Department of Paediatrics & Child Health

ANNUAL RESEARCH DAYS 2024

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Programme and Abstract Book

Tuesday, 29th and Wednesday, 30th October 2024

Venue: D3 Lecture Theatre, Red Cross War Memorial Children's Hospital (in-person only)

CPD Points for Tuesday, 29th and Wednesday, 30th October 2024

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

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Title: **SURVIVING PRETERM BIRTH: THREE-YEAR HEALTH-OUTCOMES OF VERY LOW BIRTH WEIGHT INFANTS ADMITTED TO GROOTE SCHUUR HOSPITAL: *AN OBSERVATIONAL STUDY USING THE VERMONT OXFORD NETWORK DATABASE***

Authors: Dr Yolanda Nkanuka[1], Prof Lloyd Tooke[2], Dr Dave le Roux[3]

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Background:
The first 1000 days of a child's life are vital for their well-being, particularly for preterm infants who face high mortality and morbidity rates. Despite advances in neonatal care, preterm infants still struggle with long-term health consequences. Long-term outcomes remain unknown in South Africa and other low- and middle-income countries.

Aims and Objectives:
The primary objective of this study is to estimate the mortality rate of the cohort of very low birth weight (VLBW) preterm infants during their first three years of life. The secondary objectives include exploring the complications (morbidity) of VLBW preterm infants within the same time frame, taking into consideration hospital admissions and specialist clinic visits.

Methods:
A retrospective cohort study was conducted on VLBW preterm infants admitted to Groote Schuur Hospital (GSH)in 2020, following them up until age 3. The Vermont Oxford Network (VON) was used to gather demographic information and details of their hospital stay. Multiple sources including the National Health Laboratories Service, CLINICOM, and the South African mortuary database were used to follow the infants up to 3 years of life. Telephonic contact was made with the caregivers of children not found on the databases. Data analysis was done on Excel, using descriptive statistics and bivariate analysis to examine the unadjusted association between VLBW status and long-term outcomes. The University of Cape Town Human Research Ethics Committee has granted approval (HREC 628/2024) for data collection and telephonic communication with caregivers, following ethical guidelines.

Outcomes:
The GSH nursery admitted 535 VLBW infants in 2020, the median birth weight was 1150g (IQR = 387.5) and gestational age (GA) 29 weeks (IQR = 4). Antenatal care was accessed by mothers of 474 (88.5) infants and mothers of 74.7% (n=400) received antenatal steroids. There was a 70.9% (n=381) caesarean section rate, 74.7% (n=400) were managed on continuous positive airway pressure (CPAP) and 24.8% (n=133) received surfactant therapy. Overall severe in-hospital morbidity included: severe intraventricular haemorrhage (IVH) 4.9% (n=24), cystic periventricular leukomalacia (PVL) 3.5% (n=15), severe retinopathy of prematurity (ROP) 4.8% (n=12), 2.4% (n=13) infants were on oxygen at 36weeks and 1.7% (n=9) received steroids for chronic lung disease, 52 (9.7%) had necrotising enterocolitis (NEC) of which 21% (n=11) received surgery.
The survival rate to discharge was 82.4% (n=441). Of with BW 500g – 1000g, 66.8% (n=113) survived, compared to 90.3% (n=328) of the infants with BW 1000g – 1500g. Seventy-four (16.7%) survived with significant morbidity. Post discharge mortality and secondary outcomes including hospital readmissions, specialist clinic visits and any surgical interventions will be reported.

HREC REF: 628/2024

Title: **GENE EXPRESSION, CLINICAL AND DEMOGRAPHIC DATA DISTINGUISH KAWASAKI DISEASE FROM OTHER INFLAMMATORY CONDITIONS IN SOUTH AFRICAN CHILDREN**

Authors: Timothy F Spracklen,[1,2] Simon C Mendelsohn,[3] Claire Butters,[1] Heidi Facey-Thomas,[1] Mzwandile Erasmus,[3] Mthawelanga Ndengane,[1] Liesl Zühlke,[1,2,4] Thomas J Scriba,[3] Kate Webb[1,6]

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Objective:
Diagnosis of Kawasaki Disease (KD) remains a challenge due to difficulty in distinguishing it from similar paediatric inflammatory disorders. Studies in European patients have shown the clinical utility of polygenic scores in identifying KD. Here we sought to determine the discriminatory capacity of gene expression, demographic and clinical data for KD, compared to other presenting inflammatory conditions in patients from Cape Town, South Africa.

Methods:
Between June 2020 and November 2023, RNA was collected from 13 children with KD, 42 children with multisystem inflammatory syndrome in children (MIS-C), 44 controls with other inflammatory conditions, and 74 healthy non-inflammatory paediatric controls. Expression of 80 genes with broad relevance to inflammation, immunopathology, immune regulation, and type I interferon response, was determined by real-time quantitative PCR. Differentially expressed genes (DEGs) were identified through nonparametric pairwise comparisons between experimental groups, adjusted by Holms correction. Receiver operating curve analysis was used to assess the discriminatory capacity of each gene and combinations of genes and other factors for KD or MIS-C compared to controls.

Results:
Children with KD were younger than those with MIS-C ($p = 0.0061$) and the inflammatory controls ($p = 0.0049$). Both KD and MIS-C were characterised by the presence of conjunctivitis, rash and tachycardia at baseline. A total of 32 DEGs were identified in KD compared to healthy children, but only two transcripts were up-regulated in KD compared to the inflammatory controls. A multi-factor score consisting of *CASP5* and *TREM1* expression, presence of conjunctivitis, and age could reliably differentiate KD from inflammatory controls (AUC 95.4%; 95% CI: 89.8-100%). This score did not perform as well in distinguishing KD from MIS-C (AUC 69.1%; 95% CI: 51.2-87.1%); however, a two-gene score of *IL27* and *SOCS1* expression could distinguish these disease groups (AUC 89.5%; 95% CI: 76.6-100%).

Conclusions:
These data suggest that patient demographic and clinical data can be incorporated into a diagnostic algorithm for KD and MIS-C that includes gene expression of four key genes. This has the potential to greatly improve diagnosis of KD in African children. Notably, our results do not replicate recently described gene signatures of KD and MIS-C in children of European ethnicity, partly due to the use of a limited 80 gene panel in this study. Nevertheless, this highlights the importance of conducting work of this nature in underrepresented patient populations.

HREC REF: 531/2024

Title: **REGISTRY REVIEW OF KIDNEY REPLACEMENT THERAPY FOR CHILDREN IN SOUTH AFRICA**

Authors: Mlia Phiri E[1], Davids R[2], Coetzee A[1], McCulloch MI[1], Webb K[1], Nourse P[1]

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

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Introduction:
The South African Renal Registry (SARR) collects and reports data on adults and children with kidney failure undergoing kidney replacement therapy (KRT) in the public and private healthcare sectors from all nine South African provinces. Annual updates capture and record the type of modality as at 31st December each year and any switch in treatment modality and the dates and reasons for stopping treatment are also recorded.

Aim:
To describe the state of KRT for children in South Africa from 1st January 2013 to 31st December 2022.

Methodology:
This was a retrospective cohort study using SARR. We analysed the South African Renal Registry data to provide information on the incidence, treatment modalities, factors affecting the type of KRT modality and outcome. The data was exported from the SARR database on 10/11/2023 into Microsoft Excel and analyzed using SPSS.

Results:
361 children ≤18 years started KRT between 1st January 2013 to 31st December 2022 of which 338 were alive at 1 year. The average incidence rate was 1.7 per million population (pmp). The median age was 14 years, 52.4% were male and 58.4% were black. The main primary kidney disease was glomerular diseases (42.1%) followed by chronic kidney disease (CKD)unknown cause. Kidney transplant was not done in children under 1 year. Children aged between 13-18 had almost 80% less chance of receiving a transplant than children aged 1-5 (OR 0.22, p<0.001). There was clear inequity in the access to transplants between provinces with transplant available in only 5/9 provinces. White patients had 8 times more chance of receiving a transplant (OR-8.30, 95%CI-4.27-16.15; p<0.001) and the coloured patients had 3 times more chance of receiving a transplant (OR-3.36, 95%CI- 1.93 – 5.85; p<0.001) than black patients. These discrepancies persisted despite controlling for the province of origin, age of onset and sector of healthcare. The children who received a transplant had the highest survival rates.

Conclusion:
The incidence of children starting KRT in South Africa is low compared to other well-resourced countries. There is clear inequality in access to transplant due to geographic location and demographics.

HREC REF: 794/2023

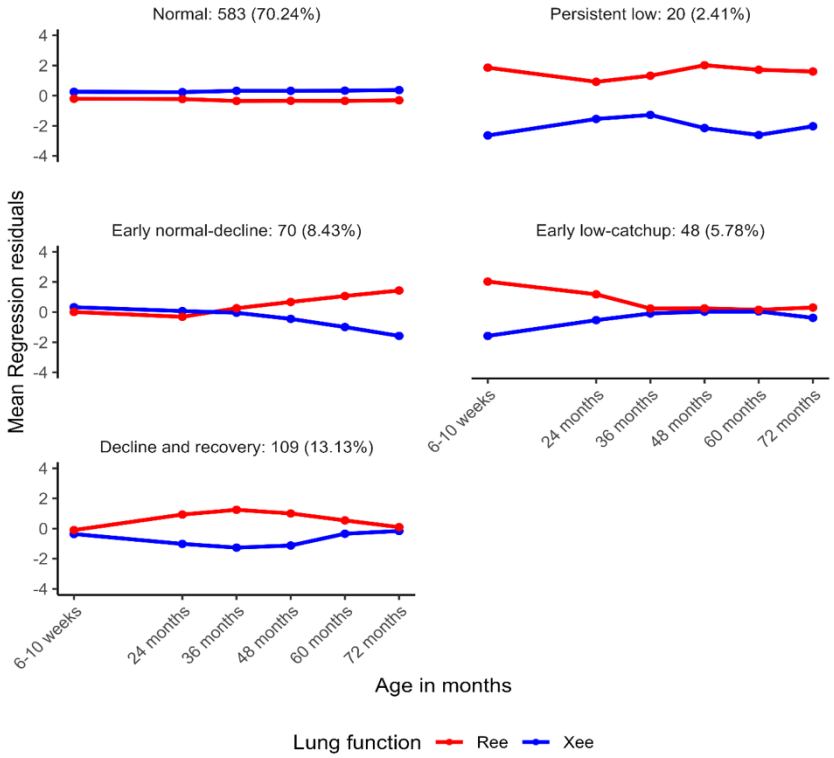
Title: LUNG FUNCTION TRAJECTORIES FROM BIRTH TO 6 YEARS IN AN AFRICAN BIRTH COHORT: GROUP BASED MULTI-TRAJECTORY MODELLING

Authors: D. Gray[1], A. Ulla[2], S. Chaya[1], C. Jacobs[1], Z. Hantos[3], N. Marozva[1], M. Botha[1], D. J. Stein[4], M. Nicol[5], A. Custovic[2], H.J. Zar[1]

Affiliation: [1]University of Cape Town, Cape Town, South Africa, [2]National Heart and Lung Institute, Imperial College, London, United Kingdom, [3]Department of Anaesthesiology and Intensive Therapy, Semmelweis University, Budapest, Hungary, [4]Dept of Psychiatry and Mental Health, and SA-MRC Unit on Risk & Resilience, Cape Town, South Africa, [5]Marshall Centre, School of Biomedical Sciences, University of Western Australia, Perth, Australia

Background: Low or worsening lung function trajectories from childhood are associated with lifelong health risk. Data is lacking on trajectories in infancy and preschool years, a time of critical lung growth with potential for interventions.
Aim: Describe lung function trajectories and determinants from birth through 6 years in the Drakenstein Child Health study, an African birth cohort.
Methodology: Pregnant mothers were enrolled from 5 March 2012 to 31 March 2015 and children were followed from birth, with lung function (intra-breath oscillometry) measured at 6 timepoints (6 weeks to 6 years), comprehensive exposure information was collected from the antenatal period through childhood. Longitudinal resistance (Ree) and reactance (Xee) at end expiration were modelled using Group-based multi-trajectory modelling to describe joint trajectories of Ree and Xee.
Results: 830 children with ≥two lung function measures were included. A model comprising 5-trajectories was the optimal solution: Normal (70.2%); Persistent low (2.4%); Early normal-declines (8.4%); Early low-catch up (5.8%); Decline and recovery (13.1%). Ninety (11%) children had low trajectories (Persistent low or Early normal-decline); risk factors were RSV-lower respiratory tract infection, preterm birth and postnatal maternal psychological distress. One hundred and fifty seven children (19%) showed catch-up to normal lung function (Early low-catch-up or Decline and recovery) through six years. Spirometry at 6-years differed by trajectory: children in the Normal trajectory had the highest FEV_1 and FVC, and those in the Persistent low, the lowest.
Conclusion: Specific early life lung function trajectories show potential for lung growth and recovery in early childhood. Modifiable factors including prematurity and RSV-LRTI negatively impact on lung trajectories.
Funding: Bill & Melinda Gates Foundation, SA-MRC, UK-MRC, Wellcome Trust
HREC REF: 048/2020

Figure 1: Mean regression residuals over time in the five respiratory system impedance trajectories (N=830, children with at least two lung function assessments).



Title: **THE INTRODUCTION OF MULTI-STRAIN PROBIOTICS TO PRETERM INFANTS IN A REGIONAL HOSPITAL: AN OBSERVATIONAL STUDY**

Authors: Meliza Abrahams[1], Prof Lloyd Tooke[2], Dr Ilse Els[3]

Affiliation: [1]Department of Paediatrics, University of Cape Town; [2]Department of Neonatology, Groote Schuur Hospital, University of Cape Town; [3]George Regional hospital, Department of Paediatrics, University of Cape Town

Background:
Worldwide 1 in 10 of all infants are born preterm. Late onset sepsis (LOS) (>3days of life) and necrotising enterocolitis (NEC) are important causes of morbidity and mortality in this vulnerable group. Probiotics may help to decrease the incidence of these conditions, although controversies remain.

Objectives:
To describe the implementation of multi-strain probiotics in George Regional Hospital (GRH) and determine the incidence of NEC, LOS and mortality in this group. Also, to compare with previous years where there were either no probiotics or only single strain probiotics.

Methods:
A retrospective observational study was conducted between February 2019 to July 2020 at George Regional Hospital, Western-Cape, South-Africa. Data were collected from infants who weighed between 800g to 1200g to observe the occurrence of LOS and NEC.

Results:
Seventy-seven inborn infants were included. They had a median weight of 1000g, IQR [900-1120g] and a median gestation of 30weeks, IQR [28-31weeks]. The ratio of male to female was 51:49. All of them received breastmilk. A total of eleven (14%) infants had positive cultures. These were predominantly gram-negative organisms and there were no positive cultures of probiotic organisms. Seventy five percent of the infections occurred in ELBW infants and their risk for mortality is higher overall. There was a total of seven deaths (9%) of which 3 were before 72hours of life. Out of all the 77 infants 4 died of LOS. None of the infants in the group had clinical or radiological NEC. Compared with the previous time periods, there was a similar rate of LOS, but a reduction of NEC and death.

Conclusion:
The introduction of probiotics to a regional hospital is possible. Less NEC was observed during the administration of multi-strain probiotics.

HREC REF: 537/2022

Title: **THE BURDEN OF ANTENATALLY UNDIAGNOSED MAJOR CONGENITAL ANOMALIES IN LIVE-BORN BABIES AT A BUSY SECONDARY LEVEL MATERNITY HOSPITAL IN THE WESTERN CAPE**

Authors: M F Amankrah[1] FCPaed, E Kalk[2] PHD, AM van Niekerk[1], FCPaed, CertPaedCardiol

Affiliation: [1]Red Cross War Memorial Children's Hospital, Department of Paediatrics and Child Health, University of Cape Town; [2]Centre for infectious Disease Epidemiology & Research, School of Public Health, University of Cape Town

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Introduction:
Major congenital anomalies (MCA) account for considerable mortality, morbidity and disability in sub-Saharan Africa. Non-lethal defects have a significant impact on quality of life, not only for the child but for their caregivers and communities. There are very limited data on MCA and their impact on neonatal services and mortality in low-to-middle income countries (LMIC).

Objective:
To determine the prevalence, characteristics, associated factors, and short-term outcomes of antenatally undiagnosed major congenital anomalies in neonates at Mowbray Maternity Hospital (MMH) in 2022. MMH is a secondary level-obstetric referral centre in the MetroWest region of the Western Cape.

Methods:
We conducted a retrospective, cross-sectional study of all live-born MCA neonates admitted to MMH neonatal services between 1 January- 31 December 2022. Stillbirths and antenatally-diagnosed MCA cases were excluded. Cases were identified from a clinical register and data collected by folder reviews using a standardized REDCap data collection form and correlating with hospital databases. Data cleaned and analysed using R and Microsoft Excel. Continuous variables were described as means and 95% confidence intervals, or medians with interquartile range as appropriate and compared using the Wilcoxon rank sum test. Categorical variables were presented as proportions and assessed using chi-square or Fishers exact tests.

Results:
The study included 73 neonates and the prevalence of MCA was 36/1000 live births. The most common defects were genitourinary defects (21%), orofacial defects (19%), musculoskeletal defects (17%), gastrointestinal defects (17%), cardiovascular defects(15%) and central nervous system defects (9%) and 47 cases were non-syndromic MCA (64%) vs 26 syndromic MCA (36%). Of the syndromic MCA, Trisomy 21 (58%) was most prevalent, followed by Trisomy 13 (12%) and Trisomy 18 (4%). Amongst these cases, the most common structural defects were cardiovascular (54%) and orofacial clefts (11%). Ninety six percent of mothers attended antenatal care and 82% had at least 1 antenatal ultrasound scan. Only 51% booked <20 weeks and 29% of neonates had fetal anomaly ultrasound scan, where the MCA was not diagnosed, the majority being neonates with Trisomy 21. A significant association was found between MCA and advance maternal age (>36 years), increased gravidity and low birth weight (< 2500g). Twenty-seven percent required admission to the neonatal intensive care and 16% required respiratory support. More than a third (34%) had a prolonged hospital stay, range 7-175 days and 21% required transfer to tertiary level hospital; of these, 93% requiring surgical intervention. The in-hospital early mortality rate was 15%.

Conclusion:
MCA prevalence in this study was 36 /1000 live-births higher than similar studies conducted in South Africa and other LMICs. More than one third of cases had prolonged hospital stay and more than a fifth required transfer for tertiary intervention. This single-facility study shows a significant MCA burden on neonatal services. Diagnosis and notification of MCA needs to improve to strengthen local surveillance, reinforce existing and potential preventative strategies as well as define appropriate referral and management guidelines.

HREC REF: 365/2022

Title: **A DESCRIPTIVE STUDY OF INFANTS WHO RECEIVED RED BLOOD CELL TRANSFUSIONS DURING 2018-2019 AT GROOTE SCHUUR HOSPITAL (GSH)**

Authors: Dr Liesl Le Roux, Dr Vashini Pillay, A/Prof Lloyd Tooke, Dr Yaseen Joolay

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

Background:
Red blood cell transfusions occur commonly in newborns admitted in neonatal units, with a higher incidence in very preterm and extremely preterm infants. Patients with clinically significant anaemia may receive red blood cell transfusions (RBCT) in their management. With improving survival of preterm newborns, the increasing numbers of patients are transfused with red cells in low to middle-income countries (LMIC) are not well documented in existing literature, we therefore aimed to describe this clinical practice.

Objectives:
The primary objective of this study was to determine the incidence of RBCT in a cohort of neonates admitted in the neonatal unit of a tertiary-level public hospital in Cape Town. Secondary objectives included describing the patient characteristics, mortality and morbidities that occurred in the patients who received RBCT.

Methods:
This was a retrospective study. The cohort was identified through a search of the Western Cape Blood Services (WCBS) database of blood products issued to patients admitted in the neonatal unit. The hospital records of infants who received RBCT between 1 January 2018 and 31 December 2019 were included for review. Additional information was gathered using the hospital's Clinicom system and Vermont Oxford Network neonatal database. Patients with incomplete records were excluded. Variables included demographic data, level of respiratory support, RBCT indications, mortality and morbidities including Bronchopulmonary Dysplasia (BPD) and severe Intraventricular Haemorrhage (IVH), sepsis and necrotising enterocolitis. Simple statistics as well as univariate and multivariate analysis were used to describe the data. Patients were categorized according to birth weight category for analysis. The study received institutional and ethics board approval HREC 487/2022.

Results:
WCBS identified 144 infants for whom red blood cell products were issued during the study period of which 116 with complete records were included. The incidence of RBCT during the 2 year study period was 2.7% of all infants admitted to the neonatal unit. 7.2% of very low birth (VLBW) infants received RBCT. Of the patients included in this analysis, 29 (25%) died during admission. Sixty-two (53%) infants were male. In VLBW infants, median gestational age at birth in which RBCT occurred was 28 completed weeks (IQR 27; 29) and birthweight was 1000g (IQR 838; 1135). A total of 143 RBCT occurred over the study period, 123 (86%) occurred in VLBW infants. The median haemoglobin at which a RBCT occurred was 8.8g/dL (IQR 7.6; 10.1). More than two-thirds (77%) of RBCT occurred in the Neonatal Intensive Care Unit Continuous Positive Airway Pressure (CPAP) and invasive mechanical ventilation was required in 41% and 45% of infants, respectively. Forty-six (40%) of infants had sepsis with a positive blood culture. Multivariate analysis demonstrated that VLBW infants who received multiple transfusions had increased odds of developing BPD (OR 5.27 (95% CI 1.20 – 22.99)), severe IVH (OR 3.75 95% CI 1.11– 12.65)) or dying (OR 3.26 (95% CI 0.99 – 10.74)).

Conclusions:
Red blood cell transfusions frequently occur in newborns, the majority occurring preterm infants. There is a high sepsis rate in these infants. Patients who receive more than one RBCT have significant morbidities, especially BPD and severe IVH. The long-term outcomes of these patients need further evaluation. The need for further research with larger patient samples is highlighted by this study.

HREC REF: 487/2022

Title: **OROPHARYNGEAL DYSPHAGIA IN NEONATES: PREVALENCE AND RISK FACTORS WITHIN A SOUTH AFRICAN CONTEXT**

Authors: Kirsten Porter[1], Mrs Vivienne Norman[2], Dr Natasha Rhoda[3]

Affiliation: [1]Master of Science in Speech Language Pathology / Postgraduate Student, University of Cape Town, Department of Health and Rehabilitation Sciences (DHRS); [2]University of Cape Town, Communication Sciences and Disorders (CSD), Department of Health and Rehabilitation Sciences (DHRS); [3]WCDoH and University of Cape Town: Department of Paediatrics and Child Health: Neonatology

Background:
The prevalence of neonatal oropharyngeal dysphagia (OPD) remains largely unexplored in lower middle-income countries, with limited published research on this topic. In the South African context, factors such as poverty, burden of disease and limited access to healthcare may elevate the risk of OPD among neonates. Improvements in neonatal medical care have led to higher survival rates for neonates with complex medical conditions, yet also increased the likelihood of feeding and swallowing difficulties. Contextual information on the prevalence, nature and risk factors for OPD is important for healthcare planning and optimal service delivery.

Research aim and objectives:
To describe OPD and the associated risk factors in neonates admitted into a neonatal unit in South Africa. The objectives of this research study were to describe the prevalence, nature and risk factors associated with OPD in neonates, including medical conditions, gestational age and birthweight.

Method:
A prospective, descriptive cross-sectional study design was used to describe OPD and the associated risk factors in 160 (*N*=160) neonates, 34 weeks or older, who were admitted into a neonatal intensive care unit (NICU) and were considered medically stable. Participants fitting the criteria between November 2021 and June 2022 were enrolled. Feeding and swallowing was assessed using a reliable and validated tool, the *Neonatal Feeding Assessment Tool* (NFAS), which allowed for the description of the nature of OPD. The prevalence of OPD and associations between OPD and various risk factors were analysed statistically.

Results:
Thirty-two participants (20%; *n*=32) were diagnosed with OPD according to the NFAS criteria, although more participants (43.1%; *n*=69) presented with some clinical signs of OPD. More than 80% of neonates with OPD were born premature (*n*=26; 81.3%) and/or with a low birthweight (*n*=28; 87.5%), while respiratory (*n*=23; 71.9%) and neurologic (*n*=9; 28.1%) complications were the most prevalent medical conditions reported in neonates with OPD in this study. Neonates born premature and/or with a low birthweight as well as those with medical conditions (neurologic, cardiorespiratory, anatomic, genetic and gastrointestinal) were at increased risk for OPD (OR>1.00). A statistically significant association between neonates with gastrointestinal complications and OPD was found (*p*=0.045). Neonates with OPD presented with suboptimal physiologic functioning (*n*=27; 84.9%), inadequate state of alertness (*n*=30; 94%) and stress cues during feeding (*n*=28; 87.5%). Nearly all neonates with OPD had non-nutritive (*n*=31; 96.9%) and nutritive suck (*n*=32; 100%) difficulties and over two-thirds of neonates with OPD presented with signs typical of OPD such as weak and/or delayed initiation of suck, coughing and poor lip closure leading to spillage during feeding.

Conclusion:
One in five neonates admitted to the neonatal unit presented with OPD, even once medically stable and over 34 weeks gestation. Neonates with multiple medical conditions or risk factors were more likely to present with OPD. The results of this study highlight the complexity of OPD in neonates and the need for timeous inclusion of oral feeding protocols in the management of neonates, and the role of speech-language therapists in the assessment and management of neonates at risk for OPD to ensure optimal management.

Ethics Approval: HREC 415/2021 (Annual renewal was submitted and awaiting new letter)

Title: **EARLY-LIFE LONGITUDINAL CYTOKINE PROFILES IN CHILDREN WHO ARE HIV-EXPOSED UNINFECTED COMPARED TO HIV-UNEXPOSED IN A SOUTH AFRICAN BIRTH COHORT**

Authors: Tusekile S. Kangwa[a,b], Catherine J. Wedderburn[b,c,d] , Kirsten A. Donald[b,c], Francesca Little[e], Heather J. Zar[c,f], Dan J. Stein[a,b,g], Petrus J.W. Naudé[a,b]

Affiliation: [a]Department of Psychiatry and Mental Health, University of Cape Town, South Africa; [b]Neuroscience Institute, University of Cape Town, South Africa; [c]Department of Paediatrics and Child Health, Red Cross War Memorial Children's Hospital, University of Cape Town, Cape Town, South Africa; [d]Department of Clinical Research, London School of Hygiene & Tropical Medicine, London, UK; [e]Department of Statistical Sciences, University of Cape Town, Cape Town, South Africa; [f]SA MRC Unit On Child & Adolescent Health, University of Cape Town, Cape Town, South Africa; [g]SA MRC Unit On Risk and Resilience in Mental Disorders, University of Cape Town, Cape Town, South Africa

Objectives:
Exposure to cytokines in utero, in the presence of maternal HIV, may trigger immunological alterations in the developing immune system and may affect the infant's immune responses. However, there are few longitudinal data that address this issue. Here we aimed firstly, to cross-sectionally assess differences in peripheral blood immune markers between pregnant women living with and without HIV; secondly, to determine longitudinal differences in immune markers between children who are HIV-exposed uninfected (HEU) and HIV-unexposed (HU); and thirdly, to longitudinally evaluate the factors/components of child immune markers separately in HEU and HU children. Secondary analysis was performed to explore the impact of ART initiation (before or during pregnancy) on immune marker levels of mothers and their children.

Methods:
415 mother-child pairs from the Drakenstein Child Health Study (DCHS) a South African birth cohort, including 193 mothers living with HIV, 222 HIV-negative mothers and their children (193 HEU, 222 HU) at ages of 6 weeks, 2, 3.5 and 5 years were included. The DCHS enrolled pregnant women from 2012 to 2015 and continues to follow the mother-child pairs through childhood and adolescence. Serum inflammatory markers: GM-CSF, IFN-γ, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12p70, IL-13, TNF-α, NGAL, MMP-9, sCD14, and sCD16, were measured using the Milliplex® Luminex and enzyme-linked immunosorbent assay (ELISA) kits. Linear regression analyses were performed to evaluate immune markers in mothers and linear mixed models were employed for longitudinal analysis, both were adjusted for covariates. Components in immune markers over time were evaluated with an ANOVA simultaneous component analysis (ASCA) framework, extended for repeated measures; this combined general linear mixed models with principal component analysis.

Results:
After correcting for covariates, pregnant women living with HIV had lower levels of GM-CSF, IL-10, IL-12p70, IL-13, IL-2, IL-4, IL-6, IL-7, NGAL, and MMP-9 (all $p<0.05$) and higher levels of TNF-α and CD14 (both $p<0.05$) compared to those who were HIV negative in pregnancy. Mixed model analyses showed lower GM-CSF, IL-10, IL-12p70, IL-1β, IL-2 and IL-4 levels (all $p<0.05$) in children who were HEU from 6 weeks to 5 years and an increase in CD14 longitudinally. Principle component analysis revealed distinct patterns in immunoregulatory profiles in HEU children over time, with IFN-γ, IL-1β, IL-2, IL-5, IL-13, IL12p70, IL-4, MMP-9, CD14, IL-7 and TNF-α explaining 80.5% of the variability during the first two years of life, whilst IL-5, IL-10, IL-6, IL-4 and IL-13 and MMP-9 explained 20.1% of the variability from 2 to 5 years. Secondary analyses showed that the initiation of antiretroviral therapy (ART) before pregnancy was associated with higher GM-CSF, IL-12p70, IL-13, IL-2, IL-4, and IL-5 (all $p<0.05$) in mothers with HIV, and no associations with immune markers in their children in this cohort.

Conclusions:
The findings that aberrant immune responses are present not only in mothers living with HIV but persist longitudinally in their children may help explain poor health outcomes in HEU children. Distinct patterns of immune dysregulation in children are consistent with heterogeneity of outcomes in these children and warrants further research. (HREC REF: 053/2023)

Title: **MATERNAL AND CHILD IMMUNE PROFILES ARE ASSOCIATED WITH MEASURES OF EARLY-LIFE BRAIN INFLAMMATION IN CHILDREN WHO ARE HIV-EXPOSED AND UNINFECTED: A SOUTH AFRICAN BIRTH COHORT**

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Background & Objectives: Children born to mothers living with HIV who remain uninfected (CHEU) face higher risks of neurodevelopmental impairment compared to HIV-unexposed (CHU) peers. The underlying biological mechanisms, particularly the impact of maternal HIV on child brain development, are not fully understood. A dysregulated immune system during pregnancy and early-life may play an important role. This study investigated the associations between maternal HIV status, peripheral blood (neuro)immune markers during pregnancy / child trajectories from birth to 2 years, and child brain metabolite ratios at age 2-3 years in a cohort of South African CHEU and CHU. We hypothesized that pro- and neuro-inflammatory peripheral blood marker trajectories would be altered in CHEU, and that increased levels would associate with elevated myo-inositol ratios —a marker for neuroinflammation— in the parietal white matter at age 2-3 years, based on prior findings.

Methods: The Drakenstein Child Health Study enrolled pregnant women between 2012 and 2015 and is following mother-child pairs into childhood and adolescence. Peripheral blood immune biomarkers were measured with Luminex and ELISA assays in a subset of mothers during pregnancy, and their children at 6 weeks and 2 years. A neuroimaging sub-study invited 156 children for single voxel magnetic resonance spectroscopy at 2-3 years, obtaining high-quality, multi-regional parietal brain metabolite spectra from 83 participants (36 CHEU, 47 CHU). Linear Mixed-Effects Models (LMM) were performed to explore differences in peripheral blood biomarker trajectories between CHEU and CHU. Factor analysis was used to identify metabolic patterns across brain regions. Robust linear models examined cross-sectional associations between blood biomarkers and brain metabolites, adjusting for confounders and correcting for multiple comparisons. Multiple Imputation by Chained Equations addressed missing data in longitudinal analyses.

Results: Significant differences in blood biomarkers were found based on maternal HIV status, including lower MMP-9 in mothers living with HIV during pregnancy ($p=0.0001$) and lower lipocalin-2 in HEU infants at 6 weeks ($p=0.03$). LMMs revealed no significant variations in peripheral blood biomarker trajectories by maternal HIV. Adjusted linear models showed cross-sectional associations between maternal pro-inflammatory IL-5 and IL-8 levels during pregnancy and CHEU myo-inositol ratios at age 2-3 years, specifically in the parietal grey matter (IL-5, $\beta=0.79$, 95% CI 0.24–1.34, $p=0.005$) and right parietal white matter (IL-8, $\beta=0.64$, 95% CI 0.10–1.17, $p=0.020$). Maternal IL-5 was also linked to a pattern of elevated myo-inositol across parietal brain regions ($\beta=0.84$, 95% CI 0.23–1.44, $p=0.0075$). CHEU MMP-9 levels at 2 years were associated with myo-inositol ratios in the parietal grey matter at 2-3 years ($\beta=1.29$, 95% CI 0.12–2.45, $p=0.031$). Other associations were found between neuroinflammatory markers (including maternal MMP-9 during pregnancy and child lipocalin-2 at age 2 years) and CHEU glutamate ratios.

Conclusions: This study highlights the important link between maternal and child immune profiles and early-life brain development in CHEU. The association of maternal pro-inflammatory cytokines during pregnancy with increased myo-inositol ratios in the parietal regions of CHEU at age 2-3 years suggests that early brain development might be influenced by exposure to maternal immune signalling proteins during pregnancy in this vulnerable population. The correlation of child MMP-9 levels with myo-inositol ratios in CHEU may indicate ongoing neuroinflammatory processes in early child development. Longitudinal analyses did not show significant variation in biomarker trajectories based on maternal HIV status, suggesting that while cross-sectional associations are evident, the dynamic changes in immune markers over time may be more complex and influenced by other factors. This could also indicate potential limitations due to sample size, or the need for additional measurements past age 2 years to fully capture these trajectories. To our knowledge, this is the first study to combine peripheral blood (neuro)immune and neurometabolite data at this young age, reporting associations between maternal and early-life immune markers and neurobiological development in CHEU.

HREC REF: 199/2024

Title: **INDUCED SPUTUM FOR DIAGNOSIS OF PULMONARY TUBERCULOSIS (PTB) AND OUTCOMES IN YOUNG CHILDREN IN A SETTING WITH A HIGH BURDEN OF HIV AND MALNUTRITION**

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Objective: Diagnosis of PTB in young children can be challenging, due to the inability to spontaneously expectorate sputum and paucibacillary disease. Children living with HIV (CLHIV), with malnutrition, or infants, are at high risk for severe disease and mortality. Induced sputum (IS) is safe and feasible, and PCR with Xpert Ultra (Ultra) offers rapid diagnosis, but there are limited data on its accuracy in high-risk groups.

Methods: Children (<15 years) with suspected PTB, attending Dora Nginza Hospital, Gqeberha, South Africa, were prospectively enrolled between 9 January 2018 - 19 January 2024. Where possible, 2 IS were performed on sequential days or at least 4 hours apart for liquid culture and Ultra. Children were categorised as 'confirmed' (Ultra or culture positive), 'unconfirmed' (clinical diagnosis) or 'unlikely TB' according to NIH consensus definitions. Diagnostic accuracy for Ultra was calculated against a culture-based reference standard. Children were followed for up to 12 months.

Results: 636 children were included; 145 (22.8%) were 'confirmed' [137/145 [94.5%] on Ultra, 88/145 [60.7%] on culture], 384 (60.4%) 'unconfirmed', and 79 (12.4%) 'unlikely TB'. Median age was 27.3 (IQR 11.7–61.6) months, 164 (25.8%) were infants and 168/634 (26.5%) were CLHIV, of whom 113/168 (80.1%) were on ART. Stunting (height-for- age Z-score <-2) occurred in 41.8% (259/627), and weight-for-age Z-score (WAZ) <-2, in 38.1% (239/627). A higher proportion of CLHIV had a WAZ<-2 (54.9% vs. 31.3%, p<0.001) or stunting (58.2% vs. 35.8%, p<0.001), compared to HIV-uninfected children. Overall, IS Ultra had high sensitivity (90.9%; 95%CI 82.9-96.0) and specificity (89.6%; 95%CI 86.7-92.0). Yield, sensitivity and specificity were similar across high-risk groups (Table). Sensitivity was lower in ambulatory compared to hospitalised children (77.8% vs 88.5%, p=0.05). IS Ultra was positive (the majority, 78.9%, trace) for 57 children with negative cultures; all improved on TB treatment. Children under 5 years with severe acute malnutrition (weight-for-height Z-score; WHZ<-3) had a higher yield on IS compared to those with WHZ>-3 (27.3% vs 17.1%; p=0.065). 276 children had valid Ultra and culture results for a second IS, which increased detection by 17.3% (52 to 61 cases) for Ultra, and 12.4% (32 to 36 cases) for culture. Risk factors for mortality amongst children diagnosed with TB (n=27) included WAZ<-2 (aOR 4.9 [95%CI 1.7-13.5]), living with HIV (aOR 3.5 [95%CI 1.5-8.3]), and infants (aOR 3.1 [95%CI 1.4-6.6]).

Conclusions: CLHIV, those malnourished, and infants, are at increased risk for mortality from PTB, highlighting the need for improved rapid diagnostics. Ultra provided a higher yield than culture on IS, and a favourable diagnostic accuracy across high-risk groups.

Diagnostic Yield and Accuracy of Ultra (vs TB culture) on induced sputum (IS)					
Yield per child, on any IS sample		**Ultra** - 137/636 **(21.5%)**		**Culture** - 88/636 **(13.8%)**	
Ultra vs TB Culture per child, on any IS sample					
N = 636	Yield (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Ultra	137/636 (21.5)	90.9 (82.9-96.0)	89.6 (86.7-92.0)	58.4 (49.7-66.8)	98.4 (96.9-99.3)
By HIV status per child, on first IS sample					
CLHIV[1,2]	28/168 (16.7)	90.9 (70.8-98.9)	94.5 (89.5-97.6)	71.4 (51.3-86.8)	98.6 (94.9-99.8)
HIV exposed uninfected	24/155 (15.5)	93.3 (68.1-99.8)	92.9 (87.3-96.5)	58.3 (36.6-77.9)	99.2 (95.8-99.9)
HIV uninfected	72/311 (23.2)	87.8 (73.8-95.9)	86.7 (82.0-90.5)	50.0 (38.0-62.0)	97.9 (95.2-99.3)
By Nutritional Status per child, on first IS sample					
WAZ[3] <-2	55/239 (23.0)	90.9 (75.7-98.1)	87.9 (82.6-92.0)	54.6 (40.6-68.0)	98.4 (95.3-99.7)
WAZ[3] >-2	68/388 (17.5)	88.9 (76.0-96.3)	91.8 (88.4-94.5)	58.8 (46.2-70.6)	98.4 (96.4-99.5)
By Age per child, on first IS sample					
<1 year	32/164 (19.5)	81.3 (54.4-96.0)	87.2 (80.7-92.1)	40.6 (23.7-59.4)	97.7 (93.5-99.50
≥1 year and < 5 years	49/307 (16.0)	92.9 (76.5-99.1)	91.8 (87.9-94.7)	53.1 (38.3-67.5)	99.2 (97.2-99.9)
≥5 years	43/165 (26.1)	91.2 (76.3-98.1)	90.8 (84.6-95.2)	72.1 (56.3-84.7)	97.5 (93.0-99.5)
By Ambulatory vs Hospitalised per child, on first IS sample					
Ambulatory	48/251 (19.1)	77.8 (60.9-89.9)	90.7 (86.0-94.2)	58.3 (43.2-72.4)	96.1 (92.4-98.3)
Hospitalised	76/385 (19.7)	88.5 (76.6-95.7)	91.0 (87.4-93.8)	60.5 (48.7-71.6)	98.1 (95.8-99.3)
Multiple risk factors, per child, on first IS sample					
CLHIV OR WFA <-2 OR <1yr	81/385 (21.0)	88.2 (76.1-95.6)	89.2 (85.4-92.3)	55.6 (44.1-66.6)	98.0 (95.8-99.3)
HIV uninfected, and WFA >-2, and >1yr	43/250 (17.2)	92.6 (75.7-99.1)	92.4 (88.1-95.5)	59.5 (43.3-74.4)	99.0 (96.6-99.9)
CLHIV[1,2] and WFA<-2	16/97 (16.5)	100.0 (73.5-100.0)	95.3 (88.4-98.7)	75.0 (47.6-92.7)	100.0 (95.6-100.0)
WFA <-2 and <1 yr	18/74 (24.3)	75.0 (34.9-96.8)	81.8 (70.4-90.2)	33.3 (13.3-59.0)	96.4 (87.7-99.6)

Data are reported as frequency and percentages (95% Confidence Intervals). [1]CLHIV = Children Living with HIV, [2]HIV status unknown for 2 children
[3]WAZ = weight-for-age Z-score

HREC REF: 045/2008

Title: **ACCEPTANCE OF COVID-19 AND INFLUENZA VACCINES DURING PREGNANCY: A PROSPECTIVE CROSS-SECTIONAL STUDY AMONG PREGNANT WOMEN ATTENDING ANTENATAL CARE IN CAPE TOWN**

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Background:
Vaccination in pregnancy protects the expectant mother, their fetuses, and their infants from infection during the first few months of life. This study aims to assess and identify factors associated with the willingness of pregnant women to receive Influenza and COVID-19 vaccines during pregnancy.

Methods:
A multi-methods cross-sectional study was conducted at Mowbray Maternity, New Somerset, and Groote Schuur hospitals in Cape Town among pregnant women attending antenatal clinics, between the 9th of October 2023 and the 29th of January 2024. Participants were asked to complete a self-administered questionnaire about their attitudes towards vaccination against Influenza and COVID-19 vaccines in pregnancy. Descriptive statistics and logistic regression were performed to assess factors associated with vaccine acceptance. Seven participants who did not participate in the quantitative component were interviewed.

Results:
500 pregnant women completed the questionnaire of whom 47,6% were vaccinated against COVID-19 before pregnancy. There were 258 (51,6%) participants who reported trusting COVID-19 vaccines, compared to 353 (70,6%) who reported trusting Influenza vaccines (p<0.001). Similarly, 245 (49%) of the pregnant women were willing to receive the Influenza vaccine during pregnancy as opposed to 18 (4%) willing to accept the COVID-19 vaccine while pregnant (p<0.001). Factors associated with the acceptance of the Influenza vaccine in pregnancy included the belief that the vaccine protects pregnant women against Influenza (OR 2.2 95%CI [1.36-3.57]) and that it is safe to receive the vaccine during pregnancy (OR 7.77 95%CI [4.85-12.69]). Being concerned about getting COVID-19 during pregnancy (OR 4.65, 95%CI [1.16-17.9]) and the belief that the COVID-19 vaccine is safe (OR 8.54 95%CI [3.67-19.96]), and important (OR 10.13 95%CI [2.27- 45.3]) during pregnancy were significantly associated with vaccine acceptance. According to the qualitative findings the common reasons for vaccine acceptance were the benefit to the baby, healthcare provider recommendation

Discussion:
Acceptance of COVID-19 and Influenza vaccines was driven by women's belief in their safety and protective effect during pregnancy. Vaccines will only be effective if pregnant women choose to get vaccinated and present their children for vaccination. Therefore, addressing determinants of vaccine acceptance and uptake, such as maternal knowledge, attitudes, and beliefs about recommended vaccines in pregnancy and childhood, should be prioritized.

HREC REF: 011/2023

Title: **IRON DEFICIENCY ANAEMIA IN MOTHERS AND INFANTS FROM A SOUTH AFRICAN BIRTH COHORT: PREVALENCE AND PROFILE IN THE CONTEXT OF INFLAMMATION**

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Objectives:
The scarcity of clinical data on anaemia in low- and middle-income countries, coupled with the poor characterisation of overlapping risk factors in high-risk settings and contrasting approaches to the assessment of iron status with inflammation, represent critical gaps to address. This study aimed to characterise the prevalence and profile of iron deficiency anaemia, including adjustment for inflammation, in pregnant and postpartum women, as well as infants from South Africa.

Methods:
Mother-child dyads (*n*=394) were recruited (2021-2022) for the Khula birth cohort study in Cape Town, South Africa**.** Haemoglobin, serum ferritin, and inflammatory biomarkers (highly sensitive C-Reactive Protein; Alpha-1 Acid Glycoprotein) were obtained from mothers antenatally and postnatally, and from infants 3-18 months after birth. World Health Organisation (WHO) guidelines were used to classify anaemia and iron deficiency. The extent to which inflammation impacted iron deficiency was assessed using two methods: Method A: use of higher serum ferritin thresholds for classifying iron status in participants with inflammation (WHO), Method B: Biomarkers Reflecting Inflammation and Nutritional Determinants of Anaemia (BRINDA) regression which corrects serum ferritin levels based on inflammatory biomarker concentrations.

Results:
Prevalence of anaemia was 34.74% (107/308) in pregnancy and 22.50% (54/240) in mothers at 3-6 months postpartum. Of their infants, 46.82% (125/267) and 48.10% (136/283) were anaemic at least once by 6-12 months and 12-18 months, respectively. When accounting for inflammation using Method A, the prevalence of maternal iron deficiency (regardless of anaemia) increased from 18.35% (20/109) to 55.04% (60/109) in pregnancy, and from 11.97% (28/234) to 46.58% (109/234) postnatally. Similarly, using Method B, the estimated prevalence of maternal iron deficiency increased to 38.53% (42/109) in pregnancy, and 25.21% (59/234) postnatally. In infants at 12-18 months, the prevalence of iron deficiency increased from 19.79% (19/96) to 31.25% (30/96) using Methods A and B. Approximately half of anaemia cases in mothers antenatally (50%; 20/40) and postnatally (45.10%; 23/51), and infants at 12-18 months (55.56%; 10/18), were attributable to iron deficiency.

Conclusion:
This is one of the first studies to report the prevalence of iron deficiency anaemia in South African mothers and infants, and the extent to which it may be underestimated if inflammation is not accounted for. Overall, the findings contribute to a global effort to understand the complex aetiology of iron deficiency anaemia, informing guidelines for optimised detection, prevention, and intervention strategies in high-risk communities.

Keywords: anaemia, iron deficiency, inflammation, maternal health, child health

HREC Reference Number: 782/2022 (New Research)

Title: **DEVELOPING A HOME-BASED PROGRAM TO MITIGATE MUSCULOSKELETAL COMPLICATIONS IN CHILDREN WITH SEVERE CEREBRAL PALSY IN RESOURCE-LIMITED SETTINGS: A MODIFIED DELPHI STUDY**

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Dates when research conducted: 01/01/22 to 31/10/23

Background:
Children living in resource-limited settings with severe cerebral palsy (CP) are at considerable risk of developing secondary musculoskeletal complications, which can cause substantial discomfort and significantly restrict age-appropriate participation opportunities. Current clinical guidelines do not specifically address this issue for this population.

Objective:
To develop the components of a home-based intervention program (HBIP) aimed at mitigating musculoskeletal complications in children with severe cerebral palsy (Gross Motor Function Classification System level III to V), suitable for use in resource-limited settings.

Methods:
A modified Delphi methodology was used to produce a consensus for a HBIP, using the Appraisal of Guidelines Research and Evaluation (AGREE 11) tool. First, a systematic scoping review of the literature was performed to identify potential program components, using the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) extension for scoping reviews. Focus group discussions were conducted with 15 caregivers of children with severe CP from a peri- urban setting in KwaZulu Natal, to explore their contextual needs and goals for a caregiver-delivered intervention. The results of the scoping review and focus group discussions were collated as statements and presented to an expert Delphi panel to rate their agreement on a Likert scale, with three Delphi rounds for modification and re-iteration until consensus was reached. The final proposed HBIP was returned to the caregivers for comment and approval before being finalised.

Results:
Fifteen multi-disciplinary healthcare experts participated in producing the final set of 66 consensus statements, grouped into five sections: the importance of the intervention; program elements; equipment needs; caregiver training; and community support mechanisms. Panelists agreed that caregivers should be trained in "24-hour postural management" and "splinting" interventions to prevent MSK deformities; given strategies to assist with activities of daily living (e.g. feeding); and provided with tools for communication, cognitive development, and social participation. Community based therapists should provide caregiver training and oversight, but community health workers should play a pivotal role in supporting program implementation.

Conclusions:
This consensus guideline document provides a detailed and actionable home-based intervention suitable for resource-limited settings, to mitigate musculoskeletal complications in children with severe CP. Implementation studies are recommended to determine feasibility, acceptability, and efficacy in real world settings.

HREC REF: 024/2022

Title: **A SCOPING REVIEW OF CEREBRAL PALSY IN AFRICAN PAEDIATRIC POPULATIONS**

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Objective:
To review the epidemiology and outcomes of African children with cerebral palsy (CP) over a 21-year period.

Methods:
PubMed, SCOPUS and Web of Science databases were searched for original research on African children with CP aged <18 years published 2000-2021.

Results:
1811 articles underwent review against explicit criteria, and 93 articles were selected for inclusion. The reported prevalence of CP ranged from 0.8-10 per 1000 children. Almost half had perinatal risk factors, but up to 26% had no identifiable risk factor. At least one-third of children with CP had ≥1 co-morbidity, most commonly epilepsy, intellectual disability and malnutrition. African children with CP demonstrate excess premature mortality ~25 times that of the general population, predominantly from infections. Hospital-based and younger populations reported larger proportions of children with severe impairment. African children with CP had inadequate access to care and education, yet showed functional improvements compared to controls for all evaluated
interventions.

Conclusion:
The prevalence of CP in Africa remains uncertain. African children with CP have different risk profiles, greater premature mortality and more severe functional impairment and co-morbidities compared to the global North. Several barriers prevent access to optimal care. Larger African
studies on validated and effective interventions are needed.

Ethics Reference No: S20/10/272 (Stellenbosch University)

Title: **REVIEW OF LIVER BIOPSIES AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL OVER A SIX YEAR PERIOD**

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Background:
Liver biopsy is the cornerstone of diagnosis in clinical hepatology. It also plays a vital role in prognostication of liver disease and guiding management.

Objectives:
To determine the role of liver biopsy in the work up of patients with liver diseases at Red Cross War Memorial Children's Hospital (RCWMCH) over a six year period.

Method:
This is a retrospective cross-sectional descriptive study of children who had liver biopsies performed at RCWMCH between the 01st/01/2018 and 31st/06/2023. Characteristics of patients with a native liver were compared to those with a graft liver.

Results:
A total of 75 patients were screened for inclusion into the study, 6 patients were excluded due to missing data and files. The final sample size was 69 patients. Sixty five percent (n=45) of the liver biopsies were performed percutaneously under ultrasound guidance and the rest were either blind or laparoscopic. Hyperbilirubinemia and suspected graft rejection were the two main indications for liver biopsy. Histopathological results directed management in 96% (n=66) of the cohort. The three main diagnoses were non-specific hepatitis, biliary atresia and autoimmune hepatitis. Participants in the native liver group were of a younger age (p=0.03) and lower weight (p=0.04) in comparison to those in the graft liver group. There were no minor complications and the rate of major complications was 2.9% (n=2).

Conclusion:
Liver biopsy has an important role in the management of liver disease with a high diagnostic yield. Complications rates are low with appropriate methods and patient selection.

HREC REF: 385/2023

Title: **CHILDREN'S PERCEPTIONS OF SAFETY, INCLUSION AND PARTICIPATION IN EARLY LEARNING: RESEARCH THROUGH CREATIVE AND PLAY- BASED METHODS**

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Objectives:
We explored the concepts of safety, inclusion and the participation of children (0-5 years) and their families in early learning spaces (centre based ECD centres and non-centre based early learning programmes) in an under-resourced local community in Cape Town. We did this to understand how Early Childhood Development (ECD) policy is given practical expression on the ground, to gather evidence to feed local level experiences into policy development and implementation processes for ECD. As part of this larger community study conducted between 2020 – 2024, we included children as participants to gather their understanding of these concepts, to give effect to their agency. This was done in recognition of a need for understanding cultural and contextual interpretations with a particular focus on young children's ways of knowing, feeling and understanding. As such, we explored the use of creative methods in relation to listening to children in their context.

Objective 1: To observe the process of, and, to test the usefulness of persona dolls as a method to conduct research with children
Objective 2: To explore children's understanding and experiences of safety, inclusion and participation

Methods: The research was carried out in Vrygrond, a vulnerable local community in Cape Town. Vrygrond is one of South Africa's first informal settlements and bears the legacy of many decades of inequality but is vibrant with an active civil society that supports development in the community.

Study design: Within the qualitative community case study, to engage with children, we used a combination of creative play-based methods, including persona dolls and images as springboards to conversation. We designed a story board with local community members to illustrate our key concepts in ways that were appropriate for young children, and we employed trained persona doll facilitators to engage with the children. They visited the children and shared the story board, which provided a stimulus for dialogue and to neutralize the researcher power status dilemma. In addition, images were used to elicit discussion with children, and we used drawing/telling in a final session where children drew a picture of anything they remembered from the sessions.

Participants and data collection:
Data from children was collected between July 2022 and December 2022. Participants included children aged four to six years. A total of 38 children participated in a total 30 group sessions. Each group of children participated in a series of five sessions. Parental assent was obtained for each child prior to data collection. Groups included children from diverse cultural and language groups in the area. Sessions were recorded whenever possible and an observer documented proceedings including children's body language, levels of engagement and key observable actions. For analysis, we developed a deductive coding framework while staying open to induction, thematic analysis was employed to derive key themes.

Findings:
Findings linked to objective 1: We found that the doll was very useful in engaging children and keeping them focused. The facilitators used the doll to engage children, using the story boards to invite them to give advice to the doll, encouraging empathy and respect for the doll and one another. The doll commanded more respect amongst children than the facilitator, they understood and imagine the doll as their friend or another child.
Findings linked to objective 2: Children found it difficult to engage with the concept of inclusion and participation but could identify instances and feelings of exclusion and shared ideas about how to include children who are excluded. Children interpreted participation as a sense of choice. While they acknowledge that they had a little sense of choice both at home and at school there were some examples of their ability to express their preferences including agency during the sessions. Key issues children focused on in relation to safety included God, their parents and their teachers. They were also aware of dangers in the community such as fires and not being able to walk alone or play in the park.

Conclusion:
This study contributes to our understanding that despite children long been situated as the subjects of research, they can be active participants in the research process. We found that using different play- based methods with children enabled them to express their lived experiences, feelings and perspectives. (HREC REF: 737/2021)

Title: **A LANDSCAPE ANALYSIS OF PAEDIATRIC AND CONGENITAL HEART DISEASE SERVICES IN AFRICA**

Authors: Thomas Aldersley[1], Sulafa Ali [2], Adila Dawood[1], Frank Edwin[3], Kathy Jenkins[4], Alexia Joachim [1], John Lawrenson [1,5], Darshan Reddy [6], Amy Verstappen[7], Bistra Zheleva[8], Liesl Zühlke[1,9], On behalf of all respondents[8]

Affiliation: [1]Department of Paediatrics University of Cape Town, South Africa; [2]University of Khartoum, Division of Paediatric Cardiology, SD; [3]University of Ghana, Division of Cardiothoracic Surgery, GH; [4]Harvard Medical School Boston, Department of Pediatrics, US; [5]Stellenbosch University, Division of Paediatric Cardiology ZA; [6]University of Kwa-Zulu Natal, Division of Cardiothoracic Surgery, ZA; [7]Global Arch, US; [8]Children's Heart Link, US; [9]South African Medical Research Council; [8]Respondent countries: Algeria, Angola, Benin, Botswana, Burkina Faso, Burundi, Cameroon, Chad, Comoros, Democratic Republic of the Congo, Egypt, Eswatini, Ethiopia, Gabon, Gambia, Ghana, Kenya, Libya, Malawi, Mali, Mauritania, Mauritius, Morocco, Mozambique, Namibia, Niger, Nigeria, Rwanda, São Tomé and Príncipe, Senegal, Seychelles, Sierra Leone, Somalia, South Africa, South Sudan, Sudan, Tanzania, Togo, Uganda, Zambia, Zimbabwe

Background:
There is geographic disparity in the provision of Paediatric and Congenital Heart Disease (PCHD) services. Previous studies show that North America and Western Europe account for 74% of the world's cardiothoracic surgical capacity. In contrast, Africa accounts for only 1% of the total global capacity. However, PCHD training and service provision in Africa has increased.

Objectives:
We conducted a cross-sectional electronic survey to evaluate Paediatric and Congenital Heart Disease (PCHD) services in Africa.

Methods:
This cross-sectional survey investigated respondent, institution, and national-level resources for paediatric cardiology, catheterisation, and cardiothoracic surgery. Survey distribution commenced on June 1st, 2023. All eligible responses received before December 1st, 2023, were incorporated into the analysis. Respondents included paediatric and adult cardiologists, cardiothoracic surgeons, paediatricians, and medical officers involved in PCHD care. Institutions were ranked by a composite score for low- and middle-income PCHD services.

Results:
There were 124 respondents from 96 institutions in 45 countries. Eighteen (40%) countries provided a full PCHD service including interventional cardiology and cardiac surgery; nine (20%) provided cardiac surgery services but no interventional cardiology service and one provided an interventional cardiology service but no cardiac surgery. Ten countries (22%) had no PCHD service. There were 0.04(IQR:0.00–0.13) paediatric cardiothoracic surgeons and 0.18(IQR:0.03–0.35) paediatric cardiologists per million population. No institution met all criteria for a level 5 PCHD national referral centre, and 8/87(9.2%) met criteria for a level 4 regional referral centre. Thirteen (29%) countries report both paediatric cardiology and cardiothoracic surgery fellowship training programmes.

Conclusions:
Only 18 (40%) countries provided full PCHD services. The number of paediatric cardiologists and cardiothoracic surgeons is below international recommendations. Only Libya and Mauritius have the recommended 2 paediatric cardiologists per million population, and no country meets the recommended 1.25 cardiothoracic surgeons per million. There is a significant shortage of fellowship training programs which must be addressed if PCHD capacity is to be increased.

HREC REF: 459/2023

Title: **BRAIN STRUCTURE OF CHEU EXPOSED TO DOLUTEGRAVIR VERSUS EFAVIRENZ: A SOUTH AFRICAN COHORT STUDY**

Authors: Layla E Bradford*, Jessica E Ringshaw, Catherine J Wedderburn, Niall Bourke, Steve Williams ,Helene Theunissen, Thokozile Malaba, Lauren Dave, Nengjie He, Helen Reynolds, Angela Colbers, Jim Read, Duolao Wang, Saye Khoo, Landon Myer, Kirsten A Donald

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Objectives:
Access to newer and more effective antiretroviral drugs for use in pregnancy have contributed to reduced vertical transmission of HIV, resulting in a growing population of children who are HIV-exposed and uninfected (CHEU). Dolutegravir (DTG) is now established as a first-line treatment for HIV in pregnancy in many countries, including South Africa, and there is a critical need to evaluate its effect on neurodevelopmental outcomes in children. However, there is no research on the structural brain outcomes of children with in-utero exposure to DTG. As a first investigation of its kind, we aimed to use magnetic resonance imaging to compare the brain structure in CHEU and their HIV-unexposed counterparts (CHU) with a particular focus on the differential impact of antiretroviral therapy (ART), comparing DTG- and efavirenz-based (EFV) regimens, on brain development in early childhood.

Methods:
We collected high-resolution magnetic resonance (T1-weighted) scans of children aged 39 to 54 months from DolPHIN-2 Plus, an infant follow-up study of the DolPHIN-2 trial (NCT03249181). DolPHIN-2 was a randomized open-label trial evaluating the efficacy and safety of DTG in comparison to EFV and enrolled mothers living with untreated HIV in the 3rd trimester of pregnancy. Children were excluded if they had a known positive HIV test or MRI contraindication. In this analysis, global and regional subcortical brain volumes, cortical thickness, and surface area were extracted. Multiple linear regression models, adjusting for age at scan, sex, and total intracranial volume, were used to investigate the effect of ART and HIV exposure on brain morphology.

Results:
Between 2021 and 2023, 25 CHEU (13 DTG, 12 EFV; mean age 45.5 months; 52% male) born in the DolPHIN-2 trial were enrolled and scanned at 3-4 years along with 33 CHU (mean age 47 months; 51.5% male). Demographic characteristics were similar for both CHEU vs CHU and DTG vs EFV groups. Results were similar between CHEU and CHU, with no differences found in total grey matter (p=0.775), white matter volume (p=0.703), subcortical volumes including the thalamus (p=742), caudate (p=0.493), putamen (p=0.373), pallidum (p=0.523), hippocampus (p=0.244) and amygdala (0.641), cortical thickness or surface area. In this small sample, there were no differences between DTG-exposed CHEU when compared to EFV-exposed CHEU in total grey matter (p=0.861), white matter volume (p=0.158), subcortical volumes including the thalamus (p=479), caudate (p=0.484), putamen (p=0.272), pallidum (p=0.292), hippocampus (p=0.885) and amygdala (0.666), cortical thickness or surface area.

Conclusion:
These are the first data comparing brain volumes in CHEU born to mothers receiving DTG- versus EFV-based ART in pregnancy. In this sample, the findings suggest that DTG is comparable to EFV in terms of its impact on brain structure in early childhood, offering novel data on this new first-line treatment in comparison to the previously widely used efavirenz. Further longitudinal studies with larger sample sizes are warranted to clarify the effects of prenatal exposure of HIV and specific ART regimens on brain development.

HREC REF: 023/2024

Title: **FEEDING AND SWALLOWING IN NEONATES WITH HIE: A DESCRIPTIVE STUDY**

Authors: Samantha Branfield, Vivienne Norman (Supervisor), Dr Natasha Rhoda (Co-supervisor); Janine Joemat (Co-supervisor)

Affiliation: University of Cape Town

Objective:
To describe the feeding and swallowing profile of neonates with Hypoxic Ischemic Encephalopathy (HIE) in a neonatal unit in Cape Town, South Africa, including characteristics of oral feeding readiness, oromotor skill, oropharyngeal swallowing and clinical signs and symptoms of oropharyngeal dysphagia (OPD), time taken to reach full oral feeds, and feeding method at discharge from the neonatal unit.

Methods:
A descriptive, exploratory, longitudinal design consisting of both prospective and retrospective data collection methods was used to examine the feeding and swallowing characteristics in a sample of 52 participants with HIE of varying severities. Clinical feeding and swallowing assessments were conducted for 13 participants using the Neonatal Feeding Assessment Scale (NFAS) between February 2022 and September 2022, and medical folder reviews were conducted for 39 participants between July 2022 and September 2022. The medical and feeding information was documented using data collection forms, including the feeding management received from the on-site speech-language therapist. Data from both data collection methods were amalgamated onto Excel spreadsheets, and information from medically similar participants was identified and grouped together for descriptive and statistical analysis. Statistical analysis comprised the nonparametric Kruskal-Wallis test and the Mann-Whitney U test.

Result:
A main effect of oral feeding readiness was indicated with a median of 4 days ($p = 0.036$), and an interquartile range of 4 – 5 days (standard deviation = 3.7 days). The median number of days to full oral feeds for the sample was 5 days ($p = 0.016$) with an interquartile range of 4 – 6.8 days (standard deviation = 4.3 days). Participants with a severely abnormal initial aEEG and who did not receive cooling treatment demonstrated the longest average time to oral feeding readiness and, subsequently, to full oral feeds. Participants of all severities presented with feeding and swallowing difficulties primarily in the oral phase of swallowing. Few pharyngeal signs and symptoms of OPD were identified. Most participants (96.2%; n = 50) were discharged on full oral feeds, while the remaining 3.8% (n = 2) were discharged on nasogastric tube feeds (NGT) while awaiting gastrostomy placement.

Conclusion:
Regardless of severity, neonates with HIE face an increased risk of feeding and swallowing difficulties. The findings highlight that neonates with HIE should be screened by a speech-language therapist for feeding and swallowing difficulties before discharge from hospital. This study contributes to the small body of research on feeding and swallowing difficulties in neonates with HIE and may guide future research.

Keywords: hypoxic-ischemic encephalopathy; neonate; feeding; swallowing; dysphagia; oropharyngeal dysphagia

HREC REF: 780/2021

Title: **THE ASSOCIATION BETWEEN MATERNAL DEPRESSION AND FRONTAL ALPHA ASYMMETRY IN INFANTS: PRELIMINARY RESULTS FROM A SOUTH AFRICAN BIRTH COHORT**

Authors: Lauren Davel[1], Sarah McCormick[2], Michal R. Zieff[1], Cara Bosco[2], Emma T. Margolis[2], Simone R. Williams[1], Reese Samuels[1], Sadeeka Williams, [1] Chloë A. Jacobs, Nwabisa Mlandu, Tracy Pan, Zamazimba Madi, Tembeka Mhlakwaphalwa, Thandeka Mazubane[1], Zayaan Goolam Nabi[1], Marlie Miles[1], Laurel J. Gabard-Durnam[2]*, Kirsten A. Donald[1]*

Affiliation: [1]Department of Paediatrics and Child Health, University of Cape Town; [2]Northeastern University Boston, United States of Amera

Objectives:
Frontal alpha electroencephalogram (EEG) asymmetry is associated with poor child outcomes. While previous studies have demonstrated a relationship between maternal depression and infant frontal alpha asymmetry, the evidence to date is limited and inconsistent. This study explored the relationship between maternal postpartum depression and frontal alpha asymmetry in a sample of young South African mother-infant dyads.

Methods:
329 Pregnant mothers and 65 postpartum mothers were recruited on the Khula LEAP longitudinal study between December 2021 and November 2022. Resting state EEG data were obtained from 242 infants (aged 58-195 days; *M* = 114.9, *SD* = 27; 51% male) enrolled in the Khula Study in Cape Town, South Africa. Mothers completed the Edinburgh Postnatal Depression Scale. A multivariate linear regression was conducted to determine the relationship between maternal depression scores and (i) average alpha power (9-12 Hz) in the left verses right dorsal-lateral prefrontal cortex, and (ii) frontal alpha asymmetry (average cluster score).

Results:
Forty-three mothers (17%) were at risk for depression. Higher maternal postpartum depression scores were associated with lower average alpha power in both the left (t = -2.22, p = 0.027) and right (t = -2.43, p = 0.015) dorsal-lateral prefrontal cortex after correcting for child sex and age. There was no significant relationship between maternal postpartum depression and frontal asymmetry.

Conclusion:
Maternal postpartum depression is associated with lower activity in the left and right dorsal-lateral prefrontal cortex. However, findings from this sample indicate no association between maternal postpartum depression and frontal asymmetry. Future investigations could use specific frontal electrodes (i.e., F3 and F4) instead of average clusters to predict a clearer association between these two variables.

HREC REF: 666/2021

Research Presented at: 5th International Developmental Paediatrics Association Congress on the 1st of December 2023

Title: **OUTCOMES OF PREGNANT WOMEN WITH CONGENITAL HEART DISEASE ATTENDING A MULTIDISCIPLINARY CARDIO-OBSTETRIC CLINIC IN CAPE TOWN SOUTH AFRICA**

Authors: Alexia Joachim[1], Thomas Aldersley[1], Hope Edwards[1], Karen Sliwa[2,3], Ayesha Osman[4], Tasneem Ahmed[4], Dominique Van Dyk [5] Blanche Cupido [3]Paul Human[6], Liesl Zühlke[1,2,7]

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Objective:
Congenital heart disease (CHD) patients are at risk for cardiovascular complications during pregnancy. Despite being the leading cause of maternal death in high-income settings, evidence from low and middle-income countries is lacking. We aimed to characterize outcomes of pregnant women with CHD referred to a multi-disciplinary combined cardio-obstetric clinic (CCOC), between 2017-2023.

Method:
Pregnant women with CHD were invited and consented to participate in the PROTEA (partnerships for children with heart disease) registry, enrolment started in 2017 and is currently ongoing. Demographics, obstetric and surgical history, WHO classification, and pre-partum, peripartum, and post-partum complications and events were recorded.

Results:
58 participants were enrolled over 7 years; median age was 27 years (IQR:24-32). Median booking BMI was 27 (IQR:23-35), with 29% overweight (BMI:25.0–29.9), and 34% obese (BMI ≥ 30). Predominant diagnoses included Ventricular Septal Defect 33% (20/61 total diagnoses), Tetralogy of Fallot 20%(12/61), Atrial Septal Defect 15%(9/61), Pulmonary Stenosis 5%(3/61), Aortic Coarctation 5%(3/61), and Atrial Ventricular Septal Defect 3%(2/61). 40 participants (69%) had a history of cardiac surgery. Most (98%, 57/58) participants had pre-existing cardiac diagnoses, however only 53% (31/58) of participants received pre-pregnancy counselling. In multigravida participants 58% (14/24) had a history of obstetric complications, with 75% (18/24) of pregnancies complicated by spontaneous abortion (9), therapeutic abortion (6) or intrauterine death (3).Comorbidities included angina (9), hypertension (7), asthma (4) and HIV (3). At enrolment 23% (13/57) of participants presented in NYHA heart failure class 2, 9% in class 3, and 2% in class 4. During their pregnancies 19% (11/58) experienced obstetric complications for which 21% (12/58) required admission. Additionally, 12% (7/58) were admitted for cardiac complications. Median gestational age at delivery was 38 weeks (IQR:35-40), 44% by elective caesarean section, 7% by emergency caesarean section. There were no maternal events during delivery; 2 experienced infective complications post-delivery. There were 0 maternal mortalities, 2 foetal mortalities and 0 neonatal mortalities.

Conclusion:
Despite suboptimal preconceptual counselling in our population of pregnant women, we present excellent outcomes for pregnant women with a variety of CHD diagnoses treated in a multidisciplinary cardio-obstetric clinic. Future interventions should optimize preconceptual counselling, awareness of healthy weight and consolidation of the multidisciplinary heart team approach.

HREC REF: R017-2014

Title: **SEQUENTIAL AND PARALLEL TESTING FOR THE MICROBIOLOGICAL DIAGNOSIS OF TB DISEASE IN CHILDREN IN A PROSPECTIVE DIAGNOSTIC ACCURACY COHORT IN LOW- AND MIDDLE- INCOME COUNTRIES**

Authors: Zoe Franckling-Smith MD[1*], Laura Olbrich DPhil[2, 3, 4, 5*], Leyla Larsson MSc[2], Issa Sabi PhD[6], Nyanda Elias Ntinginya PhD[6], Celso Khosa PhD[7], Denise Banze MD[7], Marriott Nliwasa PhD[8], Elizabeth Lucy Corbett Prof[8,9], Robina Semphere MD[8], Valsan Philip Verghese Prof[10], Joy Sarojini Michael Prof[11], Marilyn Mary Ninan PhD[11], Elmar Saathoff PhD[2,3], Timothy Daniel McHugh Prof[12], Alia Razid MSc[2,3], Stephen Michael Graham Prof[13], Rinn Song MD[4], Pamela Nabeta MD[14], Andre Trollip PhD[14], Mark Patrick Nicol PhD[15], Michael Hoelscher Prof[2,3,5,16],Christof Geldmacher PhD[2,3,5], Norbert Heinrich PhD[2,3,5°], Heather Joy Zar Prof[1°] *On behalf of the RaPaed-AIDA-TB consortium*

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Objective: Despite causing high mortality, paediatric tuberculosis (TB) is often undiagnosed. This study aimed to investigate optimal sampling and testing strategies to microbiologically confirm TB in children.

Methods: RaPaed-TB, a prospective diagnostic accuracy study, enrolled children in five healthcare centres (tertiary hospitals in Cape Town, South Africa, Blantyre, Malawi and Vellore, India; and urban health facilities in Mbeya, Tanzania, and Maputo, Mozambique). Children were eligible if <15years with signs/symptoms of pulmonary or extrapulmonary TB and excluded if weighed <2kg or received anti-TB medication. Respiratory and extrapulmonary specimens were analysed by Xpert®MTB/RIF Ultra(Ultra) and culture. The primary outcome was confirmed, unconfirmed, or unlikely TB, following NIH-consensus definitions.

Results: Of 5,313 children screened between January 2019 and June 2021, 975 were enrolled with 965 (99·0%) having a valid microbiological result in one of 2,299 samples analysed. Of these, (median age 5·0 years [IQR:1·8-9·0]; 16·1%[155/965] with HIV [CHIV];11·4%[110/965] had severe acute malnutrition [SAM]), 24·8%(239/965) had confirmed, 29·2%(282/965) unconfirmed, and 46·0% (444/965) unlikely TB. Most children were confirmed using Ultra (82·0%[196/239]: 46·0%[110/239] positive on Ultra and culture, 36·0% [86/239] on Ultra alone; 18·0%[43/239] on culture alone). "Trace" was the commonest semi-quantitative result (39·3%[77/196]). Children with HIV or SAM were primarily microbiologically confirmed by culture.
Parallel sampling and concurrent testing yielded high confirmation rates (1 specimen type: 20·3% [97/478] versus ≥2 specimen types: 28·9% [140/484] especially in children <5 years (n=129): 19/129 were Ultra-positive on 1st nasopharyngeal aspirate (14·7%), an additional 22/129(+17·1%) were Ultra-positive on 1st sputum, and a further 2/129(+1·2%) on culture. An additional 7/129(+5·5%) were culture-positive on 2nd sputum.

Conclusion: High rates of microbiological confirmation can be achieved in children using standardised parallel sampling and concurrent testing. These findings have informed updated WHO-recommendations on optimal diagnostic approach to paediatric TB.

HREC REF: 429/2018

Title: **Opportunities and Challenges for Management of Longitudinal Paediatric Data in Low- And Middle-Income Settings**

Authors: Zayaan Goolam Nabi[1], Michal R. Zieff[1], Thandeka Mazubane[1], Donna Herr[1], Kirsten A. Donald[1]

Affiliation: [1]Department of Paediatrics and Child Health, University of Cape Town

Objective:
Longitudinal paediatric research requires sustainable and ethical data management. Pregnant mothers and children constitute a vulnerable research population. This vulnerability is further compounded for participants living in poorly resourced communities and exposed to multiple risk factors. This poster discusses the opportunities and challenges of managing longitudinal data within the Khula Study, a longitudinal birth cohort study aimed at characterizing the development of emerging executive functions over the first 1000 days of life in a sample of 600 mother-infant dyads in Cape Town, South Africa and Blantyre, Malawi. This poster will present strategies from the Khula Study to collect, digitize, evaluate, integrate, and manage data.

Methods:
The Khula Study collected multimodal data, including neuroimaging, electroencephalography, biospecimens, and measures of sleep using wearable devices at multiple timepoints from December 2021 to May 2024.

Results:
Opportunities include the collection of data from cohorts that differ in terms of culture, living conditions and exposures. Major challenges included digitization, cross-site harmonization of variables, and integrating multiple data modalities processed in different places. Strategies implemented include creating a dynamic "master" centralized database with integrated clean data, using encrypted cloud-based storage platforms to share raw files with collaborators, and developing automated pipelines to quickly process large quantities of neuroimaging data.

Conclusions:
Multidimensional, longitudinal paediatric data calls for data management practices that are ethical, streamlined, and collaborative to ensure the success of the research. The Khula Study data management strategy may provide a framework for future paediatric research in low- and middle-income regions

HREC REF: 666/2021

Title: **EXPERT VOICES ON NON-SPECIALIST PAEDIATRIC EEG TRAINING**

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

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There are a limited number of child neurology specialists in sub-Saharan African (SSA) compared to the burden of neurological disease in the continent. Children with epilepsy are seen by healthcare professionals who are not equipped to read electroencephalograms (EEGs). We aim to develop a pedagogical model to improve and increase EEG interpretation skills for those treating children with epilepsy in SSA as well as in other low- and middle-income countries.

Aim:
To obtain consensus from experts on the essential curriculum content which is necessary to train non-specialists in EEG interpretation and to support safe practice for EEG training.

Method:
A qualitative, case study design was used consisting of eleven key questions on paediatric EEG, which was developed with the support of an adult education specialist. Data collected included interviews from 15 epileptology specialists across high to low-income countries between May-June 2023. Consent was obtained and an invitation to collaborate with the project offered. Data from the 11 questions were analysed using a thematic analysis. This enabled identification of various themes arising from the interview.

Results:
Findings relate to twelve aspects on paediatric EEG training; these were categorised thematically as: relevance; exposure to paediatrics; focus on paediatrics; barriers; resource limited setting; entry skills; best pedagogy; assessment; critical skills; re-inforcement of skills; training model and recommendations.

Conclusion:
The main findings from this study indicate that there is a shortage of paediatric EEG training and consequence lack of experts.

HREC REF: 481/2018

Title: **SLEEP PRACTICES OF SOUTH AFRICAN INFANTS AT THREE MONTHS OF AGE**

Authors: Rabelani Negota[1], Marlie Miles[1], Michal Zieff[1], Thandeka Mazubane[1], Thembeka Mhlakwaphalwa[1], Zamanzima Madi[2], Nwabisa Mlandu[1], Shreya Rao[3], Ayesha Sania[3], Nicolo Pini[3], William Fifer[3], Kirsten Donald[1]

Affiliation: [1]University of Cape Town, Cape Town, South Africa. [2]University of Kwa-Zulu Natal, Durban, South Africa. [3]Columbia University, New York, USA

Objective:
Sleep practices in early childhood are understudied in low-income countries. This studydescribes bedtime routines and sleep practices of South African infants at approximately three months of age.

Methods:
As part of the Khula Study in Cape Town, South Africa, we administered the Brief Infant Sleep Questionnaire Short Form (BISQ-SF) to mothers (N=276) of infants aged 2-5 months (M=3.28,SD=0.81; 53% male) during their first postnatal study visit. These visits occurred from March to May 2022. The BISQ-SF captures informationabout the infant's sleep during the previous two weeks.

Results:
Most mothers (n=167, 73%) reported having a pre-bedtime routine which often included activities such as breastfeeding (42%), bathing (40%), feeding (32%), singing, or playing lullabies (29%), changing the baby's clothes or diaper (26%), and placing the baby on the mother's back (14%). Most babies (n=249, 90%) slept for most of the night on their parents' bed. Sleep latency ranged from 0-360 minutes (M=31.03, SD=41.10). Total duration of sleep atnight-time ranged from 3-15 hours (M=9.50, SD=2.00) while the number of night-time wakingsranged between 0 to 10 times (M=2.32, SD=1.20). Lastly, total duration of day-time sleep ranged between 0-15 hours (M=03.34, SD=02.18).

Conclusion:
The BISQ-SF indicates overall healthy sleep practices in this sample. While individual variationis present, average total sleep duration and sleep latency reflect expected values for infants of this age.

HREC REF: 666/2021

Title: **RHEUMATIC HEART DISEASE CONTROL PROGRAMS IN AFRICA: A SYSTEMATIC REVIEW**

Authors: Laylah Ryklief[1], L Abdullahi[1], S Murugasen[1], Z Morar[1], K Rampersadh[2], H Moloi[3], J Abrams[1], ME Engel[24], LJ Zühlke[15]

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Background:
Rheumatic heart disease (RHD) is a significant cause of heart failure globally. Sub-Saharan Africa accounts for 23% of RHD cases worldwide, with the highest prevalence rate of 8.64 cases per 1000 people. To address the diverse challenges in prevention and management of RHD in African countries, it is crucial to establish and subsequently monitor RHD programs in each country. This approach aligns with the 2018 World Health Assembly Resolution on Rheumatic Fever and Rheumatic Heart Disease.

Objective:
This review aims to provide a comprehensive mapping of RHD control programmes within the WHO AFRO region.

Methods:
Five databases were searched from January 2012 to February 2024 for published reviews. The data were categorised and analysed according to the 25 domains of the Core Conceptual Framework for Comprehensive Rheumatic Heart Disease Control Programmes. To reduce bias, article screening, data and critical appraisal were conducted in duplicate.

Results:
We retrieved 49 reviews conducted in 38 of the 47 AFRO countries with 22 countries reporting burden of disease data. Of the 16 countries reporting RHD prevalences from school-based studies, 3 countries (Namibia, Nigeria and Cote D'Ivoire) were classified as being at low-risk populations for RHD. Twenty-two countries had evidence of tertiary cardiac services, with only seven reporting local teams with RHD-specific services. Ten countries reported either partial or full reliance on surgical services external to the country. Notably, South Africa was the only country with published primary and secondary prevention guidelines for RHD.

Conclusion:
This comprehensive mapping of RHD Control Programmes in Africa indicates that no single country provided sufficient information across all 25 domains; 11 countries had no published information in any domain, thus highlighting the numerous gaps in profiling the RHD programmes in the AFRO region, emphasising the need for more data. A search of primary studies would be useful to identify information not included in a review. Further, this review of reviews provides a framework for future formal studies or targeted supplementary data collection. Conducting interviews with key contacts in each country is recommended to assist in mapping the scope and effectiveness of RHD programmes.

AFRO/ERC REF: Protocol ID: AFR/ERC/2023/12.3

Title: **GLOBAL TRENDS AND NETWORKS IN THE LAST 20 YEARS OF RHEUMATIC HEART DISEASE RESEARCH: A BIBLIOMETRIC ANALYSIS**

Authors: Timothy F Spracklen[1,2*], Jessica Abrams[2], Mark E Engel[1,2,3], Liesl J Zühlke[1,2,3]

Affiliation: [1.]Cape Heart Institute, University of Cape Town, Cape Town, South Africa; [2.]Department of Paediatrics and Child Health, University of Cape Town, Cape Town, South Africa; [3.]South African Medical Research Council, South Africa

Objective:
Despite advances in eliminating rheumatic heart disease (RHD) in some regions, RHD remains endemic in low- and middle-income countries (LMICs). Tackling this burden requires a global effort and a multidisciplinary approach. As a step towards informing research capacity, we sought to better understand changes in trends in RHD research published over the last 20 years.

Methods:
RHD-related documents published from 2004-2023 were extracted from Scopus and PubMed, with a 1984-2003 comparison group. The Bibliometrix package of R was used for analysis.

Results:
The 2004-2023 search yielded 9,197 documents, with an annual growth rate of 2%. International collaboration was observed in 18%. In contrast, 5,077 articles were published in 1984-2003, with a growth rate of 1% and a lower rate of international co-authorship (3%). The USA produced the most scientific outputs. Of the 25 most influential articles, most were reviews or guidelines. Only seven of these papers were led by a team outside of Australia, USA or Europe. A wide global network was observed, in sharp contrast to 1984-2003, a period of markedly less international cooperation. The USA, France, UK, South Africa and Nigeria were the top five ranking countries in terms their influence on other networks. The University of Cape Town was the most productive institution; network analysis uncovered a complex system of universities, hospitals and medical schools that clustered somewhat along geographical lines. Of the top 25 authors, 12/25 were from lower- or middle-income countries and 8 were from Africa. Thematic mapping revealed retrospective and cross-sectional studies concerning surgery and epidemiology as core, well-developed topics. The genetics of RHD has recently emerged as a central topic, while immunology and mitral valve pathology have become less prevalent themes of interest.

Conclusions:
Although historically, a declining interest in RHD research in high-income countries led to fewer publication outputs, the past 20 years has seen a rapid expansion in RHD-related scientific outputs and global collaborative efforts. The USA is by far most productive in terms of scientific outputs and Australian authors and institutions are highly influential; nevertheless, we found that LMICs are well represented in RHD networks.

HREC REF: 531/2024

Title: **EARLY CLINICAL DESCRIPTION OF A SOUTH AFRICAN NEURODEVELOPMENTAL BIRTH COHORT**

Authors: Sadeeka Williams[1], Chloë A. Jacobs[1], Michal R. Zieff[1], Zayaan Goolam Nabi[1], Thandeka Mazubane[1], Marlie Miles[1], Donna Herr[1], Kirsten A. Donald[1]

Affiliation: [1]Department of Paediatrics and Child Health, University of Cape Town

Objective:
Child development in the first two years of life is a complex interplay of innate and acquired factors. The Khula Study is an observational birth cohort study in Cape Town, South Africa, tracking 293 babies from birth in an attempt to capture early predictors of emerging executive functions at 24 months of age. Data collection on the study was conducted from December 2021 until May 2024.
This sub-study describes congenital and environmental factors potentially affecting development.

Methods:
Trained medical doctors took a brief medical history, collected infant anthropometry and examined 293 infants (average age 16 weeks, SD = 3.82, 52% male) at one or two study visits in the first postnatal year. Relevant information was extracted from clinic records.

Results:
Thirty-six infants (11%) were born prematurely (< 38 weeks' gestation). There were no significant neonatal admissions. Solids were introduced between 1-32 weeks of age (M = 17.81, SD = 6.98) and 153 mothers (53%) were still breastfeeding at 6 months. One hundred and eight infants (34%) were HIV-exposed and four were infected. Nine infants (3%) were diagnosed with Foetal Alcohol Spectrum Disorder. Two infants were referred to the high-risk clinic at Red Cross Children's Hospital, a tertiary paediatric hospital in Cape Town.

Conclusions:
Although the Khula Study followed a healthy birth cohort, the impact of perinatal HIV and alcohol exposure in this sample is likely to affect the neurodevelopmental outcomes of these infants.
Identification of developmental delay enabled early referral in infants who ordinarily would only have been seen at primary care level.

HREC REF: 666/2021

Title: **EMOTIONAL AND BEHAVIOURAL DIFFICULTIES IN CHILDREN WITH AUTISM AND OTHER NEURODEVELOPMENTAL DISORDERS IN SOUTH AFRICA**

Authors: Michal R. Zieff, Emma Eastman, Alice Galvin, Björn U. Christ, Claire Fourie, Serini Murugasen, Jessica E. Ringshaw, Fatima Khan, Rizqa Sulaiman-Baradien, Raphaela Itzikowitz, Este Sauermen, Deepika Goolab, Aleya Remtulla, Zandre Bruwer, Nicole McIver, Brigitte Melly, Victoria de Menil, Celia van der Merwe, Amina Abubakar, Charles Newton, Elise Robinson & Kirsten A. Donald

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

Corresponding author: Michal R. Zieff (michal.zieff@uct.ac.za)

Objective:
Neurodevelopmental disorders (NDDs) are often comorbid with behavioural and emotional difficulties. Little is known about phenotypic characteristics of sub-Saharan African children living with NDDs. This study describes behavioural difficulties in a sample of South African children with Autism Spectrum Disorders (ASD) and other NDDs.

Methods:
This study was embedded in larger cross-sectional genetic study, *NeuroDev.* Parents of 957 South African children aged 2-17 years (M = 5.95, SD = 3.15; 75% male) with NDDs completed the Child Behaviour Checklist. We compared scores on the DSM-Oriented Scales in younger (2-5 years, n = 513) and older (6-17 years, n = 444) children by diagnosis (ASD compared to other NDDs).

Results:
In the younger age group, children with ASD obtained significantly higher average scores (indicating more difficulties) in the Affective, Anxiety, Attention Deficit/Hyperactivity, and Oppositional Defiant Scales than children with other NDDs (p < .001). In addition, 61% of young children with ASD scored in the "clinical range" in at least one diagnostic scale, compared to 42% in the non-ASD group. In the older age group, there were no group differences in average scale scores. The proportion of children with NDDs in this group who scored in the clinical range for at least one diagnostic scale, did not differ by diagnosis (56% and 59% for ASD and non-ASD groups respectively).

Conclusions:
Emotional and behavioural difficulties are prevalent in South African children living with NDDs. Differences in behavioural phenotypic profiles by age and diagnosis may help inform targeted screening tools and interventions.

HREC REF: 810/2016

Title: **HUMORAL, T CELL AND IMMUNE GENE EXPRESSION RESPONSE TO VACCINATION IN A SMALL GROUP OF CHILDREN WITH PREVIOUS MIS-C**

Authors: Claire Butters, Timothy Spracklen, Jonathan Day, Hamza Van Der Ross, Ntombi Benede, Avril Walters, Roanne Keeton, Rubina Bunjun, Thandeka Moyo-Gwete, Simone Richardson, Simon Mendelsohn, Thomas Scriba, Muki Shey, Wendy Burgers, Penny Moore, Liesl Zuhlke, Roanne Keeton, Kate Webb

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

Objectives:
The current study aims to uncover whether vaccinating children and adolescents who have previously developed multisystem inflammatory syndrome in children (MIS-C) may re-trigger an aberrant immune response.

Methods:
Children above the age of 12 years with a previous MIS-C diagnosis at Red Cross War Memorial Children's Hospital and healthy children were offered vaccination. Children received two doses of the Pfizer COMIRNATY SARS-CoV-2 vaccination three weeks apart between July and September 2022. Serum, plasma, whole blood and PAXgene samples were collected before the first dose, one week after the first dose, one week after the second dose and six weeks after the first dose. Serum from all four time points were used to measure the antibody response towards the SARS-CoV-2 vaccination (by assessing SARS-CoV-2 antibody titres and neutralising capacity) and the levels of 8 inflammatory cytokines and chemokines. PAXgene samples had whole blood RNA extracted and the expression of 96 genes was assessed. Whole blood was analysed for SARS-CoV-2-specific T cell responses.

Results:
Three participants over 12 years old with a history of an MIS-C diagnosis and four healthy children over 12 years old were enrolled. All seven participants completed the full vaccination schedule, and had samples taken at all four time points. Compared to pre-vaccination (baseline), there was a notable increase in SARS-CoV-2 IgG to Spike antibody titres. However, there was no difference between those with a history of MIS-C and healthy children. These titres remained stable throughout the vaccination schedule. Serum levels of interleukin (IL) -1β, IL-1 receptor antagonist (RA), IL-6, IL-10, IL-27, interferon gamma-induced protein (IP) -10, monocyte chemoattractant protein (MCP)-1 and tumour necrosis factor (TNF) -α remained consistent at all four time points, and there was no difference between the two groups. However, at all four time points, children with a history of MIS-C had consistently elevated levels of IL-10 compared to healthy children (p=0.011; p=0.002; p=0.067; 0.014). While this was statistically significant, the elevated levels of IL-10 were still within normal range and were markedly lower than those during acute MIS-C. *IL27* appeared upregulated in patients with previous MIS-C at the first post-vaccine visit, while *CXCR3* appeared downregulated at this timepoint; *TIMP2*, *TRMT2A*, *RAB33A* and *GZMB* all appeared downregulated in MIS-C patients at second follow-up visit; and *FCGR2A*, *IL1B*, *IFNAR1* and *GZMB* all appeared downregulated in MIS-C at the final follow-up visit. However, pairwise analysis revealed no significant differences. Only one healthy participant had a SARS-CoV-2-specific T cell response prior to vaccination. By 6 weeks post vaccination, all participants had a detectable SARS-CoV-2-specific T cell response; however, there was no difference in the magnitude of the response.

Conclusion:
In this small group, the immune response to SARS-CoV-2 mRNA vaccination in children with previous MIS-C does not appear to be significantly altered compared to healthy controls, and that antigen re-exposure does not induce an inflammatory phenotype.

HREC REF: 112/2012 and 599/2020

Title: **ADVANCED ABDOMINAL PREGNANCY AT A TERTIARY HOSPITAL IN SOUTH AFRICA: A CASE SERIES**

Authors: Shannon Harries shannon.harries-duvel@uct.ac.za, Lloyd Tooke loyd.tooke@uct.ac.za, Mushi Matjila mushi.matjila@uct.ac.za, Shakti Pillay shakti.pillay@uct.ac.za and JC Imbeault jc33335@outlook.com

Presenter's Affiliation: Department of Paediatrics and Child Health (Neonatology), University of Cape Town

Study design: Case series

Objectives: To describe the outcomes of advanced abdominal pregnancies (AAPs) over fourteen years at a tertiary neonatal unit in Cape Town, South Africa.

Background: Advanced abdominal pregnancies (beyond 20 weeks gestation) are rare in high-income countries due to extensive antenatal ultrasound screening. In low- and middle-income countries the outcome of these pregnancies are usually poor with high maternal and neonatal morbidity and mortality.
Methods: This case series retrospectively analysed 17 AAPs at Groote Schuur Hospital in Cape Town, South Africa. The analysis focused on maternal history, risk factors, delivery complications, intraoperative findings, and neonatal outcomes.
Setting: Groote Schuur Hospital (GSH) is a tertiary academic hospital with access to surgical, urological and anaesthetic specialists and provides neonatal services to half of Cape Town, South Africa (population five million). The neonatal unit has 75-beds, 20 of which are neonatal intensive care unit (NICU) beds. The hospital has an average of three thousand live births per annum, the majority of which are high-risk deliveries. Ethical approval was obtained (UCT HREC 360/2021)
Participants: All AAP cases, between January 2010 and December 2023 were included. As all AAPs require abdominal surgery, maternity theatre records over the 14-year study period were reviewed. Definite or probable AAPs were identified based on the diagnosis documented in the maternity theatre book. Maternal and neonatal medical records were then reviewed to confirm the diagnosis of an AAP.
Variables: Maternal: maternal profiles, timing of diagnosis, surgery and anaesthesia, maternal outcomes, intraoperative findings. Neonatal: fetal deaths and characteristics of babies born alive.

Statistical methods: Microsoft StatPlus was used for statistical calculations.

Results:
Participants: There were 17 cases of AAP identified
Main results: Of the 17 pregnancies, 16 were singleton births and one was a set of monochorionic-monoamniotic twins. The diagnosis was frequently missed on initial ultrasound scan. Most diagnoses were made within two days of delivery. All deliveries were open laparotomies under general anaesthaesia. All deliveries had complications with the most common complication being blood loss requiring transfusion. There were two maternal deaths due to hypovolaemic shock. Most placentae were implanted on multiple sites including the uterus, adnexa, omentum and bowel. Twelve of the 18 babies were born alive, two died in hospital and 10 were discharged home. Four babies were growth restricted.

Conclusions: Advanced abdominal pregnancies carry significant maternal and fetal risks. In this case series, despite complicated surgeries, only two mothers died, and neonatal outcomes were good. AAPs do not always have poor outcomes if managed at well-resourced hospitals.

HREC REF: 360/2021

Title : **CLOSING THE IMMUNITY GAP TO HEPATITIS B: A COMPARATIVE ANALYSIS OF IMMUNE PROTECTION AND IMPLEMENTATION COSTS OF THREE VACCINATION STRATEGIES IN FIRST YEAR HEALTH SCIENCE STUDENTS**

Authors: Sumaiyah Hendricks[1,2], Leilah Sonday[1,2], Annemie Stewart[1,4], Sipho Dlamini[5], Benjamin M. Kagina[1,2], Rudzani Muloiwa[2,3]

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Introduction:
Immunisation against Hepatitis B virus (HBV) is the most effective means of preventing HBV infection and disease. South Africa introduced the 3-dose hepatitis B vaccine into its' Expanded Programme on Immunization (EPI) schedule in 1995. Studies have shown persistence of protective immunity without booster vaccination in immunocompetent adults decades after a 3- dose schedule. South Africa, a high HBV endemic country, revaccinates health sciences students before they enter clinical training. In light of current evidence, there is a need to re-evaluate the most appropriate vaccination strategy for health science students, seen as high risk for occupational exposure to HBV.

Methods:
A retrospective observational study was performed to evaluate the immunological responses of undergraduate health science students to different HBV vaccination strategies used at the University of Cape Town in 2017, 2018, and 2019. Three groups were identified based on the year of first enrolment: Group 1 received a 3-dose vaccination schedule, Group 2 received a single "booster" dose, while Group 3 received no doses before serology testing, respectively. Serum anti-HB levels were measured at least 30 days after last dose. Students with lower than protective antibody levels (<10mlU/ml) received additional doses to complete a standard 3-dose schedule. Implementation costs viz, vaccination, serology testing and staffing, of each vaccination strategy were calculated and compared.

Results:
Group 1: After completing 3-dose vaccine schedule 342/345 (99.1%) students demonstrated protective antibody levels (≥10 mIU/ml). Group 2: Following a single booster dose 261 of 294 (88.8%) students demonstrated protective levels. Group 3: Serology testing without vaccination; 173/357(49.5%) students were seroprotected. Following a single booster dose, 261/294 (88.8%) and 129/144 (89.6%) students in Groups 2 & 3 gained protective titre levels. Group 2's strategy had the lowest cost of implementation.

Conclusion:
In areas with high infant Hepatitis B immunization coverage, the 3-dose schedule shows persistent seroprotection. Where documented seroprotection is required, a single booster dose offers similar levels of seroprotection as full revaccination, at a lower cost. Further research is needed to evaluate the significance of immunological memory on long-term protection, in the absence of additional booster doses.

HREC REF: 496/2021

Title: **COMPARATIVE ANALYSIS OF OSCILLOMETRY AND SPIROMETRY TRAJECTORIES IN LUNG FUNCTION ASSESSMENT**

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Background:
Tracking the trajectories of lung function over time is important for understanding lung function maturation. This enables us to monitor respiratory health, implement timely interventions and identify strategies to optimize respiratory health in early life. Spirometry trajectories have been described from childhood to adulthood. Given the importance of lung health in early life, more recently early life trajectories have been described using oscillometry. Understanding how these early life trajectories relate to established spirometry trajectories is not known.

Objective:
To describe tracking of oscillometry measures from 6 weeks to 10 years of age and how they relate to longitudinal (5-10 years) spirometry in an African population-based cohort.

Methods:
Lung function were measured from 6 weeks and annually to 10 years of age. Summary statistics and trajectory plots were generated to describe trajectories of oscillometry [compliance (C) and resistance (R) of the respiratory system] and forced spirometry [forced expiratory volume in 1 s (FEV1) and forced vital capacity (FVC)]. Lung function quartiles determined at 6 weeks and three years for C and R were tracked over the first 10 years of life. The relationship between C and R and subsequent spirometry measures (FEV1 and FVC) was analysed.

Results:
C trajectories remain consistent across quartiles, with children in the highest quartile maintaining highest values of C through to 10 years. R quartiles were more variable over time, with only the lowest quartile tracking consistently to 10 years. However, when tracked from 3 years of age, they remained consistent across quartiles. Children in the highest C trajectory had higher spirometry values and lower R and children in the highest R trajectories, determined at 3 years, had consistently low spirometry values from 5 to 10 years of life.

Conclusions:
These results suggest a correlation between early life oscillometry measures and subsequent spirometry values. The consistency observed in the C and R trajectories highlights the importance of early detection and monitoring to identify children at risk for respiratory issues and to implement early interventions. The study demonstrates that it is possible to track lung function along the life course from early life, thereby enhancing our understanding of respiratory health trajectories and the implications for early intervention strategies.

Dates of enrolment of the participants: March 2012 to March 2015

Funding: The study received funding from the Bill and Melinda Gates Foundation (grant number OPP1017641, OPP1017579); NIH, USA (H3 Africa grants U54HG009824 and U01AI110466), The Wellcome Trust (098479/Z/12/Z; 204755/Z/162); MRC South Africa, The National Research Foundation, South Africa; Hungarian Scientific Research Fund grant (K 128701); European Respiratory Society (INCIRCLE CRC-2013-02); Harry Crossley Clinical Research.
HREC REF: 048/2020

Title: **INTRODUCING THE AKILI PROJECT: THE GENETIC CHARACTERIZATION OF ADHD IN KENYAN AND SOUTH AFRICAN POPULATIONS**

Authors: Hendrike van Vollenhoven [1], Emma Eastman[1], Lauren Davel[1], Sadeeka Williams[1], Amina Abubakar[3,4], Elise B. Robinson[2], Kirsten A. Donald[1].

Affiliation: [1]Faculty of Health Sciences, Department of Paediatrics and Child Health, University of Cape Town, Neuroscience Institute and Red Cross War Memorial Childrens Hospital, Cape Town, South Africa; [2]Department of Psychiatry and Center for Genomic Medicine, Harvard Medical School, Massachusetts General Hospital. Stanley Center for Psychiatric Research, Broad Institute of MIT and Harvard, Cambridge, MA, USA; [3]Institute for Human Development, Aga Khan University, Nairobi, Kenya; [4]Neurosciences Unit, Clinical Department, KEMRI-Wellcome Trust Collaborative Research Programme, Kilifi, Kenya

Objective:
Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental disorder characterized by inattention, impulsivity, and hyperactivity. The diagnosis is associated with many challenges to educational, occupational, and health outcomes, particularly when untreated. Little is known of the genetic and environmental risks of ADHD. Genetic studies of ADHD have the potential to clarify the disorder's biological causes, its heterogeneity, and its relationship to other neuropsychiatric diagnoses. However genetic research into ADHD lags in terms of: (1) sample size, (2) ancestral diversity, and (3) consideration of phenotypic heterogeneity, each of which limit the returns of genetic research.

Methods:
Akili will recruit a cohort of 6,000 children ages 6-17 years living in Nairobi, Kenya, and Cape Town, South Africa. Two-thirds (4,000) of the children will meet diagnostic criteria for ADHD, and 2,000 will be age- and ancestry-matched controls. All participants will be comprehensively assessed using gold standard behavioural and cognitive assessments and DNA will be collected through saliva specimens.

Results:
Akili will perform a detailed genetic characterization of all 6,000 children by analysing exome sequencing and array-based genotyping data to discover genes associated with ADHD. Akili will also investigate the heterogeneity in the genetic architecture of ADHD by examining how the rare and common variant architectures of ADHD change in relation to differences in cognitive, behavioral, and medical outcomes across cases.

Conclusion:
The Akili project will provide an extraordinary resource for the study of ADHD in Kenya and South Africa. The data will nearly double the number of ADHD cases available for exome sequencing analysis in international genomic research databases, additionally, significantly diversifying representation from almost exclusively European ancestry to 60% European and 40% African ancestry in international genomic datasets. Ultimately, leading to the development of better treatments and management of ADHD in the future.

HREC REF: 511/2023

Title: **SELECTING APPROPRIATE TOOLS IN CLINICAL PHENOTYPING OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN A MULTI-NATION AFRICAN RESEARCH STUDY**

Authors: Sadeeka Williams[1], Lauren Davel[1], Brigitte Melly[1], Hendrike McDonald[1], Emma Eastman[1], Michal R. Zieff[1], Patricia Kipkemoi[3,4], Celia van der Merwe[2], Elise Robinson[2], Amina Abubakar[3,4], Kirsten A. Donald[1]

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Objective:
Attention Deficit Hyperactivity Disorder (ADHD) is a common condition with childhood onset that affects approximately 4% of the world's population. The aetiology of ADHD is multifactorial, with genetic and environmental elements in the first one thousand days of life emerging as important predictors. The *Akili Study* aims to characterise the genetics of ADHD in South African and Kenyan populations. Genetic and phenotypic ADHD data from the African continent is scarce and yet crucial for future diagnostic and therapeutic advancement. We describe a novel combination of clinical examination, behavioural tools, and cognitive assessments administered in the Akili study to clinically phenotype our participants.

Methods:
Akili is a cross-sectional, observational ADHD study, enrolling a cohort of 6000 children (2000 controls and 4000 cases) between the ages of 6 and 17 years of age in Cape Town, South Africa and Nairobi, Kenya. Each participant has a saliva sample taken for genetic testing and undergoes assessments for the clinical phenotype. A selection strategy for the assessment battery was based on three factors: (i) demographic, (ii) clinical, and (ii) psychometric factors. Demographic factors included age-appropriateness, cultural appropriateness, and the tools' suitability for translation into local languages (Swahili in Kenya, and Xhosa and Afrikaans in South Africa). Clinical factors included the presence of common comorbid conditions in ADHD (e.g. Autism Spectrum Disorder, Anxiety, etc.). For example, tools that require verbal fluency may be a less appropriate choice for participants with Autism who have delayed expressive communication. Finally, the tools needed to be psychometrically sound. Tools must be valid and reliable (preferably with local evidence to support excellent psychometric properties), accessible, cost-effective, and widely used to support harmonisation with existing databases in other parts of the world.

Results:
There was no single assessment tool that could adequately clinically phenotype ADHD. Our researchers went through a rigorous process of electing "gold standard" tools for each of the facets of this condition, engaging with stakeholders who had done similar work in this field and then consulting South African and Kenyan experts to ensure cultural fairness and appropriateness of the tools. Lastly, each of the tools were translated where necessary and piloted by trained researchers before commencement on the Akili study.
For behavioural measures, we chose the Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS) as a measure of impulse and attentional control and co-morbid conditions, and the Swanson, Nolhan, and Pelham Questionnaire (SNAP), a DSM-based measure of ADHD symptoms. For cognitive functioning, we selected the Behaviour Rating Inventory of Executive Function (BRIEF; a measure of executive functioning), the Flanker Task (attention and inhibition), the Trail-Making Task (visual attention), and the Ravens Progressive Matrices (non-verbal spatial reasoning). Finally, we developed a non-scored tool capturing the participant's full history of current and previous medical conditions as well as a comprehensive medical examination.

Conclusion:
We describe our selection of a novel combination of standardised tools to clinically phenotype ADHD in paediatric African populations. Our final selection took into consideration weighing the quality of measures against the suitability of measures for very specific contexts (in terms of both geographic and clinical characteristics

HREC REF: 511/2023

Title: **PRENATAL ALCOHOL EXPOSURE AFFECTS STRUCTURAL BRAIN DEVELOPMENT IN SOUTH AFRICAN INFANTS: A COMPARATIVE ANALYSIS USING LOW FIELD AND HIGH-FIELD MRI**

Authors: Simone R Williams, Michal R Zieff, Niall J. Bourke, Lauren Davel, Layla Bradford, Reese Samuels, Sadeeka Williams, Chloë A. Jacobs, Nwabisa Mlandu, Tracy Pan, Zamazimba Madi, Tembeka Mhlakwaphalwa, Thandeka Mazubane, Zayaan Goolam Nabi, Marlie Miles, Jess E Ringshaw, Daniel C. Alexander, Derek K. Jones, Steven C. R. Williams & Kirsten A. Donald

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

Objective:
Significant alterations in regional brain volumes have previously been observed in infants exposed to alcohol prenatally, with these alterations observed using high-field magnetic resonance imaging (MRI) machines not readily available in low-resourced settings, due to high infrastructural and operational costs. We aimed to determine whether subtle neurostructural alterations due to prenatal alcohol exposure could be detected using both traditional high-field MRI and affordable, portable low-field MRI technology.

Methods:
Between December 2021 and November 2022, 329 pregnant women and 65 postpartum mothers attending were recruited in Khula Leap, a multi-dimensional longitudinal birth cohort study set in Gugulethu, an informal settlement in the Western Cape, South Africa. High (3T) and low-field MRI (64mT) neuroimaging data acquired from infants at 3 months of age were included in our analysis. Using multivariable linear regression, regional cortical and subcortical volumes were compared between infants with prenatal alcohol exposure and matched controls.

Results:
Based on high-field MRI data from 67 infants (24% alcohol-exposed; mean age 116 days; 51% female), infants with alcohol exposed had lower total intracranial volumes (10% average decrease; $p = 0.02$), lower right lateral occipital volumes ($p = 0.013$), and lower subcortical volumes of the left pallidum ($p = 0.007$) and caudate ($p = 0.005$), compared to infants without exposure after correcting for sex, age and maternal HIV. Low-field MRI data from 62 infants (29% alcohol-exposed; mean age 118 days; 48% female) revealed similar occipital and caudate reductions in exposed infants.

Conclusions:
Infant brain volume alterations linked to *in utero* alcohol exposure can be detected using both MRI methods. This demonstrates that affordable low-field MRI can reliably measure these subtle neurostructural alterations, expanding research possibilities in low-resourced settings beyond traditional high-cost setups.

HREC REF: 666/2021