of seronegative children had detectable SARS-CoV-2-specific T cell responses similar in magnitude to seropositive children but with a monofunctional T cell profile. This, together with the correlation with HCoV-HKU1, may indicate cross-reactivity to endemic coronaviruses, which could contribute to the generally positive clinical outcomes of COVID-19 in children.

HREC REF: 599/2020

Title: **RETURNING INDIVIDUAL GENETIC RESULTS TO RESEARCH PARTICIPANTS: EXPERIENCES OF STIGMA IN SOUTH AFRICAN FAMILIES WITH NEURODEVELOPMENTAL DISORDERS**

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Objective:
In South Africa (SA), there is little research about the experiences of stigma in parents or caregivers of children suffering from a Neurodevelopmental Disorder (NDD). Likewise, the impact of genetic attribution on these experiences have not been extensively studied. Thus, the aim of this study was to explore the experiences of stigma of NeuroDev research participants and their families and how a positive genetic result influences/affects these experiences. To achieve this, the researcher looked at the experiences of parents or caregivers of NeuroDev research participants with stigma and the influence a positive genetic finding may have on stigma experienced by parents or caregivers of NeuroDev research participants. The role of genetic counsellors in addressing instances of stigma in NDDs and genomics research was also looked at.

Methods:
The study drew on an interpretive phenomenological approach (IPA) as this approach views individuals as "experiential experts" where researchers engage and interpret the meaning of experiences. This research was a sub-study to the NeuroDev study. The NeuroDev study aims to account for the lack of African genetic data of NDDs by exploring the phenotypic and genetic landscape of NDDs in Kenya and South Africa. Participants of the study included fathers, mothers or caregivers of children diagnosed with a neurodevelopmental disorder (NDD), who have voluntarily participated in the NeuroDev study and who have received a positive result. This is a form of purposive sampling as participants were selected based on appropriateness for the aims and objectives of this study. Data collection and exploration involved semi-structured interviews with 6 participants to ensure that the data obtained was deeply associated with personal experiences, views and beliefs. Interviews were conducted at Red Cross War Memorial Children's Hospital or at the University of Cape Town between March 15th to April 14th 2023 and were audio-recorded. Interviews continued for 1-1.5 hours so that the researcher obtained rich, meaningful data. Transcribed interviews were then analysed using an IPA-tailored thematic analysis flow to identify recurrent themes or patterns in the data.

Results:
Findings show that participants experience stigma at varying levels. It was found that how a parent rationalises a diagnosis, the difficulty in raising a child with a NDD, experiences of stigmatisation and respective coping mechanisms affect how patients perceive a genetic result and stigma. While a genetic result did not reduce public stigma, some patients expressed that assigning meaning to a genetic cause reduces internalised stigma. It was found that participants experiences of genetic counselling differ. Most expressed a lack of understanding of genetic counselling. Nonetheless, the genetic counselling session enhanced participants knowledge on NDD's, provided a human component to research and reduced internalised stigma.

Conclusion:
Findings show that there is an individualistic and dynamic interplay between a parent's rationalisation, difficulties, experiences of stigmatisation and coping mechanisms. This emphasises the multifaceted nature of stigma and that socio-economic, political and cultural factors need to be considered when conducting genetic research in SA. The genetic result was shown to only impact internalised stigma experiences with no effect on public stigma. Furthermore, findings had shown that genetic counselling enhanced participants knowledge on NDD's, provided a human component to research and impacted internalised stigma. While it was expected that genetic counselling would have a greater impact on other forms of stigma, it was not seen in this study. This study forms a basis for future research to further elucidate experiences of stigma in parents or caregivers of children suffering from a NDD and the role genetic counsellors may play in addressing this stigma.

HREC REF: 734/2022

Title: **THE CYTOKINE PROFILE OF CEREBROSPINAL FLUID IN MULTI-SYSTEM INFLAMMATORY SYNDROME IN CHILDREN**

Authors: Jonathan Day[*1], Ursula Rohlwink[2], Timothy Spracklen[1], Claire Butters[1], Raphaella Stander[1], Heidi Facey-Thomas[1], Angharad Davis[3], Chris Scott[1], Liesl Zühlke[4], Kate Webb[1]

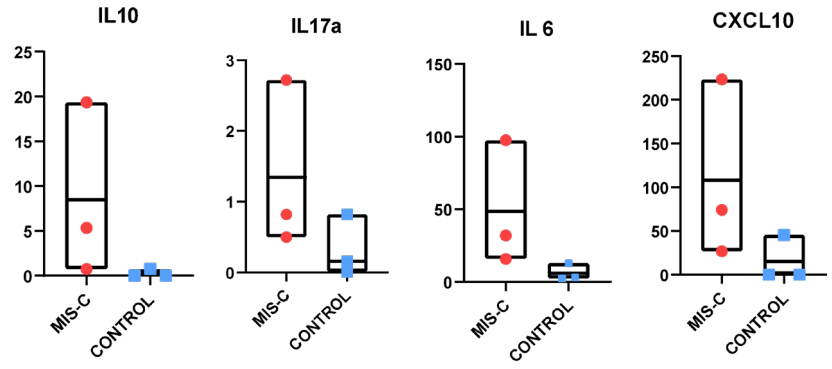
Affiliation: [1]Paediatric Rheumatology, [2]Neuroscience, University of Cape Town, Cape Town, South Africa, [3]School of Life and Medical Sciences, UCL, London, United Kingdom, [4]Paediatrics, University of Cape Town, Cape Town, South Africa

Introduction:
Multi-inflammatory syndrome in children (MIS-C) is characterized by hyperinflammation following infection or exposure to SARS-CoV-2 in children and young people. Approximately a third of MIS-C cases have central nervous system manifestations, the pathogenesis of which is unknown. Here, we characterize the cytokine profile of the cerebrospinal fluid (CSF) of a small cohort of children with MISC with neurological manifestations.

Objectives:
To characterise the cytokine milieu of cerebrospinal fluid in those with MIS-C compared to controls.

Methods:
CSF was acquired via lumbar puncture, as part of in-hospital clinical care, from 3 children who met the criteria for MIS-C with neurological manifestations and 3 control patients presenting for procedures requiring CSF; such as revision of a blocked ventriculoperitoneal shunt. Cytokine concentrations were measured via chemiluminescence and analyzed using SPSS statistical software.

Results: We noted a trend of increased cytokines IL 10, IL 17a, IL 8, CXCL10 in the CSF of patients with MIS-C compared to non-inflammatory controls.



Conclusion: In a small number of patients, we show that certain inflammatory cytokines are raised in the CSF of children with MIS-C and neurological manifestations. Understanding the specific cytokine profile of this condition may be key in efforts to understand pathogenesis and identify potential treatment targets. These data underpin the need for further studies investigating the mechanism of CNS disease in MIS-C.

HREC REF: 599/2020

Title: **SLEEP SPINDLE CHARACTERISTIC IN A NORMAL DEVELOPING INFANT COHORT FROM THE WESTERN CAPE OF SOUTH AFRICA**

Authors: Helishia Dirks[1 2], Melody Asukile[3], Jo M Wilmshurst[1 2]

Affiliation: [1]Department of Paediatrics and Child Health, University of Cape Town [2]Neurology and Neurophysiology Department Red Cross War Memorial Children's Hospital [3] Neurology Department Groote Schuur Hospital

Introduction:
Sleep spindles are oscillating potentials generated in the thalamus of the brain. They are linked to memory consolidation during sleep. Their absence in infants beyond 3 months of age indicates cognitive impairment.

Aim:
This study examines 3 to 9-month-old infants to obtain standardized criteria of the density, frequency and spindle duration for this age group in a South African population. It also examines whether sleep spindle characteristics of infants from a socioeconomically challenged setting differ from their American and European counterparts, from where most data originates.

Methodology:
Infants with normal developmental milestones and no evidence of neuro-insults were identified from routine referrals for electroencephalogram (EEG). Most patients were referred for concern of possible seizures, apneas or breath-holding events and subsequently found to have no abnormal neurology or neurological disorder. Additional exclusion criteria were any pre- or perinatal insult, or an infant born preterm. Retrospective examination of 55 children's EEGs performed between January 2018 and July 2023 was done. Manual scoring of the density, frequency and duration of each individual EEG was obtained and analyzed by a specialist pediatric EEG technologist. A qualified Neurologist independently rated the EEG scoring. Differences were resolved by a paediatric neurology specialist. Findings were statistically analyzed utilizing the Redcap and SPSS software. Of the 55 participants, 27 (49%) were male and 28 (50.9%). were female. Sleep recording was obtained via natural sleep in 35 patients (63.6%), and 20 (36.4%) were given melatonin.

Results:
Mean density, duration and frequency was recorded. Average sleep density for all age groups were between 2-6 spindles/minute with a mean of 3.8 spindles per min, average duration was 2.3 seconds and frequency mean 12.46Hz. The average sleep time was 30 minutes.

Conclusion:
There was no statistically significant difference between the density, duration and frequency of the infants between 3-9 months of age in the sample group as well as between the sample and international data, confirming similar findings from high income regions of the world. There was also no significant difference between the sleep spindle characteristics of the natural sleep group and melatonin sleep induced infants. Establishing normative data of sleep spindles density, duration and frequency in this South African population is important and provides a baseline for future studies exploring sleep spindle formation in neurologically at-risk infants.

HREC REF: 486/2022

Title: **OUTCOMES FOLLOWING NEONATAL CARDIAC SURGERY IN CAPE TOWN, SOUTH AFRICA**

Authors: Derrik du Toit, MBChB[1], MMed, Lenise C Swanson, MBChB, MMed[2], Shamiel Salie, MBChB, MPH[1], Susan Perkins, MS[2], Wisdom Basera, MPH[3,4], John B Lawrenson, MBChB, MMed[7], Thomas Aldersley, MBChB, MPH[2], Andre Brooks, MBChB[5] and Liesl J Zühlke, MBChB MPH, PhD[2,4,6]

Affiliation: [1] Department of Paediatrics and Child Health, Red Cross War Memorial Children's Hospital, Faculty of Health Sciences, University of Cape Town, South Africa; [2] Division of Paediatric Cardiology, Department of Paediatrics and Child Health, Red Cross War Memorial Children's Hospital, Faculty of Health Sciences, University of Cape Town, Observatory, Cape Town, South Africa; [3] School of Public Health and Family Medicine, Faculty of Health Sciences, University of Cape Town, South Africa; [4] South African Medical Research Council, Cape Town; [5] Chris Barnard Division of Cardiothoracic Surgery, Faculty of Health Sciences, University of Cape Town, South Africa; [6] Division of Cardiology, Department of Medicine, Groote Schuur Hospital, Faculty of Health Sciences, University of Cape Town, Observatory, Cape Town, South Africa; [7] Division of Pediatric Cardiology, Department of Paediatrics and Child Health, University of Stellenbosch

Background:
Neonatal Cardiac Surgery has developed significantly since its advent, with improved outcomes, survival, and physiological repair. Limited programs offer neonatal cardiac surgery in emerging economies. We report our experience with neonates undergoing cardiac surgery in our cardiac surgery program.

Methods:
We performed a secondary data analysis on all neonates aged ≤ 30 days undergoing congenital cardiac surgery from 1 April 2017 to 31 March 2020, including outcomes up to 30-days post-surgery.

Results:
A total of 859 patients underwent cardiac surgery at our center, of these 81 (9.4%) were neonates. The proportion of neonates increased annually (8.5%, 9.1% and 9.8%). There were 49 (60%) males, and 32 (40%) had surgery in the second week of life. Fourteen (17%) were premature, four (5%) had a major chromosomal abnormality, five (6%) a major medical illness and eight (10%) a major non-cardiac structural anomaly. The RACHS categorization of surgery was predominantly RACHS 3; n = 28 (35%) and 4 n = 25 (31%). Hours in ICU were extensive; median 188.5 [IQR 114-286] as were hours of ventilation; median 94.5 IQR 45-163]. Almost 60% (n=48) of procedures were complicated by sepsis, as defined in our database. The in-hospital mortality rate was 13% (n=13); the 30-day mortality rate was 19.8% (n=16).

Conclusions:
The proportion of neonates in our service increased over the period. Focused strategies to shorten prolonged ICU stay and decrease rates of bacterial sepsis in neonates are needed. A multi-disciplinary, collaborative heart-team approach is crucial for best outcomes.

HREC REF: 872/2019

Title: **CLINICAL PREDICTORS OF TUBERCULOSIS IN CHILDREN – A PROSPECTIVE STUDY IN FIVE LOW-MIDDLE INCOME COUNTRIES**

Authors: Franckling-Smith Z[1*], Olbrich L [2, 3, 4*], Larsson L[2], Sabi I[5], Ntinginya NE[5], Khosa C[6], Banze D[6], Nliwasa M[7], Corbett EL[7,8], Semphere R[7], Verghese VP[9], Michael JS[10], Graham SM[11], Song R[4], Nabeta P[12], Trollip A[12], Hoelscher M[2, 4, 13], Geldmacher C[2,4], Zar HJ[1°], Heinrich N[2, 4°] *On behalf of the RaPaed-AIDA-TB consortium*

Affiliation: [1] Department of Paediatrics & Child Health, SA-MRC Unit on Child & Adolescent Health, University of Cape Town, South Africa; [2] Division of Infectious Diseases and Tropical Medicine, University Hospital, LMU Munich, Germany; [3] Oxford Vaccine Group, Department of Paediatrics, and the NIHR Oxford Biomedical Research Centre, University of Oxford, Oxford, UK;[4] German Centre for Infection Research (DZIF), Partner Site Munich, Munich, Germany; [5] National Institute for Medical Research - Mbeya Medical Research Centre; [6] Instituto Nacional de Saúde (INS), Marracuene, Mozambique; [7] TB/HIV Research Group, College of Medicine, Blantyre, Malawi; [8] TB Centre, London School of Hygiene and Tropical Medicine, London, UK; [9]Pediatric Infectious Diseases, Department of Pediatrics, Christian Medical College (CMC), Vellore, India; [10] Department of Clinical Microbiology, Christian Medical College (CMC), Vellore, India; [11] Centre for International Child Health, University of Melbourne, Melbourne, Australia; [12] FIND (Foundation for Innovative New Diagnostics), Geneva, Switzerland; [13] Fraunhofer ITMP, Immunology, Infection and Pandemic Research, Munich, Germany

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Objective:
Paediatric Tuberculosis (TB) is associated with significant morbidity and mortality. Despite advances in methods of microbiological detection, diagnosis relies heavily on clinical and radiological features. Here, we describe the demographic determinants of TB disease amongst children from high burden countries, including several vulnerable populations.

Methods:
Children (<15years) with suspected TB from 5 low-middle income countries were prospectively enrolled. Baseline demographic and clinical data, and specimens for microbiological testing were collected. Participants were categorised as confirmed, unconfirmed or unlikely TB, according to NIH consensus definitions. Odds ratios were calculated using multivariable logistic regression analyses comparing 1) confirmed vs unlikely TB, and 2) TB disease (confirmed and unconfirmed TB) vs unlikely TB.

Results:
Of 976 children enrolled between 21 January 2019 and 1 July 2021, 965 (98.9%) had sufficient data for diagnostic classification; 24.8% (239/965) had confirmed TB, 32.2% (311/965) unconfirmed TB, and 43.0% (415/965) unlikely TB. The median age was 4.9 years (IQR, 1.8 to 8.8), with 51.0% (493/965) <5 years and 13.3% (128/965) <1 year. Overall, 16.3% (157/965) were children living with HIV (CLHIV) with almost half (44.9%, 70/157) antiretroviral treatment naïve. Severe acute malnutrition was present in 27.3% (264/965). Reported symptoms were similar across groups. Regression analysis found associations between confirmed TB and TST positivity (OR 6.91, 95%CI 3.65-13.10) and chest radiograph (CXR) findings attributable to TB (OR 4.06, 2.12-7.77); and TB disease and CLHIV (OR 3.53, 1.92-6.47), TST positivity (OR 3.63, 2.35-5.61), CXR (OR 3.95, 2.4-6.49), and exposure to indoor smoking (OR 1.85, 1.14-3.01).

Conclusion:
From one of the largest childhood cohorts, over half of children with TB disease were diagnosed based on clinical and radiological features alone. Findings reflected the well-described symptomology of paediatric TB.

HREC REF: 429/2018

Title: **MICROBIOLOGICAL DIAGNOSIS OF TUBERCULOSIS IN CHILDREN – A PROSPECTIVE STUDY OF MICROBIOLOGICAL YIELD IN LOW-MIDDLE INCOME COUNTRIES**

Authors: Olbrich L[1, 2, 3*], Franckling-Smith Z[4*], Sabi I[5], Ntinginya NE[5], Khosa C[6], Banze D[6], Nliwasa M[7], Corbett EL[7,8], Semphere R[7], Verghese VP[9], Michael JS[10], Graham SM[11], Song R[3], Nabeta P[12], Trollip A[12], Larsson L[1] , Hoelscher M[1, , 133], Geldmacher C[1,3], Heinrich N[1, 3°], Zar HJ[4] *On behalf of the RaPaed-AIDA-TB consortium*

Affiliation: [1]Division of Infectious Diseases and Tropical Medicine, University Hospital, LMU Munich, Germany; [2]Oxford Vaccine Group, Department of Paediatrics, and the NIHR Oxford Biomedical Research Centre, University of Oxford, Oxford, UK; [3]German Centre for Infection Research (DZIF), Partner Site Munich, Munich, Germany; [4]Department of Paediatrics & Child Health, SA-MRC Unit on Child & Adolescent Health, University of Cape Town, South Africa; [5]National Institute for Medical Research - Mbeya Medical Research Centre; [6]Instituto Nacional de Saúde (INS), Marracuene, Mozambique; [7]TB/HIV Research Group, College of Medicine, Blantyre, Malawi; [8]TB Centre, London School of Hygiene and Tropical Medicine, London, UK; [9]Pediatric Infectious Diseases, Department of Pediatrics, Christian Medical College (CMC), Vellore, India; [10]Department of Clinical Microbiology, Christian Medical College (CMC), Vellore, India; [11]Centre for International Child Health, University of Melbourne, Melbourne, Australia; [12]FIND (Foundation for Innovative New Diagnostics), Geneva, Switzerland; [13]Fraunhofer ITMP, Immunology, Infection and Pandemic Research, Munich, Germany

* Shared authorship, ° These two authors contributed equally to this work

Objective:
Childhood Tuberculosis (TB) is a major cause of morbidity and mortality. Mycobacterial culture and Xpert®MTB/RIF Ultra (Ultra) are the reference standard for diagnosis. Obtaining microbiological confirmation remains challenging. Here we describe the microbiological yields for TB in children from the RaPaed-TB cohort.

Methods:
This prospective diagnostic accuracy study enrolled children (<15yrs) with presumptive TB from 5 low-middle income countries. Two respiratory specimens (sputum or gastric lavage, GL) were collected, and one nasopharyngeal aspirate (NPA) if <5years. Extrapulmonary specimens were collected according to local guidelines and capacity. Children were categorised confirmed TB if *M. tuberculosis* (MTB) was detected on Ultra and/or culture. Incremental yield was calculated in children with samples tested by Ultra and two serial cultures.

Results:
A total of 2299 samples were collected from 965 children between 21 January 2019 and 1 July 2021, of which 94% (2157/2299) were respiratory (59%, (1273/2157) induced sputa (IS), 18% (389/2157) spontaneous sputa (SS) and 15% (332/2157) NPAs). Microbiological yield was 45% (239/527) for all children treated for TB, and 39% (102/260) in <5years. In 46% (110/239) of children with confirmed TB, MTB was detected on both Ultra and culture, 36% (86/239) on Ultra alone, and 18% (43/239) on culture alone. “Trace”, “very low” and “low” accounted for 78% of all Ultra results. Most were confirmed on IS 42%(98/239), 21% (49/239) on extrapulmonary specimens and 15% (36/239) on SS. Few (15%, 35/239) were confirmed on more than one specimen type; most on IS and NPA (5%, 13/239), and on IS and SS (3%, 8/239). Of children <5years, most were confirmed on sputum (62%, 63/102) and few on NPA (4%, 4/102), GL (3%, 3/102) or more than one specimen type (13%, 13/102). Additional yield on sputum tested by Ultra followed by first and second cultures was 3.3% and 4.8% respectively.

Conclusion:
This study across five LMICs showed one of the highest rates of microbiological confirmation reported in children. It demonstrates the paucibacillary nature of childhood TB and the added diagnostic value of Ultra “trace” detection. It highlights the need for improved diagnostic tests, particularly for those <5years.

HREC REF: 429/2018

Title: **ONLINE PAEDIATRIC EEG HANDBOOK: A SURVEY ON ITS USEFULNESS**

Authors: Veena Kander[1] MTECH (Neurophysiology), Joanne Hardman[3] PhD, Jo Wilmshurst[1,2] MD

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There is inadequate paediatric EEG training amongst doctors and technicians involved in the care of children with epilepsy in sub-Saharan Africa (Kander, 2021). An entry level handbook was originally developed for healthcare practitioners in sub-Saharan Africa. It has subsequently been encompassed as a resource on the International Child Neurology Teaching Network (ICNTN) making it accessible across the world covering high to low-income countries.

Aim:
To investigate the usefulness of a paediatric online EEG handbook.

Method:
A survey of the ICNApedia online EEG handbook was circulated in December 2021, with recurrent eblasts, via the research electronic data capture (Redcap) from the University of Cape Town to all participants who registered for the handbook (n=108; n= 39 countries). Ethical approval from UCT, Cape Town, South Africa (481/2018).

Results:
By June 2022, 64% fully and 36% partially completed the survey. Responses were from 25 countries: n=8 high income, n=7 upper-middle income, n=7 lower-middle income and n=3 from low-income. Of the 50 participants, most (n=35) had successfully completed the handbook. Seven of the survey respondents had partially and eight did not completed the handbook. Final results supported that the handbook was a good steppingstone to learning EEGs, especially supporting the unique area of paediatrics.

Conclusion:
In resource limited settings non-specialist clinicians are often required to provide extended services including EEG interpretation. To date the survey supports that the handbook is supporting this niche skills area.

HREC REF: 481/2018

Title: **RESILIENCE AND FAMILY QUALITY OF LIFE IN PARENTS OF CHILDREN WITH DEVELOPMENTAL DISABILITIES: A SOUTH AFRICAN PILOT STUDY**

Authors: S. Moodley [1], K. Reichmuth [1], M. Hendricks [1], K.A. Donald [1,2]

Affiliations: [1.]Department of Paediatrics and Child Health, University of Cape Town; [2.]Neuroscience Institute, University of Cape Town

Objective:
To understand resilience in parents of children with disabilities in a time of socio-economic crisis.

Methods:
A quantitative approach was used in a group of thirteen parents being trained by a disability organization, to lead parent networks within the community, towards the end of COVID-19 pandemic in South Africa. Data were collected using telephonic interviews and included a 10-item Connor Davidson Resilience Scale and Beach Family quality of life survey.

Results:
Thirteen mothers (mean age 39 years, range 30-64 years) participated in the study, with (n=6, 46%) mothers reporting unemployment. Mothers reported only 15% (n = 2) of fathers were involved in their children's care. Dependent children (mean age 12 years, range 4-27 years), lived with cerebral palsy, epilepsy, intellectual disability, Down syndrome, autism, and/or albinism. Mothers who were employed, had a college education, paternal support for their children, and had children returning to school, scored higher on the resilience scale (third quartile) compared to those who did not (first quartile). Resilience and family quality of life were correlated. Depression, stress and loneliness were reported in parents scoring lower in the resilience scale.

Conclusion:
Poor socio-economic factors and mental health negatively affect family quality of life and resilience in mothers of children with disabilities. Interventions that include caregivers and support factors which could improve the potential to enhance resilience may improve the family quality of life and strengthen the environment of children with disabilities.

Acknowledgement: Shonaquip Social Enterprise Parent Network

Funding: Research Award 2021, Department of Paediatrics and Child Health Research Committee, University of Cape Town

HREC REF: 443/2021

Title: **ADVANCED AND SPECIALIST NURSING ROLE CONCEPTS IN AFRICA**

Authors: Natasha North[1], Minette Coetzee[1] and Petra Brysiewicz[2]

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Introduction:
Development of advanced and specialist nursing roles is globally advocated. These roles are being introduced in African health systems. Global bodies advise adaptation of high level role definitions to local contexts. Differences between emerging roles in African contexts and globally defined roles have not been systematically analysed.

Objective:
This phase of a larger mixed methods study aimed to enable structured comparison of the relationship between an existing global Clinical Nurse Specialist (CNS) role description and reported characteristics of advanced and specialist nursing roles in Africa.

Methods:
We used concept mapping to assess the fit between the domains of a global CNS role description, primary data from the qualitative phase of the larger study, and published descriptions of African advanced and specialist nursing roles. Results are reported using GRAMMS reporting standards.

Findings:
Concept mapping supported identification of similarities and differences between key concepts and characteristics of the global CNS role description and African role descriptions. Four modified domains (direct care and consulting; strengthening specialist service; education and teaching; and professional leadership and management) resulted, representing an empirically derived role description for advanced and specialist nurses in Africa at a particular point in time.

Conclusion:
These modified domains are presented as a transitional role description with implications for ongoing work to develop advanced and specialist nursing roles in Africa. The transitional role description could contribute to ongoing work to develop advanced and specialist nursing roles in Africa, with the goal of increasing role acceptance and reducing role confusion. Further role descriptions are required to improve the empirical basis for African role descriptions.

Ethics approval number: Ethical approval for the study was provided by the Human Research Ethics Committee of the University of Cape Town (HREC REF: 022/2020), the Research Board of Kamuzu College of Nursing, and the Research Committee of the College of Medicine, Kamuzu University of Health Sciences.

Title: **WHITE MATTER MICROSTRUCTURAL CHANGES IN 6-YEAR-OLD CHILDREN WHO ARE HIV-EXPOSED UNINFECTED IN A SOUTH AFRICAN BIRTH COHORT – A DIFFUSION TENSOR IMAGING STUDY**

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Objective:
Magnetic resonance imaging (MRI) studies have described some of the effects of in utero HIV exposure on children who are HIV-exposed uninfected (CHEU). However, there have been relatively few longitudinal neuroimaging studies of CHEU. White matter microstructural differences have previously been observed in the Drakenstein Child Health study (DCHS) in 2-4-week-old CHEU compared to children not exposed (CHUU). The aim of this cross-sectional follow-up study was to investigate whether these HIV exposure-related white matter microstructural changes persist in the same cohort at age 6 years.

Methods:
A total of 228 6-year-olds underwent MRI scanning between August 2018 and July 2022, as part of a longitudinal nested neuroimaging study, of which 129 children (43 CHEU; 86 CHUU) met inclusion criteria and had usable diffusion-weighted imaging (DWI) scans. DWI scans were pre-processed using TORTOISE software, and diffusion parameters were extracted using the FMRIB Software Library Diffusion Toolbox and Tract-Based Spatial Statistics pipeline. Multivariate analysis of variance (MANOVA) models were conducted to assess group differences in diffusion parameters, adjusting for age at scanning, sex, height and prenatal. An exploratory partial correlation analysis controlling for HIV-exposure was also conducted, assessing the association of tract diffusion parameters with cognition, as measured using the Weschler Preschool and Primary Scale of Intelligence (WPPSI), and behaviour, as measured using the Child Behaviour Checklist (CBCL).

Results:
The CHEU group demonstrated lower AD in the right posterior limb of the internal capsule, as well as lower mean diffusivity (MD) and radial diffusivity (RD) in the right inferior cerebellar peduncle compared to the CHUU group. Findings held on adjustment for covariates, but not False Discovery Rate correction. AD in the right posterior limb of internal capsule was negatively correlated with the WPPSI_similarities score, and positively correlated with CBCL_externalising summary and CBCL_aggressive behaviour subscale. Right posterior limb of internal capsule MD and RD correlated with the somatic complaint's subscale score. Separately, AD and MD in the right inferior cerebellar peduncles positively correlated with the aggressive behaviour subscale.

Conclusions:
WM changes in the cerebellar region in this study are consistent with previously reported findings in neonates in the same cohort. While CHEU neonates showed alterations in the middle cerebellar peduncle, at 6 years CHEU showed alterations in the inferior cerebellar peduncle. The consistency of cerebellar findings suggests the possibility of persistence of WM changes which could have implications on behavioural outcomes considering the partial correlation analysis findings. Further longitudinal studies are required to investigate underlying biological mechanisms of in utero HIV-exposure in the maturing brain.

HREC REF: 738/2021

Title: **LONG TERM QUALITY OF LIFE IN CHILDREN WITH PREVIOUS MIS-C IN CAPE TOWN, SOUTH AFRICA**

Authors: Frank Phoya[*1], Claire Butters[1,2], Timothy Spracklen[1,3], Hamza van der Ross[1], Kate Webb[1]

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Introduction:
Multisystem inflammatory syndrome in children (MIS-C) is a severe, hyperinflammatory disease that occurs after exposure to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Over the past 2 years, the acute effects of MIS-C have been well documented but very little data has been shown on the chronic effect of MIS-C on the quality of life of patients.

Objectives:
To document the long-term effect on the quality of life of children with previous MIS-C, including their physical, emotional, social, and school functioning.

Methods:
A descriptive prospective study was performed. Participants who were previously diagnosed with MIS-C between June 2020 and March 2022 by fulfilling the World Health Organization criteria were recalled to complete a (paediatric quality of life) PedsQL generic inventory score and to get a physical review between March 2023 to July 2023. This was used to evaluate the effect on their Physical, Emotional, Social, and School Functioning.

Results:
Out of the 66 recruited patients with previous MIS-C we managed to recall 36% (24) of them to complete the PedsQL generic inventory. There was a mean duration of 22 months since admission, (minimum 8 months, maximum 32 months). Sixteen percent of our cohort were male and the average age of the group was 9,6 years old (minimum 3 years old, maximum 16 years old). During their illness, the average length of admission was 9 days and 20% needed ICU admission. At follow up, all the participants had a full recovery, no medical complaints, and a normal physical examination. The results from the PedsQL showed that 16% of the children had a deficit in their physical domain score (with the lowest score of 47% deficit) and 12% had a deficit in their psychosocial functional score which included emotional, social, and educational scores (with the lowest showing a 37% deficit).

Conclusion:
Although children with previous MIS-C had no obvious medical sequelae, there was a prolonged effect on the quality of life in this single center cohort.

HREC REF: 599/2020

Title: **NORMAL OUTCOME WITH PRENATAL INTERVENTION FOR RIBOFLAVIN TRANSPORTER DEFECT**

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Introduction*:*
Riboflavin transporter deficiency is a rare but severe neurometabolic disorder. We report two siblings with pathogenic variants in *SLC52A3* gene, resulting in riboflavin transporter 3 deficiency.

Case Summaries:
The first sibling was diagnosed at 11 months of age with severe respiratory compromise and regression of developmental milestones. His symptoms significantly improved with riboflavin supplementation therapy. The younger sibling was diagnosed by antenatal genetic analysis; riboflavin supplementation was initiated in utero and continued from birth. Now 2 years of age, he remains clinically asymptomatic despite genetic confirmation of riboflavin transporter deficiency.

Discussion:
Antenatal riboflavin supplementation is a safe and effective treatment for the prevention of symptomatic manifestations of riboflavin transporter deficiency. These participants have now been recruited as genetically confirmed cases to the International Centre for Genomic Medicine in Neuromuscular Diseases (ICGNMD) to increase opportunities for participant access to future trials and research.

HREC REF: 722/2023

Title: **A RETROSPECTIVE REVIEW OF ALL CHILDREN ADMITTED WITH ACUTE SEVERE ASTHMA TO THE PAEDIATRIC INTENSIVE CARE UNIT, RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL BETWEEN 2009-2019**

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Background and Aim:
Asthma is one of the commonest chronic conditions of childhood and affects children worldwide. The majority of children who experience an acute exacerbation of asthma do not require admission to a paediatric intensive care unit (PICU). There is limited data on the admission rates, treatment modalities and length of PICU stay, for children who have acute severe asthma (ASA) in a South African context. In this study, we aim to describe the patient profiles and treatment of all children admitted to the PICU with ASA.

Method:
We conducted a retrospective audit of all children admitted with ASA to the paediatric intensive care unit at Red Cross War Memorial Children's Hospital in Cape Town, South Africa between 01 January 2009 - 31 December 2019.
Results
There were 14592 PICU admissions over the 11-year period, of which 180 admissions (1,2%) were for acute severe asthma. There were 96 male (53,3%) admissions and the median, interquartile range (IQR) age on admission was 67 (37 – 93) months. Nearly all the patients received nebulisations, steroids, and magnesium sulphate before PICU admission. Half of the patients were loaded with IV salbutamol (n=96; 53,3%) and about a third (n=61; 34%) received a salbutamol infusion before admission to PICU. Similar proportions received nebulisations and steroids in PICU, 34 patients (19%) received magnesium sulphate again in PICU and a total of 130 patients (72,2%) received a salbutamol infusion. Most children received non-invasive respiratory support (n=167; 90,3%), and 18 children (9,7%) required mechanical ventilation for a median (IQR) of 3 (2 – 4) days. The median PICU stay was 1 (IQR 1 – 2) days and median hospital stay was 4 (IQR 3 – 6) days. No children died.

Conclusion:
There has been an increasing number of children admitted to PICU with ASA over the 11-year period. There has been increased utilization of non-invasive ventilation (NIV) strategies, mainly HFNC and the duration of PICU support is short.

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Title: CHARACTERIZATION OF LATENT CLASSES OF ANTHROPOMETRIC GROWTH IN EARLY CHILDHOOD IN A BIRTH COHORT THE DRAKENSTEIN CHILD HEALTH STUDY

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Background:
Early childhood growth sets a trajectory for lifelong health, but there are limited data of growth trajectories and determinants from low- and middle-income country settings.

Objective:
We present an analysis to determine whether groups of children that follow similar longitudinal trends (ie. latent growth classes) exist within Standardized Height and Weight measures from birth through five years in a South African birth cohort study. Additionally, we provide a characterization of such classes considering child health, maternal, socioeconomic, environmental and child feeding factors as well as features of abnormal growth such as rapid weight gain, stunting, underweight and overweight.

Methods:
The Drakenstein Child Health Study (DCHS) is a prospective South African birth cohort in which pregnant women were enrolled between March 2012 and March 2015 and followed through birth and childhood (follow-up visits are described in Figure 1). Latent Class Mixed Modelling was used to identify underlying latent profiles of growth for standardized height and standardized weight measurements from birth to five years for a sample of 1143 children from the DCHS. Multinomial Logistic Regression allowed the identification of key exposure variables that describe allocation to the identified latent growth classes.

Results:
Four classes of growth within standardized height (n_1=516, n_2=112, n_3=187, n_4=321) and standardized weight (n_1=263, n_2=150, n_3=584, n_4=142) were identified, each with distinct trajectories over early childhood. A strong association was found between various growth classes and abnormal growth features such as rapid weight gain, stunting, underweight or overweight. Exposures associated with weight trajectories were prematurity, TB disease in childhood, prenatal alcohol exposure or breast feeding. Premature birth, pneumonia in early childhood, gravida and prenatal smoke exposure were associated with height trajectories.

Conclusions:
Better understanding of distinct childhood growth trajectories and their predictors may be gained, through identification of these classes, informing interventions to promote optimal childhood growth.

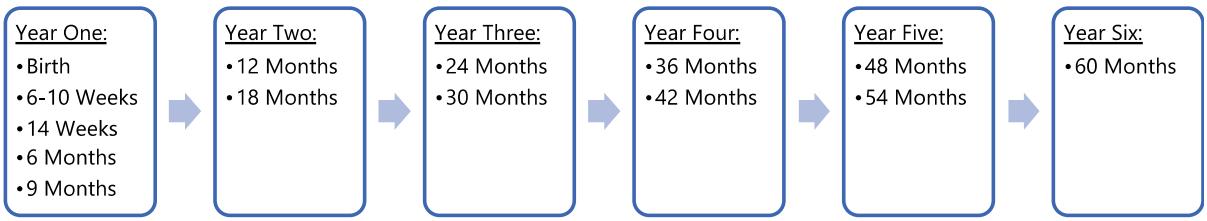

Figure 1: Timeline of follow-up visits for subjects within the DCHS.

Title: **ADOLESCENT HEALTH RELATED QUALITY OF LIFE: MIND THE GAP!**

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Background:
It is widely recognised that the health care and emotional needs in adolescence is distinctly different from younger children and adults. Clinical care during this transition period has transformed to ensure that adolescents needs are met. Decision making bodies around the world, such as the National Institute for Health Care Excellence (NICE), rely on Health Related Quality of Life (HRQoL) for funding decisions. They endorse the generic EuroQol HRQoL questionnaires which have both an adult (EQ-5D-3L) and youth version (EQ-5D-Y-3L). Similar appraisal decisions are currently being considered for national health insurance (NHI) in South Africa. This study aims to investigate whether adolescents living with HIV (ALHIV) and Diabetes Mellitus (ALDM) answer the adult and youth questionnaires differently and whether they can detect known-group validity with comparison to a general population sample.

Methods:
Adolescents aged 13-18 years were recruited between June 2021 and May 2022 from the Infectious Diseases and Endocrine transition care clinics at Groote Schuur and Red Cross War Memorial Children's Hospitals. The general population sample was recruited from schools in the same geographical catchment area as the hospitals. The EQ-5D-3L and EQ-5D-Y-3L were presented to consenting adolescents in random order and separated by a cognitive task (word problem). Clinical information was extracted from the medical folder. The redistribution of responses between questionnaires was tabulated and Kruskal-Wallis H test was used to assess the known group-validity by health condition and clinical characteristics.

Results:
Responses were collected from ALHIV (n=85), ALDM (n=107) and general population (n=294). The majority of the ALHIV sample had perinatally acquired HIV and prescribed anti-retroviral therapy (ARTs) for a median (IQR) of 14 years (12,16). They were classified in WHO stage 1/2 (n=11, 13%), stage 3 (n=45, 53%) or stage 4 (n=29, 34%) and had a viral load <50 (n=18, 21%), 51-100 (n=57, 67%) or >1000 (n=10, 12%). A range of HIV related co-morbidities were recorded in 45% of the sample (n=38) and included HIV encephalopathy (n=9, 11%), HIV associated neurocognitive disorder (n=3, 4%) and chronic lung disease (n=3, 4%). ALHIV most frequently reported problems with pain/discomfort (n=20, 24%) and mental health (n=24, 28%). There was however a 11% (n=9) and 20% (n=17) discrepancy in reporting problems on these respective dimensions on the youth and adult questionnaires with the youth version detecting more problems. ALDM had been living with the condition for a median (IQR) of 5 years (3,9) and had a median (IQR) HbA1c of 10.2 (8.2, 12.1). Co-morbidities were reported in 18% of the sample (n=19) and included leg pain, rash or acanthosis, diabetic ketoacidosis and headache (all <3%). ALDM most frequently reported problems doing their usual activities (n=20, 19%), pain/discomfort (n=39, 37%) and mental health (n=48, 45%). There was 9% discrepancy in responses for usual activities (n=10) and pain/discomfort (n-11) and 34% for mental health (n=36) between the youth and adult questionnaires with the youth version detecting more problems. However, in ALDM 10% (n=11) reported some anxiety and depression and not being worried, sad or unhappy. There were no significant differences between clinical characteristics and total HRQoL scores in ALHIV nor ALDM. ALHIV reported significantly better general health ($p<0.001$) than ALDM and the general population. However, ALHIV ($p=0.001$) and ALDM ($p=0.048$) showed a significantly poorer total HRQoL score on the adult EQ-5D-3L than the general population. Although approximately 40% of adolescents had no preference for the youth and adult versions, 45% of ALDM (n=48) and 31% of ALHIV (n=27) preferred the wording of the youth version.

Conclusion:
The EQ-5D-Y-3L describes mental health as worried, sad or unhappy whereas the adult EQ-5D-3L describes it as anxiety or depression. This results in the youth version detecting more problems with mental health compared to the adult version. However, the youth version did not detect any mental health concerns in 10% of ALDM who reported some problems with anxiety or depression, which may arguably be more clinically relevant. Despite the pain/discomfort question being identical in the two questionnaires there was a discrepancy noted for both ALHIV and ALDM. These discrepancy in responses needs to be investigated in responsiveness analysis in clinical trials as the choice of questionnaire could influence health resource allocation. Although the questionnaire showed validity in its ability to differentiate health between ALHIV, ALDM and the general population consideration needs to be given to the development of adolescent specific HRQoL measures.

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