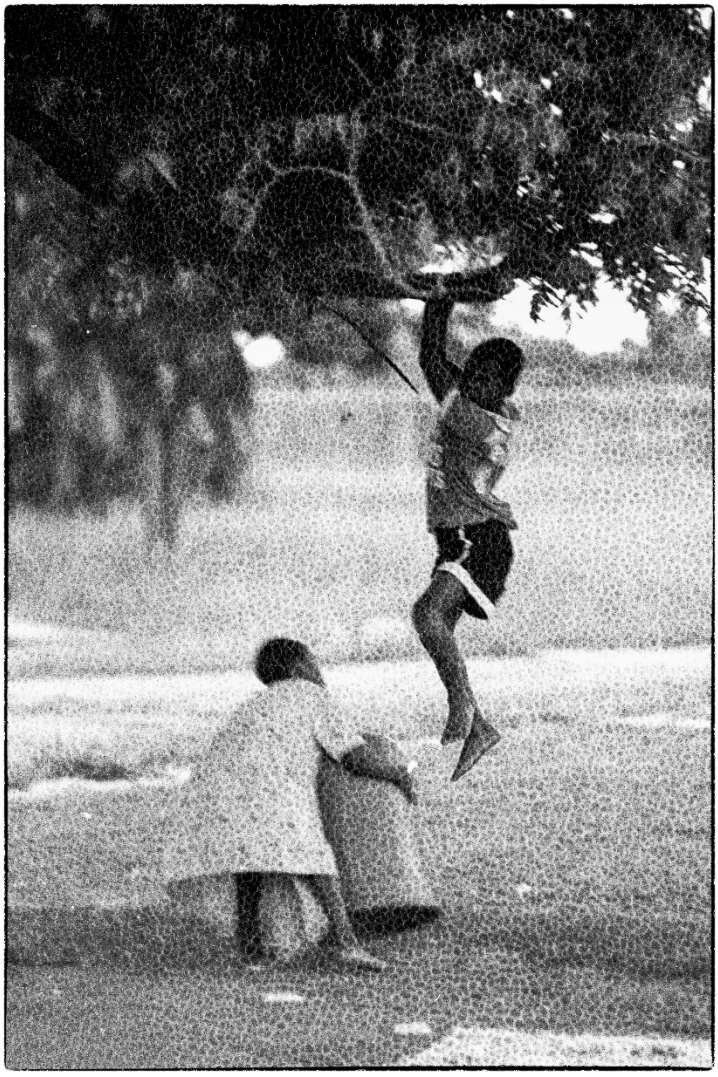
Department of Paediatrics & Child Health

UNIVERSITY OF CAPE TOWN

ANNUAL RESEARCH DAY 2020



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Programme and Abstract Book

Wednesday, 04 November 2020

VIRTUAL MEETING (ZOOM)

Registered for CPD Points

Please complete online registration form to claim your points.

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15H25 – 15H45 **TEA BREAK (VIRTUAL)**

Session 4: Chairperson: **D. le Roux**

15H45 – 16H15 Ethics Talk: *"Conflicts of Interests."* *M. Blockman*

16H15 – 16H30 **Feedback on Research Day presentations, with Award & Research Prizes by guest judges (C Hlela and R Solomons) & Thanks and Closing Remarks (D le Roux)**

Electronic Poster Presentations (VIRTUAL ROOM) **Page No.**

Title: **ABDOMINAL SURGERY IN VERY LOW BIRTH WEIGHT NEONATES IN A DEVELOPING WORLD NEONATAL UNIT - SHORT TERM OUTCOMES AND RISK FACTORS FOR MORTALITY**

Authors: Nazneen Allie[1]: MBChB (UCT), DCH (SA) Yaseen Joolay: MBChB (US), FCPaed (SA), MPhil Neonatology (UCT) Cert. of Neonatology (SA)

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

Background:
The surgical neonate requires care in specialized neonatal units. Very low birth weight infants (VLBW) are a group particularly vulnerable to risks and outcomes associated with prematurity. There is an increased number of abdominal emergencies attributed to improved survival in this birthweight category.

Objectives:
To describe the short-term survival to discharge in VLBW infants following abdominal surgery at a South African public tertiary hospital and to examine the utility of common scoring systems for prognostication.

Methods:
A retrospective study of VLBW infants with abdominal surgery was conducted in patients admitted to the neonatal unit at Groote Schuur Hospital between 2012 and 2016. CRIB And SNAPPE scores were calculated for patients where sufficient data was available.

Results:
Fifty-two patients were included. The mean gestational age (GA) and birthweight (BW) were 29.5 weeks (SD 2.1) and 1102g (SD 197.8) respectively. Necrotizing enterocolitis was the most common (50%) surgical emergency. The leading postoperative complication was sepsis (37%). Fourty-two (81%) infants survived to discharge, the mean age at presentation 21 days (SD 21.1) with a mean hospital stay of 74 days in survivors vs 52 days in the non-survivors (p=0.06). There was a non-statistically significant difference in SNAPPE scores between survivors and non-survivors.

Conclusion:
Abdominal emergencies have a high mortality and adds to the overall length of stay in VLBW patients. Neonatal scoring systems have proven to be useful adjuncts in predicting neonatal mortality, further study is warranted in neonates who deteriorate due to surgical abdominal complications.

HREC 399/2018

Title: **OUTCOMES AND RISK FACTORS OF VERY LOW BIRTH WEIGHT INFANTS WITH INTRAVENTRICULAR HAEMORRHAGE WHO RECEIVED RESPIRATORY SUPPORT IN A MIDDLE-INCOME COUNTRY NEONATAL UNIT**

Authors: D Goolab[1], MB BCh, DCH (SA); L Tooke, MB ChB, FCPaeds, MMed (Paeds), Cert Neonatol (SA); S Le Roux, MB ChB, MPH; Y Joolay, MB ChB, FCPaeds, MPhil (Neonatol), Cert Neonatol (SA)

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

Background:
Prematurity is a major risk factor for intraventricular haemorrhage (IVH). Premature infants often require respiratory support. There is little information on neonates with IVH who require respiratory support in low and middle income countries.

Objective:
To describe the characteristics and short-term outcomes of very low birth weight (VLBW) infants with IVH who required respiratory support in a tertiary neonatal unit with resource limitations.

Methods:
This was a matched retrospective observational study. The population included VLBW infants with IVH, who received positive pressure respiratory support between January 2014 and December 2016. Outcomes of infants with severe IVH was compared to those with mild IVH. Outcomes were further analysed according to mode of ventilation.

Results:
150 infants were included in the study, 56 (37%) received continuous positive airway pressure (CPAP) only and 94 (63%) mechanical ventilation. Severe IVH was associated with surfactant therapy across both ventilation groups (p=0.03). Oxygen requirement at 28 days was more frequent in infants with severe IVH compared to mild IVH (79% vs 38%, p=0.01) (OR 6.11 (95% CI 1.19-31.34), p=0.03). Severe IVH and the presence of coagulopathy were the strongest predictors of death in both ventilation groups (p <0.0001). Pulmonary haemorrhage was the commonest cause of death in those with severe IVH and blood culture confirmed sepsis in those with mild IVH. Periventricular leukomalacia (PVL) was associated with severe IVH in those receiving invasive ventilation (OR 6.67 (95% CI 1.11-40.17)).

Conclusion:
Mechanical ventilation, coagulopathy and pulmonary haemorrhage were strongly associated with death in VLBW infants with severe IVH in a resource-limited setting. These prognostic factors may have a role in end of life decisions.

HREC: 725/2017

Title: **MORBIDITY AND MORTALITY IN SMALL FOR GESTATIONAL AGE VERY LOW BIRTH WEIGHT INFANTS AT GROOTE SCHUUR HOSPITAL**

Authors: M. Mangiza[1], D.Ehret, E. Edwards, N. Rhoda & L. Tooke

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

Background:
Small for gestational age (SGA) is defined as a birth weight which is below the 10th percentile for gestational age. The burden of small for gestational age is very high in low and middle income countries. The mortality risk associated with being premature and small for gestational age is substantially higher than either alone , and yet the outcomes of these infants is not well described in low resource settings.

Objectives:
We sought to evaluate the impact of SGA on outcomes of Very Low Birth Weight (VLBW) Infants at Groote Schuur Hospital. We compared the mortality and morbidity rates of SGA infants with appropriate for gestational age infants (AGA).

Methods:
Data was obtained retrospectively from the Vermont Oxford Network (VON) Groote Schuur database from 2012 to 2018. VON VLBW database enrolls neonates with birth weights between 501 and 1500g if they are born at participating institutions or transferred there within the first 28 days of life. Neonates with congenital anomalies were excluded. Fenton growth charts were used to classify neonates as SGA. Gestational age was estimated using an early ultrasound (<20 weeks) as the gold standard, when it was not available Ballard score or postnatal foot length were used. The information was analyzed using Stata. Risk ratios and their Confidence Intervals were calculated, adjustments were made for confounding factors.

Results:
The mortality rate was significantly higher in the SGA compared to the AGA group (28.9% vs 18.5% RR 2.1 CI 1.6-2.7). Bronchopulmonary dysplasia (14% vs 4.5% RR 3.7 CI 2.3-6.1), Necrotizing Enterocolitis (10.1% vs 6.6% RR 1.7 CI 1.1-2.7) and late onset sepsis (16.7% vs 9.6% CI 1.6-3.3) were significantly higher in the SGA group. On analyzing the morbidities among survivors only Bronchopulmonary dysplasia (14.1 vs 4.2% RR 4 CI 2.5-6.7) and late onset sepsis (15.3% vs 6.5% RR3.3 CI 2.1-5.2) remained significant.

Conclusion:
SGA infants have a significantly higher risk of mortality and morbidity among the VLBW infants at Groote Schuur Hospital. The observed increased risks may be useful for the perinatal management of these infants.

HREC REF: 102/2019

Title: **A COMPARISON OF THE ACCURACY OF VARIOUS METHODS OF POSTNATAL GESTATIONAL AGE ESTIMATION**

Authors: Alexander Stevenson[1], Yaseen Joolay[1], Candice Levetan[1], Caris Price[1,] Lloyd Tooke [1]

Affiliation: [1]Division of Neonatal Medicine, Department of Paediatrics, University of Cape Town

Objective:
Which are the most accurate methods of postnatal gestational age estimation in our setting? Is their reliability affected by babies being small for gestational age?

Methods:
A prospectively designed diagnostic accuracy study in a tertiary referral hospital in a developing country. Early ultrasound (<20 weeks) was the clinical reference standard. Methods evaluated included anthropometric measurements (including foot-length), vascularity of the anterior lens, the New Ballard Score and Last Menstrual Period. Clinicians' non-structured global impression "End of Bed" Assessment was also evaluated. Babies were recruited in the Groote Schuur neonatal nursery Researchers were blinded to the results of the ultrasound scan. Correlation with gold standard and mean bias of the different methods were compared.

Results:
106 babies were included in the study. Ballard Score and "End of Bed" Assessment had the smallest mean biases of -0.14 and 0.06 weeks respectively but wide 95% limits of agreement. Foot-length was particularly poor in Small for Gestational Age infants. None of the methods studied were superior to a non-structured clinician's informal "End of Bed" Assessment.

Conclusion:
None of the methods studied met the a priori definition of clinical usefulness. Improving access to early ultrasound remains a priority. Instead of focusing on chronological accuracy, future research should compare the ability of early ultrasound and Ballard score to predict morbidity and mortality.

Title: **REFERENCE RANGE FOR OSCILLOMETRY IN HEALTHY SOUTH AFRICAN PRESCHOOL CHILDREN**

Authors: Chaya S[1], MacGinty R[1], Jacobs C[1] Hantos Z[2], Simpson SJ [3], Zar HJ[1], Gray DM[1]

Affiliation: [1]Department of Paediatrics and Child Health, Red Cross War Memorial Children's Hospital and MRC Unit on Child and Adolescent Health, University of Cape Town, Cape Town, South Africa; [2]Department of Anaesthesiology and Intensive Therapy, Semmelweis University, Budapest, Hungary; [3]Telethon Kids Institute, School of Physiotherapy and Exercise Science, Curtin University, Perth, Australia

Introduction:
Oscillometry is a non-invasive measure of respiratory impedance and can be used in young children from 3 years. Its clinical application is limited by the lack of reference data for non-Caucasian children.

Objective:
To develop appropriate reference equations for oscillometry outcomes in South African preschool children.

Methods:
Children(3 to 6 years)not acutely or chronically ill, enrolled in the Drakenstein Child Health study had respiratory resistance(R)and reactance(X)measured using intra-breath(10 Hz)and standard oscillometry(6-32 Hz).Intra-breath R at end inspiration(R_{ei})and at end expiration(R_{ee}),X at end expiration(X_{ee})and end inspiration(X_{ei}),and standard oscillometry measures[R at 10 Hz(R_{10}), X at 10 Hz(X_{10}), mean resistance(R_m),and compliance(C)]were assessed.Fit with current European reference range(Calogero 2013) was assessed.Linear regression was used to develop reference equations.

Results:
599 children were included:males 50.1%,mixed ancestry 35.2%;African 64.8%;mean(SD)height z-score -0.8(1.1).European reference was a poor predictor of R_{10} and X_{10} in this cohort(z-score R_{10}_log 1.07; z-score TX_{10}-0.17).

Reference equations for oscillometry in African preschool children

Variable	Equation	#P-Value	Adjusted R-squared
$\mathbf{R_{ee}}$	29.42- 0.1791*ht	p<0.001	0.36
$\mathbf{R_{ei}}$	26.90-0.1720*ht	p<0.001	0.28
$\mathbf{*X_{ee}}$	4.35-0.0088*ht	p<0.001	0.13
$\mathbf{*X_{ei}}$	4.64-0.03*race-0.0104*ht	p<0.001	0.25
$\mathbf{R_{10}}$	26.77-0.146*ht	p<0.001	0.34
$\mathbf{*X_{10}}$	4.35-0.0088253*ht	p<0.001	0.13
R	25.50-0.1455256*ht	p<0.001	0.39
C	-7.21+0.1341573 *ht	p<0.001	0.16

#Linear regression model adjusted for height,age,race,sex.See text for definitions.*transformed(T)variables: $X_T=(|X|- 10)^{1/2}$; ht:height in cm ,Units for R, X:hPa.L.s^{-1} ;C:ml.hPa.L^{-1}

Conclusion:
The reference data for oscillometry in African preschool children were inconsistent with European reference data.
Funding: Gates Foundation (OPP1017641), Wellcome Trust (#204755/Z/162), ERS Clinical Research Collaboration Award (INCIRCLE), South African Medical Research Council, Hungarian Scientific Research Fund (#105403, #128701), Harry Crossley Research Grant

Title: **LONGITUDINAL STUDY OF NASOPHARYNGEAL BACTERIAL PROFILES IN A SOUTH AFRICAN BIRTH COHORT EARLY IN LIFE**

Authors: Shantelle Claassen-Weitz[1], Sugnet Gardner-Lubbe, Kilaza S. Mwaikono, Heather J. Zar and Mark P. Nicol

Affiliation: [1]Department of Pathology, University of Cape Town

Rationale:
Nasopharyngeal (NP) colonization with potentially pathogenic bacteria is a pre-requisite for transmission and may precede the development of pneumonia or invasive disease. Whilst individual bacteria have been studied, there are few data describing the longitudinal patterns of NP bacterial communities, particularly in children in Africa.

Objectives:
To study bacterial succession of NP microbiota within a South-African birth cohort, the Drakenstein Child Health Study (DCHS), during the first 30 months of life and to identify key environmental factors associated with changes in these profiles.

Methods:
We collected NP specimens from 100 children enrolled in the DCHS with no reports of lower respiratory tract infection during the first three years of life. We collected NP specimens monthly during the first year of life and six-monthly up until 2.5 years of life. We performed nucleic acid extraction and sequenced the V4 hypervariable region of the 16S rRNA gene on MiSeq. Bioinformatic processing was performed on DADA2 (Divisive Amplicon Denoising Algorithm 2) to resolve amplicon sequence variants (ASVs). Potential "contaminant ASVs" were removed from the dataset via the decontam package in R.

Results:
A total of 1333 NP specimens were included, from which 1079 ASVs were identified. We identified age-related changes in overall bacterial community composition. For individual taxa, we observed high relative abundance of *Corynebacterium* spp. during the first six months of life. *Staphylococcus* spp. followed a similar pattern with high abundance in early life, declining over the first six months of life. We observed increasing mean relative abundances of *Moraxella catarrhalis* over the first six months of life. We observed a relatively novel species, *M. lincolnii* which had no clear age-related pattern of carriage. A gradual increase in mean relative abundance was observed for *Haemophilus influenzae* during the first 2.5 years of life. No clear changes in mean relative abundance was observed for *Streptococcus pneumoniae* during the first 2.5 years of life. We further observed that tuberculosis diagnosis ($p = 0.0239$) and maternal work status ($p=0.0188$) were associated with within-sample (alpha) diversity (Shannon diversity index) during the first year of life. Higher alpha diversity indices were observed at 6-12 months of life from infants diagnosed with tuberculosis when compared to uninfected infants. Infants born to working mothers had higher alpha diversity between three and nine months of life compared to infants born to non-working mothers. Alpha diversity measured during the first year of life was not associated with HIV-exposure, gender, mode of delivery, mode of feeding, household size, smoking exposure, indoor air pollution nor maternal psychosocial variables.

Conclusion:
These results highlight changes in nasopharyngeal bacterial profiles in a South African birth cohort during early life, with tuberculosis infection and maternal work status impacting on alpha diversity.
Ethics approval number: HREC 585/2015
Funding: H3Africa U01 award from the National Institutes of Health of the USA (1U01AI110466-01A1), the Bill and Melinda Gates Foundation Global Health Grant (OPP1017641; OPP1017579), the National Research Foundation South Africa, the South African Medical Research Council, L'OréalUNESCO For Women in Science (South African Young Talents Award)

This is new research

Title: **DESCRIPTIVE ANALYSIS OF ROUTINE CHILDHOOD IMMUNISATION TIMELINESS IN THE WESTERN CAPE, SOUTH AFRICA**

Authors: Ntombifuthi Blose,[1] Edina Amponsah-Dacosta[1], Benjamin M. Kagina[1], Rudzani Muloiwa [1,2]

Affiliation: [1] Vaccines for Africa Initiative, School of Public Health and Family Medicine, Faculty of Health Sciences, University of Cape Town; [2] Department of Paediatrics and Child Health, Groote Schuur Hospital, Faculty of Health Sciences, University of Cape Town

Objective:
Receiving routine immunisation at the correct age is critical in ensuring effectiveness of vaccines in controlling vaccine preventable diseases. We therefore sought to assess the timeliness of age-specific routine immunisation in a paediatric population in Cape Town, South Africa.

Methods:
We reviewed 704 participant records from a prospective health-facility based study conducted between 2012 and 2016 in Cape Town, South Africa. The primary outcome of interest was receiving age-specific immunisations within 4 weeks (28 days) of that recommended for age as per the South African Expanded Programme on Immunisation (EPI) schedule. Bacillus Calmette–Guérin (BCG) was used to assess birth dose timeliness while Diphtheria/Tetanus, Pertussis, Inactivated Poliomyelitis vaccine and Haemophilus Type B (DTP/IPV/HiB) was used as a proxy for the 6, 10- and 14- weeks immunisations. The measles vaccine was used as proxy at 9 and 18 months. Proportions of delayed immunisations for each vaccine was calculated as a percentage of total number of eligible participants at specific immunisation time points. The degree of delay for each vaccine was calculated as the difference between expected date and the actual date of receipt of age-specific immunisation. The length of delay was described using medians and interquartile ranges (IQR) in weeks. The study was approved by the University of Cape Towns' Human Research Ethics Committee of the Faculty of Health Sciences [HREC 027/2020].

Results:
A total of 652 participants with a median age of 11 [IQR 4.5 – 28.0] months had sufficient data for inclusion in the study. BCG had an immunisation coverage of 619/652 (94.9%). Immunisation coverage for DTP/IPV/HiB 1, DTP/IPV/HiB 2 and DTP/IPV/HiB 3 were 599/634 (94.5%), 537/594 (90.4%) and 471/556 (84.7%) respectively. Measles 1 and 2 immunisation coverage was 314/370 (84.9%) and 167/232 (72.0%). BCG was delayed in 40 (6.5%) participants. The delay in DTP/IPV/HiB 1, DTP/IPV/HiB 2 and DTP/IPV/HiB 3 was 87 (14.5%), 139 (25.9%), and 163 (34.6%) respectively. The proportion of delay in measles 1 was 70 (22.3%), while measles 2 had 49 (29.3%) delayed participants. BCG had a median delay of 6.6 [IQR 5.4 – 9.1] while, DTP/IPV/HiB 1, DTP/IPV/HiB 2 and DTP/IPV/HiB 3 had median delays of 7.0 [IQR 4.7 – 11.2], 7.6 [IQR 5.0 – 12.4] and 7.9 [IQR 5.3 – 17.1] weeks respectively. Measles 1 was delayed by a median of 8.6 [IQR 5.5- 25.3] weeks, and measles 2 by a median of 12.9 [IQR 6.7 – 38.6] weeks.

Conclusion:
Despite the relatively high immunisation coverage in early childhood vaccines, there is significant delay in receiving age specific vaccine doses. In addition to the known decline in vaccine coverage with age, we observed proportional increase in delayed immunisation and increased length of delay in receiving age specific vaccines. A combination of the three findings has the potential to greatly undermine the effectiveness of the EPI program. There is an urgent need to address both vaccine coverage and timing of vaccination particularly in late infancy and second year of life. Further study is required to assess modifiable factors to improve vaccination uptake within the study population.

Title: **TUBERCULOSIS INFECTION AND DISEASE IN SOUTH AFRICAN PERINATALLY HIV-INFECTED ADOLESCENTS ON ANTIRETROVIRAL THERAPY: A COHORT STUDY**

Authors: Lisa Frigati, MMED[1,2], Katalin A. Wilkinson PhD[3,4], Stanzi le Roux, MBChB[5]; Karryn Brown MPH[5], Sheena Ruzive (BScMedSciHons) [3], Leah Githinji, PhD[1], Wonita Petersen NDip [1], Prof Mark F Cotton PhD[2], Prof Landon Myer PhD[5], Prof Heather J Zar, PhD [1,6].

Affiliation: [1.]Department of Paediatrics and Child Health, University of Cape Town, Cape Town, South Africa; [2.]Family Center for Research with Ubuntu (FAMCRU), Department of Paediatrics and Child Health, Stellenbosch University, Cape Town, South Africa; [3.]Wellcome Centre for Infectious Disease Research in Africa; Institute of Infectious Disease and Molecular Medicine, University of Cape Town, Cape Town 7925, South Africa; [4.]The Francis Crick Institute, London NW1 1AT, United Kingdom; [5.]Division of Epidemiology and Biostatistics, School of Public Health and Family Medicine, University of Cape Town, Cape Town, South Africa; [6.]SAMRC Unit on Child and Adolescent Health, University of Cape Town, Cape Town, South Africa

Objective:
There are limited data on Tuberculosis (TB) in adolescents with perinatal HIV (PHIV+). The objective of this study was to examine the incidence and determinants of TB infection and disease in the Cape Town Adolescent Antiretroviral Cohort (CTAAC).

Methods:
PHIV+ adolescents between 9-14 years on antiretroviral therapy (ART) for more than 6 months in public sector care, and age-matched HIV-negative adolescents, were enrolled between 2013-2015 and followed 6-monthly. Symptom screening, chest radiograph, viral load, CD4 count, QuantiFERON (QFT) and sputum for Xpert MTB/RIF, microscopy, culture and sensitivity were performed at enrolment and annually. TB infection was defined by a QFT of >0.35 IU/ml. TB diagnosis was defined as confirmed (culture or Xpert MTB/RIF positive) or unconfirmed (clinical diagnosis and started on TB treatment). Analyses examined the incidence and determinants of TB infection and disease.

Results:
Overall 496 HIV+ and 103 HIV-negative participants (median age at enrolment 12 (interquartile range, IQR 10.6-13.3) years were followed for a median of 3.1 years (IQR 3.0-3.4); 50% (298/599) were male. HIV+ participants initiated ART at median age 4.4 (IQR 2.1-7.6) years. At enrolment, 376/496 (76%) had HIV viral load <40 copies/ml, median CD4 count was 713 cells/mm^3, and 179/559 (32%) were QFT+, with no difference by HIV status (HIV+ 154/468, 33%; HIV negative 25/91, 27%; p=0.31). The cumulative QFT+ prevalence was similar (HIV+ 225/492, 46%; 95%CI 41% to 50%; HIV negative 44/98, 45%; 95% CI 35% to 55%; p=0.88). HIV+ adolescents had a higher incidence of all TB disease than HIV-negative adolescents (2.2/100PY, 95% CI 1.6 to 3.1 vs 0.3/100PY, 95% CI 0.04 to 2.2; IRR 7.36, 95% CI 1.01 to 53.55). The rate of bacteriologically confirmed TB in PHIV+ adolescents was 1.3/100 PY compared to 0.3/100PY for HIV-negative adolescents, suggesting a 4-fold increased risk of developing TB disease in PHIV+ adolescents despite access to ART. In addition, a positive QFT at enrolment was not predictive of TB in this population.

Conclusions:
High incidence rates of TB disease occur in PHIV+ adolescents despite similar QFT conversion rates to HIV-negative adolescents. Strategies to prevent TB in this vulnerable group must be strengthened.

Title: **ESTABLISHMENT OF A TB RESEARCH SITE IN THE EASTERN CAPE TO IMPROVE MICRIOBIOLOGICAL DIAGNOSIS AND TREATMENT OF CHILDHOOD TB**

Authors: Juaneta Luiz[1], Lesley Workman[1], Jacinta Munro[1], Cynthia Whitman[1], Yekiwe Hlombe[1], Margaretha Prins[1], Nomlindo Makhubalo[2], Zaahir Abrahams[2], Judi Van Heerden[3], Widaad Zemanay[3], Helen Cox[3], Mark P Nicol[3], Heather J Zar[1]

Affiliation: [1]Department of Paediatrics and Child Health, Red Cross Children's Hospital: SA-MRC Unit on Child & Adolescent Health AND TB-RePORT consortium, Cape Town, South Africa; [2]Department of Paediatrics, Dora Nginza Hospital, Port Elizabeth, South Africa; [3]Division of Medical Microbiology and Institute for Infectious Diseases and Molecular Medicine, University of Cape Town and National Health Laboratory Service South Africa

Background:
Microbiological diagnosis of pulmonary TB in children is challenging and often poorly done in healthcare facilities in high TB burden settings. New rapid diagnostics and improved methods for sampling have strengthened diagnostic options.

Objectives:
To establish and evaluate a program for microbiological confirmation of TB in children in a high burden setting.

Methods:
A research site was established at Dora Nginza Hospital in Port Elizabeth, South Africa for paediatric TB. Study and district hospital staff were trained in diagnosis and induced sputum (IS) with ongoing training and support. Children presenting to hospital with clinical suspicion of TB were prospectively enrolled, and clinical, radiological and microbiological investigations performed. Two sequential induced sputum (IS) specimens were obtained from each child, with each sample processed for culture and Xpert MTB/RIF (Ultra from January 2018). Children were classified as confirmed TB, unconfirmed TB or unlikely TB based on NIH consensus definitions. Children were followed-up regularly until six months post treatment completion.

Results:
Between 1 February 2017 and 31 December 2019, 1483 children were screened, and 422 enrolled. Median age was 32 months; 50% were male. 126 (30%) were HIV exposed uninfected (HEU), and 100 (24%) were HIV-infected of whom 29% were diagnosed with HIV at enrolment. ART coverage was 35%; 38% had a CD4% < 15%. There was a high prevalence of malnutrition; 153 (36%) stunted, with 51% and 33% in the HIV-infected and uninfected group respectively [p<0.001]. TST positivity was significantly lower in HIV-infected children (34%), but similar between HEU (65%) and HIV negative children (64%) [p<0,001].

Of the total cohort, 126 (30%) were confirmed TB, 257 (61%) unconfirmed TB and 39 (9%) unlikely TB. IS was successfully performed in 421 (99.7%) of children with at least one valid result for Xpert obtained for 416 (99.6%), and for Xpert and culture obtained for 406 (96.4%). The sensitivity and specificity of Xpert compared to culture from the first IS sample was 84% (95% CI, 72-91%) and 100% (95% CI, 92-100%) respectively. Amongst children with microbiologically confirmed TB, 107/126 (85%) were diagnosed on induced sputum. Xpert yield increased from 17% (27/156) in 2017 (culture yield, 23%) to 31% (80/260) in 2018-2019 (culture yield, 29%) with the introduction of Xpert Ultra, providing rapid microbiological diagnosis. Xpert detected an additional 20 cases not detected by culture, increasing the overall yield by 15%. There were higher rates of extra-pulmonary TB among HIV positive (36/100, 36%) versus HIV negative (80/309, 26%) children [p=0.05]. There were 19 DR TB cases (5%), 13 of which were microbiologically confirmed. Cohort retention was 73% at end-of-treatment. Mortality was 20/422 (5%); with 35% being HIV infected.

Conclusion:
A fully functional research site, was effectively established, with substantial capacity development, leading to increased rates of diagnosis and treatment of childhood TB and increased diagnosis of childhood HIV. Sputum induction with Xpert and culture, yielded high rates of microbiologic confirmation including drug-resistant TB. Microbiologic yield increased over time with use of Xpert Ultra providing one of the highest reported yields globally.

Funding: SA-MRC; NIH; TB-Report

Title: **WHEEZE PHENOTYPES AND THEIR EARLY-LIFE DETERMINANTS IN A SOUTH AFRICAN BIRTH COHORT STUDY**

Authors: Carlyle McCready[2], Sadia Haider[3], Francesca Little[2], Lesley Workman[1], Diane Gray[1], Shaakira Chaya[1], Adnan Custovic[3], Heather J Zar[1]

Affiliation: [1]SA-MRC Unit on Child & Adolescent Health, and Dept Paediatrics & Child health, University of Cape Town, South Africa; [2]Dept of Statistical Science, University of Cape Town; [3]Imperial College London, UK

Background: Wheezing illness is very common in young children, representing a spectrum of airway disease. Wheezing phenotypes and determinants have not been well studied in African children.

Objective: We aimed to investigate patterns of wheezing in a well characterised South African birth cohort, the Drakenstein Child Health Study (DCHS), followed from birth to 5 years, with comprehensive longitudinal measurement of associated risk factors from the antenatal period onwards.

Methods: Children enrolled in the DCHS were followed from birth through childhood, with active surveillance for intercurrent lower respiratory tract infection or wheezing. Wheezing was longitudinally identified by caregiver report using a validated questionnaire as well as by health worker ascertainment at health facilities at routine study visits and during intercurrent illness. Caregiver-reported questionnaires were completed at 14 different scheduled visits from birth up to and including 5-years of age, 6 of which occurred in the first 12-months and then at 6-monthly intervals, as well as during intercurrent illness. Exposure to tobacco smoke was measured by maternal self-report. Lung function was measured from 6 weeks and annually in healthy unsedated children.

Longitudinal profiles of presence/absence of wheeze were summarised using 6 characteristic indicators. Based on these indicators, the partitioning around mediods (PAM) algorithm was used to cluster the children into homogenous wheezing phenotypes by mapping a distance matrix into a user-specified number of wheezing classes. To characterise each identified wheezing phenotypes further, supervised analyses using multinomial logistic regression was used to identify phenotype specific risk-factors. Forward stepwise and backward stepwise approaches were used to select variables for entry into the model in addition to considering the inclusion of variables of specific clinical interest. Lung function variables were used to validate wheezing phenotypes using linear regression models adjusted for confounding by subject height and sex at 5-years.

Results: There were 1143 children enrolled, of whom 193/1143 were lost to follow-up or had incomplete data, providing a cohort of 950. Four unique wheezing phenotypes were identified: Phenotype 1 (n=495/950, 52.1%) were children with no wheezing symptoms; phenotype 2 (n=203/950, 21.3%) were children who experienced early wheeze soon after birth (from 6-weeks), phenotype 3 (n=106/950, 10.9%) experienced delayed wheeze (after 1-year), or phenotype 4 (n=146/950, 15.7%) with recurrent wheezing throughout the 5-year period.
Multinomial logistic regression identified phenotype specific early-life risk factors for wheeze. Ancestry, season of birth, HIV exposure, a child's BMI at first wheeze, postnatal tobacco smoke exposure or rhinovirus LRTI were associated risk factors for phenotype 2. Ancestry, prematurity, or rhinovirus LRTI were risk factors for phenotype 3. Sex, ancestry, or rhinovirus LRTI were risk factors for phenotype 4. The strongest and most consistent risk-factors were Black-African children (vs Mixed ancestry) or children who had a rhinovirus LRTI having significantly higher risks of developing wheeze.

Clinical validation of these phenotypes was completed using **XeI** (Respiratory reactance at the end of inspiration (zero-flow), hPa.s.L-1), **XeE** (Respiratory reactance at the end of expiration (zero-flow), hPa.s.L-1) and **XeI**, (**XeE**-**XeI**) differences, **FRC** (functional residual capacity, litres), and **Rei** (Respiratory resistance at the end of inspiration (zero-flow), hPa.s.L-1). Statistically-significant differences were observed between phenotypes, *Table 1*.

Conclusions: Childhood wheezing represents a heterogenous airway disease with phenotype-specific risk factors in African children. Early life LRTI, environmental or genetic factors influence wheezing risk.

Funding: Gates Foundation; UK-MRC; SA-MRC

Table 1: Coefficients and confidence intervals obtained using a linear regression model.

	Lung Function Measures at 60 months			
	FRC	Xei	dx Mean (XeE - XeI)	Rei
Phenotype 2 (vs Phenotype 1)	-0.011	-0.306**	0.226*	0.536**
	(-0.033, 0.011)	(-0.567, -0.044)	(-0.035, 0.487)	(0.062, 1.010)
Phenotype 3 (vs Phenotype 1)	0.030**	-0.429**	0.335**	0.448
	(0.003, 0.057)	(-0.754, -0.104)	(0.010, 0.660)	(-0.141, 1.036)
Phenotype 4 (vs Phenotype 1)	0.004	-0.137	-0.025	0.461*
	(-0.021, 0.029)	(-0.435, 0.161)	(-0.322, 0.272)	(-0.078, 1.000)
Sex (Male vs Female)	0.035***	0.177*	-0.051	-0.418**
	(0.018, 0.053)	(-0.030, 0.384)	(-0.257, 0.156)	(-0.793, -0.042)
Height at 60 months (cm)	0.010***	0.051***	0.002	-0.143***
	(0.008, 0.011)	(0.031, 0.072)	(-0.019, 0.022)	(-0.180, -0.106)
Constant	-0.440***	-7.300***	-0.186	24.235***
	(-0.624, -0.257)	(-9.482, -5.118)	(-2.364, 1.991)	(20.276, 28.195)
Observations	515	580	580	584
Note:				*p<0.1; **p<0.05; ***p<0.01

Title: **PERSONAL MONOTORING OF PARTICULATE MATTER ($PM_{2.5}$) EXPOSURE IN MOTHERS AND YOUNG CHILDREN IN A SOUTH AFRICAN BIRTH COHORT STUDY – A PILOT STUDY**

Authors: Aneesa Vanker[1], Whitney Barnett, Ryan Chartier, Rae MacGinty, Heather J. Zar

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Air pollution is an important cause of morbidity and mortality globally and a recognized risk factor for lower respiratory tract infections (LRTI). In children, LRTI are the leading cause of under-5 mortality,however, assessing personal exposure to air pollution is difficult. Particulate matter ($PM_{2.5}$), an important respirable component of air pollution, has been linked to adverse health outcomes. The MicroPEM® and Enhanced Children's MicroPEM® (ECM) are personal particulate matter exposure monitors. This pilot study aimed to assess the use and accessibility of the MicroPEM and ECM in mothers and children enrolled in the Drakenstein Child Health Study(DCHS), an African birth cohort study, and to investigate correlates of exposure to measured particulate matter.

Methods:
Mother-child pairs, already enrolled in the DCHS, were recruited to participate in the pilot study, with a MicroPEM(mother) and ECM(child) issued to each pair to be worn over 24 hours. Questionnaires were administered to assess home environment, wearability, and wearing compliance of the devices (quantitative and qualitative). Stepwise logistic regression identified risk factors for $PM_{2.5}$ exposure in both mothers and children.

Results:
From August – November 2016, results were obtained from 86 mothers and 75 children ranging in age from 1-4 years. Fossil fuels were used in 21% of homes and maternal smoking (37%) and exposure to household tobacco smoke (89%) was high. Wearing compliance of the devices (more than 40% of the time) was 56% in children and 48% in mothers. Measured particulate matter ($PM_{2.5}$) levels were above threshold (median 25ug/m^3 IQR [15.9-41.3 ug/m^3]) in 19/75 (25%) of children and was significantly associated with Winter; aOR 5.65 (95% CI 1.16; 27.50) p = 0.032 and with fossil fuels used for heating; aOR 12.06 (95% CI: 1.45; 100.01) p = 0.021. The measured concentrations of $PM_{2.5}$ in children and mothers were significantly correlated (Spearman's Correlation: rho=0.43; p-value= <0.0001).

Conclusion:
The MicroPEM® and ECM provide wearable low-burden personal exposure monitoring tools for women and children with relatively high rates of acceptability among at-risk populations.

Title: **CYSTIC FIBROSIS IN SOUTH AFRICA (SA): FIRST ANALYSIS FROM THE SA CF REGISTRY (SACFR)**

Authors: Zampoli M [(1)], Verstraete J [(1)], Frauendorf M [(2)], Kassanjee R [(3)], Workman L [(1)], Zar HJ [(1)] and Morrow B [(1)] and SA CF Steering Committee

Affiliation: [(1)]Department of Paediatrics and Child Health, MRC Unit for Child and Adolescent Health; University of Cape Town; [(2)]Milpark Netcare Hospital, Johannesburg, South Africa; [(3)]Centre for Infectious Disease Epidemiology and Research (CIDER); School of Public Health and Family Medicine; University of Cape Town

Introduction:
The epidemiology and spectrum of CF in SA was unknown prior to establishing the SACFR in 2018. South Africa is a low-middle income country characterized by diverse ethnicity, income inequality and unequal access to healthcare. Newborn screening is not offered in SA and access to CF diagnostic tests, multidisciplinary care and expensive therapies is limited or not available. This study aimed to describe the spectrum of CF in SA and report nutrition and lung function (LF) outcomes of individuals captured in the SACFR.

Methods:
The SACFR is a multi-center public-private collaboration which adopted similar data collection methods to the European CF registry. Demographics, diagnosis information and annual review data on nutrition, LF, microbiology, complications, therapies and mortality were prospectively collected from 2017. Cross-sectional and multiple regression analysis was conducted to explore factors associated with poor LF (Global Lung Initiative FEV1 z-score ≤ -3, from age 6 years and nutrition (WHO WAZ ≤-1.0 age < 2 years ; BMI z-score ≤ -1, children 2-18 years; BMI ≤ 18.5 kg/m^2, adults ≥ 18 years) outcomes in 2018.

Results:
By December 2019, 475 individuals were captured in the SACFR; 270 (57%) < 18 years age. Ethnicity was caucasian (327; 69%); mixed (96; 20%); black African (46; 10 %) and other (6; 1%). Genotype was p.Phe508del homozygous (220; 46%); p.Phe508del heterozygous (153; 32%) and neither p.Phe508del or unknown *CFTR* variant in 102 (22%); 3120+1G>A+1G>A was the second most frequent *CFTR* variant (allele frequency 10%) and most common in black Africans [26 (56.5%) homozygous; 14 (30%) heterozygous]. Median diagnosis age was 7.7 months (IQR 2.9-39.7); 270 (57 %) diagnosed under 1 year of age. In 2018, median age of the cohort was 15 years (IQR 8-26); 173 (39%) receiving care exclusively in the public sector. Poor LF (excluding 10 lung transplant recipients) and nutrition was present in 96/292 (33%; 26 children; 70 adults) and 91/398 (23%; 63 children; 28 adults) individuals, respectively. Poor LF was independently associated with chronic MRSA (OR 16.7; 95%CI 1.7-161), chronic *P.aeruginosa* infection (OR 1.9; 95% CI 0.9-4.3), poor nutrition (OR 5.2; 95%CI 2.2-12.1) and older age (OR 2.2 per 10-years; 95%CI 1.5-3.3). Poor nutrition was associated with lower WAZ at diagnosis, non-caucasian ethnicity, chronic *P.aeruginosa* infection and lower socioeconomic indicators including exclusive public healthcare and receiving a social welfare grant.

Conclusion:
Based on genotype, most (80%) people with CF in SA are eligible for CFTR modulator therapy which is currently not available in SA. Interventions to improve nutrition and improved treatment of MRSA and *P.aeruginosa* infections may improve lung function outcomes in SA.

Funding: Cystic Fibrosis Foundation (ZAMPOL19K0); National Research Foundation SA (UID: 117885); Harry Crossley Foundation, University of Cape Town; and SA CF Association.
No conflicts of interest declared; HREC 032/2019; abstract submitted to North American CF Congress, October 2020.

Title: **INTIMATE PARTNER VIOLENCE AND GROWTH OUTCOMES THROUGH INFANCY: A LONGITUDINAL INVESTIGATION OF MULTIPLE MEDIATORS IN A SOUTH AFRICAN BIRTH COHORT**

Authors: W. Barnett[1], S.L. Halligan, R. Nhapi, A. Fraser, J. Pellowski, H.J. Zar, K.A. Donald, D.J. Stein

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

Background:
Growth faltering during early childhood represents a significant indicator of both short and long-term health. Intimate partner violence (IPV) has been linked to poor fetal and infant growth outcomes. However, the factors underlying this relationship are not well understood, particularly in the postnatal time period. In a high-adversity South African birth cohort, we investigated: IPV in pregnancy and postnatally in relation to growth outcomes at birth and 12 months and the potential explanatory role of maternal depression, tobacco use, alcohol use or infant admission to hospital in IPV-growth relationships.

Methods:
Mothers were enrolled into the Drakenstein Child Health Study during their second trimester and mother-infant pairs were followed from pregnancy until 12 months of age. Maternal IPV (emotional, physical and sexual) was measured during pregnancy and at 10 weeks postpartum; depression, alcohol and tobacco use were measured during pregnancy and at 6 months postpartum. Child weight and length were measured at birth and 12 months. Linear regression and structural equation modelling were used to investigate predictors of weight-for-age z-scores (WFAZ) and length-for-age z-scores (LFAZ) at birth and at 12 months.

Results:
At birth, among 1,111 mother-infant pairs, both maternal emotional and physical IPV were associated with reduced WFAZ. Only physical IPV was associated with LFAZ at birth. Maternal alcohol use and tobacco use during pregnancy were key contributors to the relationship between IPV and birth WFAZ, with alcohol use being an explanatory variable for the relationship between physical IPV and LFAZ at birth. Postnatally, among 783 mother-infant pairs, both emotional and physical IPV were associated with reduced WFAZ at 12 months, Only emotional IPV was associated with LFAZ at 12 months. Postnatal maternal tobacco use emerged as the key explanatory variable in these relationships.

Conclusion:
Our findings contribute to a growing body of evidence showing that maternal IPV is detrimental to fetal growth, highlighting the role of emotional IPV in addition to physical IPV as a risk factor for compromised infant growth. Further, whereas alcohol and tobacco use emerged as explanatory factors in these relationships, maternal depression and child hospitalisations in this cohort, did not. These findings suggest the importance of interrelated psychosocial and environmental risk factors, which are prevalent and often co-occur in high-risk settings, in understanding drivers of compromised fetal and infant growth.

Ethics: The DCHS was approved by the Faculty of Health Sciences, Human Research Ethics Committee, University of Cape Town (401/2009) and by the Western Cape Provincial Health Research committee.

Title: **MAPPING CORTICAL STRUCTURE AND NEUROCOGNITIVE DEVELOPMENT OF HIV-EXPOSED UNINFECTED CHILDREN: NEUROIMAGING OUTCOMES FROM A SOUTH AFRICAN BIRTH COHORT**

Authors: Catherine J Wedderburn,[1,2,3] Shunmay Yeung,[2] Sivenesi Subramoney,[1] Jean-Paul Fouche,[3,4] Shantanu H. Joshi,[5] Katherine L. Narr,[5] Andrea M Rehman,[2] Annerine Roos,[1,3,6] Diana M Gibb,[7] Heather J Zar,[1,8] Dan J Stein,[3,4,6] Kirsten A Donald[1,3]

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Background:
There are an estimated 15.2 million HIV-exposed uninfected (HEU) children worldwide. HIV-exposure without infection has been associated with developmental delay, however, the neurobiological mechanisms are not yet understood and neuroimaging studies are lacking.

Objectives:
We compared the neuroanatomy of HEU and HIV-unexposed (HU) children aged 2-3 years and investigated associations with neurocognitive development.

Methods:
Children from the Drakenstein Child Health population-based birth cohort study underwent magnetic resonance imaging (MRI). Structural T1-weighted images were acquired on a 3-Tesla machine at the Cape Universities Brain Imaging Centre, South Africa during natural sleep. All mothers received HIV testing and antiretroviral therapy (ART) per local guidelines; HIV-exposed children were confirmed uninfected. Acquired structural T1-weighted images were processed using FreeSurfer software. Cortical thickness and surface area, components of cortical brain structure, were extracted from segmented images bilaterally. Given frontal brain structure supports many cognitive and language processes, regions-of-interest within the frontal lobe were compared between groups using multivariable linear regression adjusting for child age and sex. Neurocognitive development, assessed using the Bayley Scales of Infant and Toddler Development-III, was correlated with cortical structure.

Results:
MRI scans from 162 children (70 HEU, 92 HU) (mean age 34.1 months; 94 [58%] male) were included. Demographic characteristics of HEU and HU children were similar, including child sex, gestation and socioeconomic status (all $p>0.05$). HEU children had significantly higher cortical thickness measurements in the medial orbitofrontal cortex (mOFC) bilaterally (left: $p=0.04$, Cohen's d effect size 0.33 [95% CI 0.02 to 0.64]; right: $p=0.02$, effect size 0.38 [0.06 to 0.69]) compared to HU children. These results held after correcting for household income, maternal education and maternal age (effect sizes >0.35; all $p<0.05$). There were no group differences in cortical surface area. Further analyses revealed HEU children had lower language scores compared to HU children (effect size -0.38 [95% CI -0.73 to -0.04], $p=0.02$), and cortical thickness in the mOFC was negatively correlated with language development bilaterally (left mOFC: $r = -0.30$, $p=0.02$; right mOFC: $r = -0.35$, $p=0.008$).

Conclusions:
At age 2-3 years HEU children had increased cortical thickness in the prefrontal cortex compared to HU children, which correlated with poorer language outcomes. These findings are consistent with studies of child development that have shown cortical thickness in the frontal lobe is negatively associated with language abilities. This suggests that *in utero* HIV/ART exposure may affect cortical maturation processes of specific regions, impacting neurological development and cortical thickness trajectories, with implications to the growing HEU population.

Ethics approval number: HREC 044/2017

Title: **THE NURSES' ROLE IN SUPPORTING MOTHERS IN ADMINISTERING ORAL MEDICATION TO THEIR HOSPITALISED CHILDREN: MODIFICATION AND DEVELOPMENT OF A CONTEXTUALISED EVIDENCE-BASED PRACTICE GUIDELINE**

Authors: Andrea Amos[1,2], Nadia Harris[1,2], Nina Power and Natasha North

Affiliation: [1]The Harry Crossley Children's Nursing Development Unit, Department of Paediatrics and Child Health, University of Cape Town; [2]Division of Nursing & Midwifery, Department of Health and Rehabilitation Sciences, University of Cape Town

Background:
Adverse drug events and potential adverse drug events represent a considerable hazard for the paediatric inpatient population. In the paediatric wards medication has to be checked by two registered nurses before it is administered, often resulting in delays in medication administration since a second nurse is not always available on the floor. Children are often reluctant to receive medication from nurses and eventually medication is given by the parents. It has been acknowledged that current practice in many wards is for nurses to hand over medication to mothers to give to their children, but this is an 'informal' practice and lacks evidence-based guidelines.

Purpose:
The purpose of this project was to develop a contextualised and adapted evidence-based guideline to enable nurses to partner with mothers/carers, for the mother/carer to be competent and safely administer oral medication to their hospitalised child under the supervision of a competent nurse. Good medicines management is essential for high standards of clinical care.

Methods:
A structured, transparent and replicable search (PubMed and CINAHL) was conducted to identify existing guidelines relating to the topic of concern. The AGREE II instrument was used to appraise the quality of the identified guidelines and policy document. Appraisal was carried out by two to three independent reviewers who were all children's nurses and postgraduate students. The three-tiered process of guideline adaptation recommended by Dizon, Machingaidze & Grimmer (2016) was followed, involving compilation of the evidence base, obtaining expert input and developing end user guidance documents. A list of adapted recommendations was developed and scored according to levels of evidence and grade of recommendation using evidence from the appraised guidelines, as well as supplementary searching, with the addition of the legislative and regulatory frameworks which govern nursing practices in South Africa. A flowchart was developed as an easy to understand process map, visually representing the recommendations in the form of step by step instructions.

Results:
Six guidelines were screened and three items were found to eligible and subjected to full appraisal. It was found that there is a lack of evidence-based practice guidelines regarding the practice of mothers administering oral medication to their hospitalised children. Two guidelines were identified as suitable for adaptation: *Medicines optimisation: the safe and effective use of medicines to enable the best possible outcomes* (National Institute for Health and Care Excellence); and *Clinical Guideline for Self/Carer Administration of Medicines* (Guy's and St Thomas' NHS Foundation Trust.) A policy document was also included as it contained relevant resources**:** *Supporting Children and Young People with Health Care Needs and Managing Medicines in Educational Establishments* (NHS Grampian Aberdeenshire Council: Scotland). Expert consultation confirmed that the resulting adapted guideline was sound, easy to understand and well presented for the target audience.

Conclusion:
Clinical practice guidelines provide a systematic approach to different clinical circumstances and disease profiles of patients in the healthcare system. Developing new clinical practice guidelines can be time-consuming and expensive. A more efficient approach could be to adopt, adapt or contextualize recommendations from existing good quality CPGs so that the resultant guidance is tailored to the local context. An evidence based practice guideline which enables nurses to partner with mothers/carers, for the mother/carer to be competent and safely administer oral medication to their hospitalised child under the supervision of a competent nurse in lower-resourced African settings, will assist with building rapport between nurses and mothers/carers. The mother/carer will have a sense of purpose and feel included in the care of their children whilst admitted in hospital and the EBPG may help avoid potential adverse drug events, assist with the issue of medication not being given on time due to shortage of staff, and aid in treatment compliance in children not only in the hospital but upon discharge as well. This is new research. Ethical approval was not required due to the nature of the work.

Statement of contributions: AA and NP undertook all aspects of the work together in accordance with UCT's guidance on collaborative and group work, supervised by Natasha North and Nina Power. Adess Mwale, Busisiwe Jama and Elijeshca Crous assisted with co-appraisal of guidelines.

Title: **A NEW STYLE OF HOSPITAL JOURNAL CLUB: ENGAGING NURSES IN RESEARCH AWARENESS**

Authors: Angela Leonard[1], Natasha North, Candice Bonaconsa and Minette Coetzee

Affiliation: [1]The Harry Crossley Children's Nursing Development Unit, Department of Paediatrics and Child Health, University of Cape Town

Objective:
Nurses, especially nurses in Africa, face barriers when trying to access and apply literature. These challenges include paywalls limiting access to journals; complex academic language; unfamiliar research terms and processes, and journal content which originates from high-income countries and is hard to translate to local realities. These factors may contribute to nurses feeling and being distanced from academic literature, reinforcing the evidence to practice gap. The journal club established at the Red Cross War Memorial Children's Hospital (RCWMCH), by researchers from the Children's Nursing Development Unit, aimed to break down the barriers to accessing research by providing an ongoing opportunity for nurses to access and explore scientific literature together in a relaxed, non-threatening environment, using a consistent and recognisable structure and participatory format. The aim of this study was to investigate of the impact of a monthly hospital wide journal club on nurses' access to scientific literature, personal and organisational habits of reading, and collaborative exploration of clinical practice.

Methods:
A descriptive questionnaire study using a quantitative questionnaire design was conducted at the RCWMCH. The questionnaire survey was developed by the research team. Survey questions were designed using the Total Survey Design methodology to examine the impact of journal clubs on nurses' access to scientific literature, personal and organisational habits of reading, and collaborative exploration of clinical practice. All cadres of nurses who had attended six or more hospital journal club sessions over the previous two years were purposefully recruited.

Results:
155 participants completed the survey (96.87% response rate). Participants self-reported an improved ability to answer questions about a journal article ($p<0.002$) and a significant increase in talking to colleagues about evidence-based nursing practice after attending journal club compared with before ($p<0.0004$). Enjoyment of attending the innovative journal club was reported by 87% of the participants. Results further demonstrate that the nurses understanding of the research article was improved using the innovative visual facilitation method (large-scale graphic).

Conclusions:
Attendance at a journal club appears to be of value and potentially contributes to increased access to scientific literature, personal and organisational habits of reading, and collaborative exploration of clinical practice for all categories of nurses.

This study was approved by the Human Research Ethics Committee of the University of Cape Town (HREC REF: 577/2019). This work was presented at the 5th Commonwealth Nurses and Midwives Conference in London in March 2020 with support from a DPCH Travel Award.

Title: **UNDERNUTRITION IN KHAYELITSHA, CROSSROADS AND BROWNS FARM: A REVIEW OF NUTRITIONAL OUTCOMES OF CHILDREN TREATED AT PHILANI CLINICS FROM 2008 TO 2018**

Authors: Claudine Bill[1], Rebecca Sher[1], Rudzani Muloiwa[1]

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

Objective:
Acute and chronic malnutrition continue to impede child health and well-being in South Africa. While rates of severe acute malnutrition have declined, moderate malnutrition has persisted at unacceptably high rates. This study aims to assess the nutritional outcomes of children under five years of age referred for underweight or growth faltering who were followed up at Philani clinics in Khayelitsha, Crossroads and Browns Farm, between 2008 and 2018.

Methods:
We conducted a retrospective cohort study, using Philani medical records, of children under 5 years who attended a Philani clinic between 2008 and 2018. The nutritional status of each child was assessed using World Health Organisation's weight for age z-scores (WAZ). Children with WAZ below – 2 WAZ were classified as moderately underweight for age, while below – 3 WAZ were classified as severely underweight for age. The outcome was rehabilitation of weight to WAZ> -2. Data were collected from folders randomly selected from 933 children under 5 years, who attended a clinic and were followed up for minimum of three months. Continuous data were summarised using medians and interquartile ranges while percentages depict categorical data.

Results:
Of the 410 folders reviewed 224 (54.6%) were of girls . HIV status was known for 296 (72.2%) of whom 37 (12.5%) were HIV positive. The median age of the children at the time of entry was 9.6 (interquartile range (IQR) 4.2-16.0) months, with the follow-up period of median 11.2 (IQR 6.9-18.0) months. A total of 365 (89.0%) were assessed as moderately to severely underweight for age. In 151/365 (41.4%) of the children, WAZ was rehabilitated to > -2 while 214 (58.6%) were not rehabilitated although 109 (29.9%) there was some improvement in their centiles without gaining full rehabilitation. Children who were rehabilitated were first seen at the age of 7.6 (IQR 3.1-12.8) months while those not rehabilitated presented at 12.9 (IQR 6.9-20.9) months; P=0.0001. The follow-up period for children whose nutrition was rehabilitated was 10.1 (IQR 6.7-14.9) months compared to 12.7 (IQR 8.1-21.2) who were not rehabilitated; P=0.0024. Seven children (1.9%) died, all without rehabilitation. In total 134 (62.6%) of the ones who failed rehabilitation exited by being lost to follow-up compared to lost to follow up in 48 (31.8) who were rehabilitated at exit; P<0.001.

Conclusions:
Failure of rehabilitation in children with severe to moderate malnutrition was associated with older age of referral to the Clinic and a longer follow-up period. The risk of loss to follow-up in those who failed rehabilitation was double that in the success rate. There is a need to explore reasons underlying this observed pattern.

HREC Ref:033/2020.

This is new research.

Title: **INVESTIGATION OF COPY NUMBER VARIATION IN SOUTH AFRICAN PATIENTS WITH CONGENITAL HEART DEFECTS**

Authors: Nicole Saacks[1]; Timothy Spracklen; James Eales; Thomas Aldersley; John Lawrenson; Blanche Cupido; George Comitis; Rik De Decker; Barend Fourie; Lenise Swanson; Alexia Joachim; Phaphama Magadla; Raj Ramesar; Gasnat Shaboodien; Bernard Keavney; Liesl Zuhlke

Affiliation: [1]Department of Medicine, University of Cape Town

Objectives:
Congenital Heart Disease (CHD) is the leading non-infectious cause of paediatric morbidity and mortality worldwide. The aetiology of CHD is poorly understood, though heritable genetic factors including copy number variants (CNVs) have been shown to contribute to the risk of CHD in individuals of European ancestry. However, the role of rare CNVs in the development of CHD in South Africa is unknown. Partnerships for Congenital Heart Disease in Africa (PROTEA) is a collaborative project between the University of Cape Town (UCT) and the University of Manchester designed to address the gaps in CHD epidemiology as well as better understand the genetic underpinnings of CHD in Africa. This sub-study of the PROTEA projects aims to identify pathogenic and likely pathogenic CNVs in South African cases of CHD. To our knowledge, this is the first study to investigate the genetic basis of CHD in a South African cohort.

Methods:
The PROTEA study cohort included 105 patients with non-syndromic isolated CHD (n = 76), CHD with additional extra-cardiac anomalies (n = 17) and positive controls with syndromic CHD (n = 12). Genotyping was performed using the Affymetrix CytoScan HD platform. Rare CNVs were filtered using stringent criteria for their size and algorithm-specific quality score, and were compared against a gene panel of known associated CHD genes. Candidate genes were considered based on pLI scores and reported CHD phenotypes in mouse models. The identified CNVs were validated by quantifying the read-coverage of available whole-exome sequencing data of a similar overlapping cohort.

Results:
Chromosomal microarray analysis was successful for 101 participants (including 89 non-syndromic CHD cases and 12 control cases), and led to the identification of eight CNVs overlapping genes known to be causal for CHD, and four CNVs encompassing candidate genes likely to play a role in the development of CHD. The CNVs were identified in nine unrelated individuals, five of the CNVs were classified as pathogenic or likely pathogenic (5.6% of the cohort) and four were classified as variants of unknown significance (4.6%). CNVs of interest were validated using the available whole-exome sequencing data.

Conclusions:
In this sub-study of the PROTEA project, we show that chromosomal microarray analysis can be performed locally in South Africa, producing results similar to those seen in international CHD studies. The findings of this thesis highlight the genetic heterogeneity of CHD and the growing importance of CHD genetic studies for both research and clinical purpose. Advancing our understanding of CHD aetiology will help define disease risk in South Africa and improve the way we care for and assess our cardiac patients.

HREC Ethics approval number: 339/2019
**This is new research*

Title: **FAVOURABLE OUTCOMES FOR CHILDREN WITH BIOPSY PROVEN MALIGNANT EXTRACRANIAL GERM CELL TUMOURS 1990-2015: A FIRST NATIONAL REPORT BY THE SOUTH AFRICAN CHILDREN'S CANCER STUDY GROUP (SACCSG)**

Authors: Hendricks M[1], Cois A[2,14], Geel J[3], du Plessis J[4], Bassingthwaighte M[5], Naidu G[5], Rowe B[5], Buchner A[6], Omar F[6], Thomas K[7], Uys R[8], van Zyl A[8], van Heerden J[9,13], Mahlachana N[5], Vermeulen J, Davidson A[1], Frazier L[11], Donald K[12], Kruger M[6]

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Objectives:
The management of malignant extracranial germ cell tumours (MEGCTs) requires a comprehensive multidisciplinary team approach to achieve the best possible survival rates. In preparation for harmonised national treatment protocol development, a South African national retrospective analysis was performed to investigate treatment outcomes of children and adolescents with MEGCTs.

Methods:
Retrospective data from nine South African paediatric oncology units was collected and interrogated to establish the range of treatment protocols used, 5-year overall survival (OS) and prognostic factors.

Results:
Between January 2000 and December 2015, 217 children were diagnosed with MEGCTs. The male to female ratio was 1:2.6 (60 males with median age 22.5 months and 157 females with median age 97.0 months). Female sex was associated with a significantly lower risk of death (OR = 2.26, p=0.035). Advanced stage significantly affected 5-year OS: Stage I (n=59; 96%), stage II (n=37; 94.3%), Stage III, (n=74; 75.5%; p=0.017) and Stage IV (n=46; 60.1%; p<0.001). Patients with a pre-operative serum AFP level of >33,000 ng/ml at diagnosis had poorer outcomes (p=0.002).
Chemotherapy regimens included JEb (42.4%), BEP (41.8%), PEb (3.6%) and other (6.2%). Thirty six patients (16.5%) died, mostly from progressive disease (31). The remaining five deaths were treatment related: infection (3), secondary acute myeloid leukaemia (1), pulmonary fibrosis (1) and a surgical complication (1). Only 15/91 (16.4%) patients who received cisplatin-based chemotherapy had a documented glomerular filtration rate (GFR) at diagnosis and only 11/91 (12.1%) an audiogram. Nineteen patients receiving cisplatin-based chemotherapy developed hearing deficits, 4 were severe.

Conclusions:
This study is the largest cohort of paediatric MEGCTs reported from sub-Saharan Africa demonstrates a favourable 5-year OS of 80.3% with Stage IV patients achieving a 60.1% OS. Female sex was associated with a significantly lower risk of death. Stage and elevated serum AFP levels were independently predictive of outcome. A standardised national protocol will be implemented to further improve survival, especially for those with advanced disease.

Title: **ASSOCIATION BETWEEN DURATION OF VIROLOGICAL FAILURE AND CLINICAL OUTCOMES IN A COHORT OF ADOLESCENTS ON ANTI-RETROVIRAL THERAPY**

Authors: Rebecca Sher[1], Sipho Dlamini, Rudzani Muloiwa

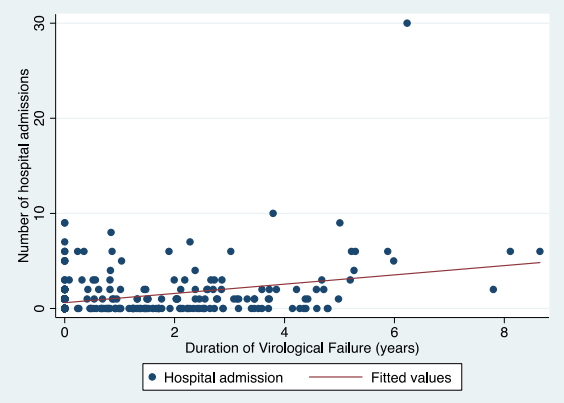
Affiliation: [1]Department of Paediatrics & Child Health, University of Cape Town

Objectives:
Despite advances in treatment options and access to anti-retroviral therapy (ART), adolescents living with HIV continue to have worse outcomes than children and adults. There is lack of longitudinal data around adolescent adherence and the dynamics of viraemia over time. In particular, the impact of the duration of virological failure (VF) has been poorly explored. We aimed to investigate the association between the duration of virological failure and clinical outcomes in a cohort of adolescents on ART.

Methods:
We conducted a retrospective cohort study of all patients on ART aged 10-19 years. Participants were included if they underwent at least two HIV viral load (VL) measurements and attended the Groote Schuur Hospital HIV Clinic for at least 24 months between 2002 and 2016. VF was defined as a confirmed VL >100 copies/ml, in line with the lower limit of detection of assays in use over the follow-up period. The primary outcome was a clinical event defined as TB diagnosis or hospital admission due to any cause.

Results:
Of 482 screened subjects, 327 met inclusion criteria. Most subjects were vertically infected (n= 314; 96%), and 170 (52%) were male. Overall, 203 episodes of VF involving 159 (49% [95% CI 43%–54%]) subjects were experienced during the follow-up period. Total follow-up time was 1723 person years (PY), of which 880 (51%) were contributed by the 159 subjects who experienced VF. Overall time with VF was 370 PY. This comprised 22% of total follow-up time, but 42% of the follow-up time contributed by those who experienced VF.

Overall, 381 hospital admissions occurred, involving 143 (44%) subjects. Total incidence of hospital admission was 22.1 per 100 PY. The most common diagnosis on hospital admission was lower respiratory tract infection excluding TB (n=59, 16%), followed by unspecified HIV infection (n=56, 15%) and all forms of TB (n=30, 8%). There were 49 diagnoses of TB involving 46 (14%) participants, for a total incidence of 2.8 per 100 PY. Participants experiencing detectable VL during the follow up period were 1.45 times more likely to have at least one hospital admission (95% CI 1.12–1.87, p=0.004) and 1.98 times more likely to be diagnosed with TB (95% CI 1.12-3.49 p=0.015). The incidence of hospital admissions and TB diagnoses increased with increasing duration of VF (Figure).



Conclusion:
VF is common in adolescence, and adolescents who experience it spend significant proportions of time in this state. Monitoring the duration of VF may help to identify adolescents at especially high risk of adverse clinical outcomes.

Title: **NEONATAL MORTALITY IN THE CAPE TOWN METRO WEST GEOGRAPHICAL SERVICE AREA 2014-2017**

Authors: C. Afonso[1], M.K. Hendricks, N. Rhoda, A. Masu

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Background:
Each neonatal death counts, as recognised by the Every Newborn Action Plan (ENAP). This is an important aspect in attaining the third Sustainable Development Goal by 2030. Accurate neonatal mortality data as well as an understanding of the causality and context is essential to plan interventions to reduce neonatal deaths and attain the third Sustainable Development Goals (SDG) of a neonatal mortality rate of less than 12 per 1000 livebirths by 2035.
Objectives
The objectives of this study were: (i) to determine neonatal mortality occurring in and out of health facilities in the Metro West GSA using the three audit programmes; Perinatal Problem Identification Programme (PPIP), Child Healthcare Problem Identification Programme (Child PIP) and Forensic Pathology Services (ii) to ascertain the cause of death specific neonatal mortality (iii) to describe the avoidable factors in each death as coded by the three audit programmes (iv) to make recommendations for the alignment of existing audit databases to obtain accurate neonatal statistics for the Metro West GSA.

Methods:
This was a retrospective descriptive study of neonatal deaths undertaken in the public healthcare setting in the Cape Town Metro West GSA from January 2014 till December 2017. Existing data from PPIP, Child PIP and the CDR/FPS was used. Neonatal deaths were defined as in the first 28 days of life where there had been signs of life at delivery and a birthweight greater than 500g. Neonatal deaths were excluded where birth had occurred outside of the GSA or in the private health care setting. The audit data with regards to cause of death and avoidable or modifiable factors was obtained for each death.

Results:
From a total of 134843 live deliveries, 1243 neonatal deaths were identified: 976(78%) from PPIP, 58(5%) from Child PIP and 209 (17%) from CDR/FPS. Sixteen per cent of the deaths occurred outside of healthcare facilities. The neonatal mortality rate (NMR) for PPIP was 7.2, Child PIP 0.43 and CDR 1,6 per 1000 livebirths. When the audit systems were combined, the annual NMR over the study period varied from 8.05 to 10.1 with a mean of 9.2 per 1000 livebirths over the entire period. Seventy-eight per cent of the deaths occurred in the early neonatal period with a mean early neonatal mortality rate of 7.2 per 1000 livebirths. The mean late NMR was 2 per 1000 livebirths. Where all neonatal deaths were considered for those more than 500g, the main cause of death was immaturity related, then infection related followed by congenital disorders and then hypoxia related. Seventy-four per cent of deaths occurred in those less than 2500g at birth and 41% were less than 1000g and defined as extremely low birthweight. In the group of neonates greater than 1000g, the main cause of death was infection related deaths, closely followed by congenital disorders and then hypoxia, followed by immaturity. Most of infection related deaths were collected by the CDR and Child PIP. A third of Child PIP and PPIP deaths and half of the CDR deaths were coded as avoidable. The prevalence of deaths due to abandonment either by passive or active neonaticide contributed towards the higher proportion of preventable deaths in the CDR group.

Conclusions:
The burden of deaths due to immaturity is high and may be attributed to the finding that 41% of neonatal deaths were in the ELBW group. Current viability criteria that aim at optimum use of resources may improve survival amongst this group. Infection related deaths were shown by this study to have a greater burden than recorded from PPIP data; most of these deaths were derived from Child PIP and CDR data. Also, where 10% of neonatal deaths were sudden unexpected deaths (SUDIs), a better understanding and definition of this group is urgently required as many of these deaths were subsequently found to be secondary to lower respiratory infections. It is further relevant that where 20% of CDR deaths or 3% of all the study deaths were due to active and passive neonaticide, this entity should be monitored and investigated. The study showed that the GSA has achieved the SDG for NMR of less than 12 per 1000 livebirth. However, a mean NMR of 9.2 per 1000 livebirths is not comparable to other upper middle-income countries. As 38% of the deaths were coded as avoidable, appropriate programmes to address these factors could reduce the NMR to 5.7 per 1000 livebirths. A strong recommendation from this study would be to use all three audit systems to calculate the NMR, understand the causes of neonatal deaths and plan programmes to improve neonatal survival in this GSA.

Title: **AETIOLOGY OF PLEURAL INFECTIONS IN CHILDREN AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL IN THE POST-PCV ERA: A PROSPECTIVE STUDY**

Authors: Golden L[1], Chaya S, Reichmuth K, Ayuk A, Kwarteng Owusu S, Marangu D, Affendi N, Lakhan A, Gray D. Vanker A, Zar HJ and Zampoli M.

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

Background and Objective:
Pleural effusions (PE) in children are commonly caused by bacterial infections and *M. tuberculosis* (TB). Parapneumonic effusion (PPE) and empyema are recognised complications of pneumonia, resulting in prolonged hospital stay and increase in morbidity. Distinguishing TB and bacterial PE is difficult without microbiological confirmation. We investigated the aetiology of PE and describe clinical features that distinguish TB and bacterial PE in children which could be useful to guide medical treatment.

Methods:
This was a prospective, descriptive observational study. Children admitted to Red Cross War Memorial Children's Hospital with PE between December 2016 and December 2019 were enrolled. Comparison of routine blood, pleural fluid and microbiological investigations of PE aetiology categories was undertaken. PE aetiology was categorised as confirmed or unconfirmed: bacterial, TB or unclassified according to study-defined clinical definitions.

Results:
Ninety-one patients were included in the study, of which 56(61%) were male. Median age was 31 months (IQR 11,8 - 102,1). Aetiology (confirmed and unconfirmed) was classified as bacterial in 37 (40%), TB in 36 (40%) and unclassified in 18 (20%). Among the bacterial group, 14/31(45%) blood and 25/37 (68%) pleural fluid samples were culture-positive; *S.aureus* was the most common bacterial isolate, confirmed in 24/37(65%) of bacterial group patients. Among the TB group, microbiological confirmation by GeneXpert/GeneXpert-Ultra or TB culture was possible in 12/36 (33%) patients. Pleural fluid was GeneXpert/GeneXpert-ultra positive in 5 (14%), and TB culture positive in 8 (22%) of all TB cases. Mantoux was positive in 24/36 (67%) TB cases, 2/18 (11%) unclassified cases and negative in all bacterial cases. Compared to bacterial group, patients with TB were: older (91.6 vs 11.8 months, p=0.0001), reported more weight loss (28 vs 12 patients, p <0.0001) , chest pain (22 vs 7 patients, p= <0.00001) and longer cough duration (10 vs 4 days, p= 0.01). Comparison of selected laboratory findings of bacterial, TB and unclassified groups is presented in table below.

	Bacterial	TB	Unclassified	Total	-value
WCC	16,6 (10,6 - 27,7)	10,3 (7,9-13,1)	14,4 (5,0-21,7)	12,0 (8,1-23,5)	0.0049
CRP	250,5 (188,5-305)	122 (75-156)	125,5 (54-236)	171 (102-257)	0.0001
PCT	11,6 (3,4-29,4)	0,46 (0,24-1,43)	4,8 (0,17-14,31)	2,7 (0,39-12,73)	0.0001
Fluid TP	46,5 (37-51)	55 (51-58)	55 (47-60)	51,5 (42-57)	0.007
Fluid LDH	7280 (3433-16844)	544 (386-820)	325,5 (358,5-951)	1071 (473-855)	0.0001
Fluid glucose	1,25 (0,6-3,15)	4 (3-5)	5,05 (4-5,6)	3,5 (1,7-4,7)	0.0001
Fluid ADA	162,2 (60,5-339)	47,9 (41,7-59)			0.0003
Fluid polys	1340 (605-3280)	27 (5,5-120)	260 (106-400)	133 (11-530)	0.0001
Fluid lymphs	460 (115-720)	832 (419-1522)	400 (155-800)	664 (224-1185)	0.1419

Overall, clinical and laboratory findings of the Unclassified group tended to in the range between TB and bacterial, with exception of more patients in this group (78%) receiving prior antibiotics compared to TB (44%) and bacterial groups (54%), p=0.06.

Conclusion:
In the post-PCV era, *S. aureus* is the dominant cause of PPE and empyema in children. Despite useful clinical and laboratory differences between TB and bacterial PE, the cause of PE in a proportion of children was undetermined. Molecular (PCR) testing of pleural fluid for pathogens may be useful in children with undetermined PE aetiology.

Ethics approval number: HREC REF 661/2019; This is new research
Funding: Dept Paediatrics Research Award

Title: **OUTCOMES OF CHILDREN WITH BIOPSY PROVEN LANGERHANS CELL HISTIOCYTOSIS (LCH) TREATED AT THE RED CROSS CHILDREN'S HOSPITAL FROM 1998 – 2017**

Authors: Loyce Hlatywayo[1], Alan Davidson[1]

Affiliation: [1]Haematology-Oncology Service, Department of Paediatrics and Child Health, Red Cross Children's Hospital and the University of Cape Town

Objective:
Present the course of disease and the outcomes of treatment in children who had Langerhans Cell Histiocytosis (LCH) at Red Cross Children's Hospital from 1998 to 2017.

Methods:
A retrospective document review of all children diagnosed with LCH at Red Cross War Memorial Children's Hospital (RCWMCH) between 1998 and 2017. Data was collected from patient folders and entered into Microsoft access database. Data was transferred and analyzed in Statistica. Where two groups were compared, using the log rank test a p value of 0.05 was regarded as significant.

Results:
There were 30 patients between the ages of 1 month and 12 years with a median age of 2 years. The male to female ratio (M:F) was 1:1.5.Seventeen patients(56.7%) presented with multisystem disease with risk organ involvement(MS RO LCH).Twelve patients (40%) had single system LCH(SS LCH) and only one patient had multisystem disease with no risk organ involvement. The patients were treated with modified versions of serial Histiocyte Society LCH – protocols.
Overall mortality of the whole group was 16.7% with a 5 year overall survival (OS) of 83% and a 5 year EFS of 58%. SS- LCH patients fared better with 5 year OS of 100% and EFS of 90%.Considering the whole group ,the 5 year OS was lower in patients < 1 year of age (44 % versus 100 % in children >1 year of age (p value of 0.002),as was EFS (15% versus 77% p value of 0.008).

Conclusion:
Patients with MS RO LCH had a poorer outcome despite more intensive therapy. The 5-year OS and EFS were consistently lower in those patients less than 1 year of age at diagnosis.

HREC REF: 014/2020
New Research

Title: **PATTERNS OF MORTALITY IN CHILDREN PRESENTING TO A TERTIARY PAEDIATRIC EMERGENCY UNIT IN SUB-SAHARAN AFRICA: A CROSS SECTIONAL STUDY**

Authors: Tracey Josephs [1,] Adelaide Masu[2], Rudzani Muloiwa[3] , Heloise Buys[4]

Affiliation: [1] Paediatrics, Khayelitsha District Hospital; [2] Child Health Unit, Department of Paediatrics and Child Health, University of Cape Town; [3] Groote Schuur Hospital & Department of Paediatrics and Child Health, University of Cape Town; [4] Red Cross War Memorial Children's Hospital & Department of Paediatrics and Child Health, University of Cape Town

Objectives:
Pneumonia, diarrhoea and perinatal factors are the foremost killers of South African children as in other low- to middle-income countries. This is mainly due to pre-hospital predisposing factors such as poverty and poor access to care. However healthcare related factors such as inadequate pre and in-hospital treatment contribute to the burden of disease. This study aimed to describe the in-hospital mortality, clinical presentation and the management of children admitted via the medical emergency unit (MEU) of the Red Cross War Memorial Children's Hospital (RCH)

Methods:
We did a retrospective study undertaking a cross-sectional review of children who died following admission via RCH MEU in 2008. Demographic information, clinical data, time factors and mortality data were reviewed and summarised by descriptive and inferential statistics. The unit utilised the WHO Emergency Triage Assessment and Treatment (ETAT) triage tool, categorising children into Red (emergency), orange (priority) and Green (non-urgent). Patient management was assessed by means of ETAT and the Integrated Management of Childhood Illness (IMCI) tool, which is used to identify severity of illness and strategize treatment plans accordingly.

Results:
A total of 135 children met the inclusion criteria. The crude in hospital mortality rate was 3.8 per 1000 MEU attendees. Of the 135 children who died, 119 (88%) were under five years of age, 33(24%) were HIV-infected, of whom 29 (88%) were under 5 years old. In 67 (50%), a chronic medical condition could be identified while 67 (50 %) were moderately or severely malnourished. There were 29 (22%) deaths within 24 hours of arrival at the MEU. Fifty-five (41%) presented after hours. Community health centres referred 65 (48%) patients, general practitioners referred 20 (15%) and 38 (28%) were self-referred. Ambulance services provided pre-hospital transport to 69 (51%). The two top presenting illnesses in 88 (65%) of the children were acute respiratory illness and acute gastroenteritis. Prior to referral, oxygen was not provided in 57 (59%) children, 35 (71%) with suspected sepsis did not receive antibiotics and glucose was not checked in 39 (80%) with depressed level of consciousness. The median time to ward transfer was 3.23 (IQR: 2.12-4.92) hours. Twelve deaths (9%) occurred in the MEU, 57 (42%) in intensive care unit, 56 (42%) in medical wards and 10 (7%) in specialist wards. The five most common causes of death were acute respiratory infections in 45(33%), acute gastroenteritis in 27(20%), septicaemia in 22 (16%), cardiac conditions in 12 (9%) and meningitis in 12 (9%) children.

Conclusion:
The top causes of mortality in this hospital cohort in 2008 were pneumonia, acute gastroenteritis, and septicaemia. Using the IMCI and ETAT standard of care, suboptimal management was identified in pre-hospital management. Appropriate training and protocol implementation to improve morbidity and mortality should be undertaken.

Title: **CLINICAL USE AND INDICATIONS FOR HEAD COMPUTED TOMOGRAPHY IN CHILDREN PRESENTING WITH ACUTE MEDICAL ILLNESS IN A LOW- AND MIDDLE-INCOME SETTING**

Authors: Pamela Machingaidze[1,2], Heloise Buys[1,2*], Tracy Kilborn[2,3], Rudzani Muloiwa[1,4]

Affiliation: [1]Department of Paediatrics and Child Health, University of Cape Town, South Africa; [2]Red Cross War Memorial Children's Hospital; [3]Department of Radiology, University of Cape Town, South Africa; [4]Department of Paediatrics, Groote Schuur Hospital

Objectives:
Computed tomography (CT) imaging is an indispensable tool in the management of acute paediatric neurological illness providing rapid answers that facilitate timely decisions and interventions that may be lifesaving. While clear guidelines exist for use of CT in trauma to maximise individual benefits against the risk of radiation exposure and the cost to the healthcare system, the same is not the case for medical emergency. This study primarily aimed to retrospectively describe indications for non-trauma head CT and the findings at a tertiary paediatric hospital.

Methods:
Records of children presenting with acute illness to the medical emergency unit of Red Cross War Children's Hospital, Cape Town, over one year (2013) were retrospectively reviewed. Participants were included if they underwent head CT scan within 24 hours of presentation with a non-trauma event. Clinical data and reports of CT findings were extracted.

Results:
Inclusion criteria were met by 311 patients; 188 (60.5%) were boys. The median age was 39.2 (IQR 12.6-84.0) months. Most common indications for head CT were seizures (n=169; 54.3%), reduced level of consciousness (n=140;45.0%), headache (n=74;23.8%) and suspected ventriculoperitoneal shunt (VPS) malfunction (n=61;19.7%). In 217 (69.8%) patients CT showed no abnormal findings.
In the 94 (30.2%) with abnormal CT results the predominant findings were hydrocephalus (n=54;57.4%) and cerebral oedema (n=29;30.9%). Papilloedema was more common in patients with abnormal CT (3/56; 5.4%) compared with none in those with normal CT; P=0.015; while long tract signs were found in 42/169 (24.9%) and 23/56 (41.1%) of patients with normal and abnormal CT findings, respectively; P= 0.020. Post-CT surgery was required by 47(15.1%) of which 40 (85.1%) needed a ventricular drainage. A larger proportion of patients with VPS (25/62; 40.3%) required surgery compared to patients without VPS (22/249; 8.8%; P<0.001).

Conclusion:
A majority of head CT scans in children with medical emergency with acute neurological illness were normal. Patients with VPS constituted the majority of patients with abnormal CT scans that required subsequent neurosurgical intervention. Evidence-based guidelines are required to guide the best use of head CT in the management of children without head trauma.

Title: **RETROSPECTIVE ANALYSIS OF INFECTION RELATED DEATHS OF SUDDEN UNEXPECTED DEATH IN INFANCY CASES AT SALT RIVER MORTUARY**

Presenter: Miss Sefule Anastacia Matlebjane[1] **(Supervisor:** Dr Laura Heathfield)

Affiliation: [1]Department of Pathology, University of Cape Town

Objective:
Sudden unexpected death in infancy (SUDI) remains a global public health and unfortunately, South Africa experiences high rates of SUDI cases. Infections have been previously linked to SUDI deaths, but there is a lack of empirical data in a South African context. This study aimed to explore the burden and risk factors of infection related infant death at Salt River Mortuary between the 1st of January 2017 and 31st of December 2018.

Methods:
In order to identify pathogens associated with SUDI in a local setting, medico-legal case files from the Salt River Mortuary (Cape Town, South Africa) between the 1 January 2017 and 31 December 2018 were reviewed. Included cases involved infants between 1 day and 365 days old where an infectious cause of death was suspected (n = 286). Variables pertaining to cause of death, scope of post-mortem investigation, clinical history and risk factors were collected. Microsoft Excel® and STATA version 15 were used for descriptive analysis and data visualisation.

Results:
Respiratory infections were the most common cause of death, in 73% of the cases. While infection was suspected in over 95% of the cases, ancillary investigations were conducted in only 22.7% (n = 65/286) of the cases and pathogens were found in 78% (n = 51/65) of these cases. The most common pathogens identified in these cases were Gram positive cocci, Gram positive and negative bacilli, *Staphylococcus aureus,* coagulase negative staphylococcus and cytomegalovirus. In addition, several modifiable risk factors were identified, and these included the sleeping position of the infant (side= 44.1%; prone= 23.8%), exposure to second-hand tobacco smoke (42%), as well as co-sleeping (91.6%). The majority of the infants succumbed to death while under 4 months old (62%) with 34% of these infants under 2 months old.

Conclusion:
There is a need for a nationally accepted standard protocol for the investigation of sudden unexpected deaths in infancy. This protocol will ensure a consistent approach to investigating these deaths and the information obtained could be used in the public health sector for identifying at-risk individuals and promote awareness. The risk factors identified are modifiable, therefore, an understanding of these factors on their role in sudden infant death in a local context can be used in preventive strategies**.**

This study was approved by the Human Research Ethics Committee of University of Cape Town (HREC REF: 248/2020)

Title: **PAEDIATRIC ACUTE LIVER FAILURE; A RETROSPECTIVE REVIEW FROM A SOUTH AFRICAN TERTIARY CENTRE**

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Acute liver failure describes a fatal clinical syndrome resulting from extensive loss of functional parenchymal liver mass due to severe liver damage triggered by various factors. Early recognition and initiation of specific therapy may improve outcomes and reduce the need for liver transplantation, a treatment modality not universally available in resource constraint areas. There is paucity of data describing this syndrome in Sub-Saharan Africa in children.

Objective:
This study aims to retrospectively review and determine the clinical presentation, aetiology, complications & outcome of Acute liver failure in children admitted at the Red Cross War Memorial Children's Hospital (RCWMCH).

Methods:
All records of children from 0 to 13 years admitted at the RCWMCH over the period from January 2005 to December 2016 with acute liver failure were retrospectively reviewed, after obtaining ethical approval. Patients with preexisting evidence of chronic liver disease were excluded. Demographic variables as well as clinical presentation and investigations were captured, with determination of outcomes at 3 weeks and 6 weeks of diagnosis.

Results:
Study included 24 children, age range varied from 0.2 months to 135 months (Average 25.6 months) Diarrhoea, jaundice, respiratory distress, hepatomegaly and encephalopathy were common clinical features. Aetiology was infection in 37.5 % of cases (n=9, 2 of whom had autoimmune hepatitis comorbidity) and hepatitis A was most common infectious cause (n=4, 50%). Causes were indeterminate in 29.2%. Two patients had autoimmune hepatitis without co-morbidity; Reye syndrome 12.5% and 17% had miscellaneous causes.

Conclusion:
Viral hepatitis A is the leading infective cause of acute liver failure in this study cohort and 29.2% of cases were indeterminable. INR >4 and Bilirubin > 210umol/l were predictors of poor outcome. Follow up study is recommended to better understand clinical spectrum and outcomes of children with acute liver failure in this setting.

Title: **INTERNATIONAL NORMALISED RATIO MONITORING IN CHILDREN: COMPARING THE ACCURACY OF PORTABLE POINT-OF-CARE MONITORS TO STANDARD OF CARE LABORATORY MONITORING AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL**

Presenter: Dr Ryan Moore

Affiliation: Paediatric Cardiology, Department of Paediatrics & Child Health, University of Cape Town

Background:
There is an increasing trend in the use of long-term oral anticoagulation therapy in children. Monitoring the international normalised ratio (INR) is an integral part in management of these patients, but standard laboratory testing of the INR presents challenges in this age group. Point-of-care INR monitors such as the Mission® PT/INR monitor provide advantages in efficiency and accessibility but have not been evaluated for accuracy in the South African paediatric setting.

Objectives:
This is a feasibility study with the aim to evaluate the accuracy of the Mission® PT/INR Monitor in comparison to standard laboratory INR measurement, in children presenting for INR testing.

Methods:
We compared the accuracy of the Mission® PT/INR monitor to the Sysmex Cs- 2100i laboratory analyser in 37 children aged between 1 year and 17 years, who presented for INR testing. The sample size was limited due to time constraints. 40 paired POC INR and laboratory INR values were obtained.

Results:
The majority of participants in the study were outpatients (62%) and required INR testing as part of screening in non-cardiac disease (81%) - the majority had chronic liver disease, and a minority were on warfarin therapy (13.5%). The mean INR value on the Mission® PT/INR was 1.49 (standard deviation (SD) 0.73) and was comparable to the Sysmex Cs-2100i (mean INR value 1.39 with SD 0.69). The Bland-Altman difference plot revealed good agreement. Bias between the two methods was 0.13 (SD 0.23). In total, 92.5% of POC INR values were within 0.5 units of laboratory INR value.

Conclusion:
The Mission® PT/INR point-of-care monitor has a clinically acceptable level of accuracy in children when compared with laboratory INR measurement, but larger studies are needed in the paediatric setting to evaluate patient safety and clinical outcomes. There is a need for implementing POC INR monitoring in outpatient settings but this practice will require robust assessment of infrastructure and quality control before application.

Title: **RESPIRATORY SYNCITIAL VIRUS INFECTION IN CHILDREN HOSPITALISED WITH SEVERE LOWER RESPIRATORY TRACT INFECTION AT THE RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL (2012-2013)**

Authors: Nicole Morgan[1], Heloise Buys[1,2], Stephen Korsman[3], Rudzani Muloiwa[1,4]

Affiliation: [1]Department of Paediatrics & Child Health, University of Cape Town; [2]Red Cross War Memorial Children's Hospital, Cape Town; [3]Medical Virology, Groote Schuur Hospital/National Health Laboratory Services, University of Cape Town; [4]Groote Schuur Hospital, Cape Town

Objective:
This study aimed to determine the proportion of infants and children admitted to Red Cross War Memorial Children's Hospital during one calendar year with acute lower respiratory tract infection, who were infected with Respiratory Syncitial virus (RSV). We also aimed to determine the potential risk factors for RSV in this population. These risk factors include an association of RSV infection with age, HIV status, nutritional status, underlying chronic conditions and tobacco and bio fuel exposure. We hypothesised that RSV infection is involved in a substantial number of cases of severe lower respiratory tract infection in children requiring hospitalisation.

Methods:
Children hospitalised with lower respiratory tract infections in Cape Town, South Africa were enrolled over a one year period (2012-2013) after informed consent was obtained. Existing data that was prospectively collected was used for this study. Clinical data was collected by means of a history and clinical examination of the patient. Anthropometry was assessed. All children were tested for HIV. A nasopharyngeal swab (NP) and induced sputum (IS) were taken for molecular diagnostic testing. Children were followed up until discharge from hospital.

Results:
460 children with median age 8 (IQR 4-18) months were studied of whom 258 (56.1%) were male. RSV was detected in 142 (30.8%). There were only 57 (12.4) identified on NP while IS identified 135 (29.4%) positive cases. The median of RSV positive children was 4.7 (IQR 2.6-10.3) months while the age of PCR negative ones was 10.3 (IQR 4.4-20.6) months; P<0.001.

RSV was detected in 10.5% (n=2/19) of HIV infected children, 31.8% (n=140/441) of HIV uninfected; P=0.050.

Conclusions:
RSV remains common in South African children hospitalized with LRTI and particularly affects younger children with severe LRTI. PCR on IS specimen provides confirmation with a better overall diagnostic yield.

Title: **POST CARDIAC SURGERY STERNAL WOUND SEPSIS BURDEN, RISK FACTORS AND OUTCOMES AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL, CAPE TOWN, SOUTH AFRICA: A FIVE-YEAR EXPERIENCE**

Presenter: Fefekazi Mpisane

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

Purpose:
Sternal wound infection (SWI) is associated with significant morbidity and mortality in post-operative cardiac patients. We aimed to describe the burden, risk factors and outcomes of SWI in post-operative paediatric cardiac patients at a tertiary children's hospital.

Methods:
We conducted a retrospective record review of cardiac surgeries via median sternotomy over a five-year period to identify cases of SWI.

Results:
Between 2011-16, 1319 patients underwent median sternotomy. Thirty-four (2.6%) patients developed SWI; eighteen (1.3%) patients developed deep sternal wound infection (DSWI), and sixteen (1.2%) developed superficial sternal wound infections (SSWI). Twenty-two (1.6%) of SWIs were apparent within a week post-surgery before discharge, the remaining were re-admitted post-discharge. Seven (0.5%) patients died from complications.

Conclusion:
Significant morbidity was associated with SWI. Furthermore, with a mortality rate of 20 % in the case of DSWI. We strongly support quality improvement procedures such as the Sternal Wound Prevention Bundle (SWPB) that was introduced in late 2014. However, the rate of SWI implies that ongoing monitoring and evaluation of the SWPB is necessary and more stringent adherence to the protocol may result in better outcomes.

Title: **CLINICAL PROFILE OF CHILDREN WITH AUTISM SPECTRUM DISORDER IN A DEVELOPMENTAL CLINIC IN WESTERN CAPE**

Authors: Louisa Rudo Mudawarima[1], Reneva Petersen, Kirsten A Donald

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

Objective:
To describe the clinical profile of children diagnosed with autism spectrum disorder (ASD at the Red Cross War Memorial Children's Hospital (RCWMCH) Developmental Clinic.

Methods:
We carried out a cross-sectional study of children diagnosed with an ASD in the neurodevelopmental clinic at Red Cross War Memorial Children's Hospital in the Cape Town metropolitan area in the Western Cape Province. This is one of 2 hospitals with dedicated paediatric development assessment services for the public sector in the city. The majority of clients in the neurodevelopmental clinic are of low socioeconomic status.

Participants with a diagnosis of autism spectrum disorder using DSM 5 criteria were drawn from the clinic and invited to participate in the study. A study questionnaire was administered initially, and the child was also assessed using an Autism Diagnostic Observation Schedule version 2 (ADOS-2).

Results:
A total of 32 patients were recruited into the study with 26 out of 32 (81%) being boys. The age range was 25 to 105 months with the median age being 64 months. The mean time between symptom onset and attainment of a diagnosis was 22 months.

All participants met all three of the DSM 5 social communication and interaction criteria for the diagnosis of autism spectrum disorder. For the restricted, repetitive patterns of behaviour, interests, or activities criteria, 29 participants (90%) had stereotyped or repetitive movements, 28 (88%) had insistence on sameness, 30 (94%) had restricted fixated interests and 31 (97%) had sensory hyper- or hypo-reactivity. More than half of participants (17 (53%)) required very substantial support in day to day activities.

Most participants (94%) did not experience overall developmental regression but a substantial proportion (39%) had regression of language milestones. Almost half of participants (48%) had self-injurious behaviour, 25% had some form of associated motor difficulty and 10% had comorbid epilepsy.

Most participants (81%) were administered the ADOS module 1 which is recommended for children who are either preverbal or use only single words, the remainder had phrase speech and therefore were assessed using module 2. In the group, 59% (19 participants) used either single words with very few (less than five) words used in the interaction or no words. All participants fulfilled the ADOS criteria for autism spectrum.

Conclusions:
Children who are seen in the clinic tend to represent the more severe end of the autism spectrum and a significant proportion have associated comorbidities such as epilepsy, and motor difficulty. The findings on the ADOS 2correlated well with clinical assessments.

Title: **DEVELOPMENT OF A CONTEXTUALIZED EVIDENCE-BASED PRACTICE PROTOCOL ON THE NURSE'S ROLE IN PARTNERING WITH MOTHERS TO KEEP FLUID BALANCE RECORDS FOR A HOSPITALIZED CHILD**

Authors: Adess Mwale[1,2], Busisiwe Jama[1,2], Nina Power and Natasha North

Affiliation: [1]The Harry Crossley Children's Nursing Development Unit, Department of Paediatrics and Child Health, University of Cape Town; [2]Division of Nursing & Midwifery, Department of Health and Rehabilitation Sciences, University of Cape Town

Aim:
To create an evidence-based protocol that shows how nurses can partner with mothers in monitoring and recording fluid balance records of hospitalized children in a lower-resourced hospital setting, in order to improve patient care.

Objectives:
To identify existing protocols and guidelines from higher-resourced settings and follow a rigorous and transparent process of adaptation and contextualisation to produce a high-quality protocol suited to implementation in paediatric wards in Zambia and South Africa. To ensure that the resulting protocol explicitly recognised that mothers/caregivers accompanying a child in hospital in African settings are often expected to play an active role in taking care of their hospitalised child including taking note of the child's fluid intake and output.

Methods:
We conducted a structured and replicable search of bibliographic databases for guidelines relevant to the topic using Mesh terms and keywords. This was supplemented by consultation including with international expert nurse practitioners. Initial screening of identified guidelines was conducted using Domains 1 and 3 of the AGREE II tool. Included guidelines were then fully appraised using all 6 domains of the AGREE II tool. The process of guidelines adaptation and modification followed the approach recommended by the MRC South African Guidelines Excellence Project (SAGE).

Results:
Bibliographic databases searching and consultation identified three guidelines which were appraised for: relevant scope and purpose; extent of stakeholder involvement; rigour of development; presentation; applicability and relevance; and editorial independence by the two researchers plus a third colleague. After screening, two guidelines were included: The Royal Marsden Manual of Clinical Nursing Procedures: Nutrition, fluid balance and blood transfusion (West-Oram, Lister & Dougherty, 2015) and Assessing and documenting fluid balance procedures: Central Manchester University Hospitals NHS Foundation Trust (Pinnington, Ingleby, Hanumapura & Waring, 2016). A third guideline was appraised: Intravenous Fluid Therapy in Children and Young People in Hospital. NG29. (National Institute of Clinical Excellence (NICE), 2015) but was excluded as it scored low on relevance and applicability. Both the included guidelines were specific to higher-resourced settings in the UK and did not deal with the role of mothers/caregivers so a need to adapt them was identified. The main areas for adaptation and contextualisation involved improving communication between nurses and mothers, developing or identifying simple tools and figures to illustrate what information mothers should record recognising that in our settings many mothers have literacy challenges, and processes to support nurses in teaching mothers to use the chart. An assessment of competence was developed to ensure that mothers are safe to record what the patient is drinking and passing out. A flow chart was developed to highlight key steps in the process. Expert consultation ensured that the resulting protocol was clinically sound, of high quality and was understandable and well presented.

Conclusion:
The process resulted in a contextually-relevant adapted protocol to assist nurses in partnering with mothers in monitoring and recording fluid balance records of hospitalized children in a lower-resourced hospital setting, in order to improve patient care. Nurses have the overall responsibility to teach mothers how to monitor intake and output. The nurse should use the information provided by the mother to maintain an accurate fluid balance record for the patient so that they can be able to calculate the total intake and output at the end of the 24hour shift. It is our hope that this will improve the quality of record keeping for fluid balance records thus inform clinical decision making, help to prevent dehydration and fluid overload in hospital, and improve patient care and communication between nurses, mothers and the wider healthcare team. This is new research. No ethical approval was required.

Statement of contributions: AM and BJ undertook all aspects of the work together in accordance with UCT's guidance on collaborative and group work, supervised by Natasha North and Nina Power. Andrea Amos, Elijeshca Crous and Nadia Harris assisted with co-appraisal of guidelines. This is a joint presentation of work produced in accordance with UCT's policy on assessment of collaborative and group work.

Title: **PREVALENCE AND CORRELATES OF VITAMIN D DEFICIENCY AMONG SOUTH AFRICAN INFANTS – A BIRTH COHORT STUDY**

Authors: Jabulani Ncayiyana[a], Leonardo Martinez[b], Elizabeth Goddard[c], Heather Zar[c], Landon Myer[a]

Affiliation: [a]Division of Epidemiology and Biostatistics, School of Public Health and Family Medicine, University of Cape Town, Cape Town, South Africa; [b]Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine, Stanford, CA, USA; [c]Department of Paediatrics and Child Health, Red Cross War Memorial Children's Hospital and MRC Unit on Child and Adolescent Health, University of Cape Town, Cape Town, South Africa

Objective:
Early-life vitamin D deficiency (VDD) is associated with adverse child health outcomes, but the prevalence of VDD and its correlates in infants remains underexplored, particularly in sub-Saharan Africa.

Methods:
As part of the Drakenstein Child Health Study, a population-based prospective birth cohort in two peri-urban sites near Cape Town, South Africa, we measured serum 25(OH)D concentrations (nmol/L) in 744 infants ages 6-10 weeks. Using a Tobit regression models, we examined the correlates of serum $25(OH)D_3$ levels.

Results:
The overall prevalence of VDD in infants was 81% (95% CI:78%-83%); boys had significantly lower serum $25(OH)D_3$ concentrations than girls (median (IQR) 35 (23-46) vs 40 (28-50), p=0.002). Multivariate analysis showed that serum $25(OH)D_3$ concentration was independently associated with site, season of birth, socioeconomic status (SES), age, sex, and feeding practices. Birth in winter and exclusive breastfeeding were the strongest predictors of lower serum $25(OH)D_3$ concentration levels.

Conclusions:
VDD in infants is very common in this setting, under-recognised and strongly associated with infant feeding practices or birth season. Nutritional interventions to improve early life vitamin D status in infants are urgently needed.

Title: **CLINICAL OUTCOMES AND HEALTHCARE COSTS ASSOCIATED WITH HEPATITIS A IN CAPE TOWN, SOUTH AFRICA**

Authors: Jenna Patterson[1], Susan Cleary, Gregory D. Hussey, Annabel Enoch, Stephen Korsman, Liz Goddard, Mashiko Setshedi, C. Wendy Spearman, Benjamin M. Kagina, Rudzani Muloiwa

Affiliation: [1]Department of Epidemiology, School of Public Health & Family Medicine, University of Cape Town

Objectives:
In order to generate evidence for the consideration of the inclusion of hepatitis A into the South African Expanded Programme on Immunisation (EPI), the primary objective of this study was to assess the clinical severity and outcomes of hepatitis A cases presenting to Groote Schuur Hospital (GSH) and Red Cross War Memorial Children's Hospital (RCWMCH). Secondly, the study aimed to estimate the average cost per hepatitis A case managed at these tertiary healthcare centers.

Methods:
We conducted a retrospective folder review of acute hepatitis A cases that presented to GSH and RXCH between 2008-2018. All hepatitis A samples received from GSH and RCWMCH were identified with the help of the National Health Laboratory Services. The most recent cases were selected for inclusion beginning 1 January 2018 until the desired sample size of 250 adult folders (GSH) and 250 child folders (RCWMCH) was fulfilled. Data including demographics, clinical presentation, and case management/treatment were extracted from the folders. Hepatitis A treatment was costed using a combination of ingredients and step-down methods.

Results:
A total of 451 folders (GSH=212; RCWMCH=239) were included in the study. Thirty-eight folders were dropped from GSH and 11 folders were dropped from RCWMCH due to duplications or missing hepatitis A notes. The mean ages of patients were 7 years old at RCWMCH and 30 years old at GSH. Of the adult patients at GSH, 29 (13.68%) developed complicated hepatitis A and three died during treatment (1.41%). Of the paediatric patients at RCWMCH, 27 (11.03%) developed complicated hepatitis A and one died during treatment (0.42%). A majority of patients presenting to either facility (GSH = 79.72%; RCWMCH = 81.17%) were on H1 accounts. Hepatitis A patients included in this study stayed an average 7.45 days at GSH and an average 3.11 days at RCWMCH. The cost per day for hepatitis A hospitalization at GSH was ZAR 4,124.39 and ZAR 6,259.16 at RCWMCH.

Conclusion:
Contrary to previous belief, children in this study did not experience more mild hepatitis A as compared to adults in the study. Given the severity of childhood hepatitis A and the health system cost of treatment, hepatitis A immunisation should be considered further for introduction into the South African EPI.

Ethical approval: This study has been approved by the University of Cape Human Research Ethics Committee and relevant committees at GSH and RCWMCH. As this is a retrospective study, patient care or management was not affected. Findings will be disseminated through publication in a peer-reviewed journal.

Title: **OUTCOMES FOLLOWING ADMISSION TO PAEDIATRIC INTENSIVE CARE: A SYSTEMIC REVIEW**

Authors: Claire Procter[1], Brenda Morrow[2], Genee Pienaar[3], Mary Shelton[4], Andrew Argent[1]

Affiliation: [1]PICU, Red Cross War Memorial Children's Hospital, Cape Town, South Africa

Introduction:
Paediatric Intensive Care has developed rapidly in recent years with a dramatic increase in survival rates. However, there are increasing concerns regarding the impact that admission to a Paediatric Intensive Care Unit (PICU) has on both the child and their family. Following discharge from intensive care, children may be living with complex medical problems as well as dealing with the psychosocial impact that their illness has had on them and their family.

Objectives:
To describe the long-term health outcomes of children admitted to a paediatric intensive care unit.

Methods:
A full literature search was conducted including the databases; MEDLINE via PubMed, Cochrane Central Register of Controlled Trials, (CENTRAL), Scopus, Web of Science, CINAHL, ERIC, Health Source Nursing/Academic, APA PsycInfo. All studies including children under 18 admitted to a paediatric intensive care unit were included. Primary outcome was short- and longer-term mortality. Secondary outcomes were neurodevelopment/cognition/school performance; physical function, psychological function/behaviour impact, quality of life outcomes and social/family implications. Studies focused on Neonatal Intensive Care Admission and articles with no English translation were excluded.

Results:
One hundred and five articles were included in the analysis. Mortality in PICU ranged from 1.3% to 50%. Mortality in high income countries reduced over time but the data did not show the same trend for low- and middle-income countries. Higher income countries were found to have lower Standardised Mortality Rates than low- and middle-income countries. Children had an ongoing risk of death for up to 10 years following intensive care admission. Children admitted to PICU also have more ongoing morbidity than their healthy counterparts with more cognitive/developmental problems, more functional health issues, poorer quality of life as well as increased psychological problems. Their parents also have an increased risk of Post Traumatic Stress Disorder.

Discussion:
Most of the studies identified are from high income countries and only include short-term follow up. More data is needed from low- and middle-income countries and over longer terms. The studies were markedly heterogenous and were all observational. Agreement is needed regarding which outcomes are most important to measure as well as standardised methods of assessing them. Further research is needed to identify the risk factors which cause children to have poorer outcomes as well as to identify predictive and modifiable factors which could be targeted in practice improvement initiatives.

Ethics committee number: 123/2018 - Ethics approval not required.

The initial findings of this research were presented at the 2019 research day (mortality data only) - the study has now been completed and the remaining results will be presented.

Title: **CHILDREN WITH LENNOX-GASTAUT SYNDROME IN THE WESTERN CAPE OF SOUTH AFRICA**

Authors: Robert Sebunya [1,2,3], Richard J Burman [1,2,4], Helishia Dirks [2], Jo M Wilmshurst [1,2]

Affiliation: [1]Paediatric Neurology, Red Cross War Memorial Children 'Hospital, Neuroscience Institute, University of Cape Town, South Africa; [2]Paediatric Neurophysiology Department, Red Cross War Memorial Children`s Hospital, Cape Town South Africa; [3]St. Francis Hospital Nsambya Department of Paediatrics and child Health, Kampala, Uganda**;** [4]Nuffield Department of Clinical Neurosciences, University of Oxford, UK

Introduction:
Lennox-Gastaut Syndrome (LGS) is one of the most common refractory epilepsies of childhood. This developmental and epileptic encephalopathy is associated with a significant morbidity and mortality and typically leads to poor quality of life (QOL) of the affected children. There is paucity of data of this syndrome in resource limited settings (RLS).

Objective:
To delineate the phenomenology, diagnosis, management and outcomes of children diagnosed as LGS in the Western Cape Province of South Africa.

Methods:
This retrospective observational cohort included all children between 1 to < 18 years of age in the neurology database with an entry point diagnosis of LGS between 2000-2018. The group were critiqued for those who met the diagnostic criteria of LGS namely (1) multiple seizure types to include, tonic, atonic and atypical absence and (2) SSW complex at < 3Hz, paroxysmal fast rhythm of >10Hz plus or minus cognitive impairment. The group were categorized into those with confirmed LGS and remainder were non- LGS. Data of the social demographics, age of seizure onset, aetiology, preceeding history of epileptic spasms, and semiology of epilepsy types, management interventions and outcome were reviewed to identify key diagnostic indicators to permit early and targeted interventions for children with this epilepsy syndrome.

Results:
Of 2551 children managed with epilepsy in the neurology service, 110 children were suspected at presentation to have LGS of these 83 children records were available for assessment**.** 58(70%) met the criteria LGS and 25(30%) as non-LGS. Patients who present in infancy (*OR* 5.31, $p = 0.01$) and with epileptic spasms (*OR* 14.57, $p = 0.02$) are more likely to be diagnosed with LGS. In addition, underlying structural aetiology, current level of cognitive impairment and seizure control are also significantly associated with LGS diagnosis. Notably, patients with structural abnormalities are more likely to lead to a diagnosis of LGS (*OR* 3.8, $p = 0.01$). Further patients with moderate or severe cognitive impairment are more likely to be associated with a diagnosis of LGS (*OR* 20.91, $p = 0.006$ and *OR* = 46.10, $p = 0.001$). Lastly, patients in the LGS group are more likely to have intractable seizures (*OR* = 4.38, $p = 0.004$). The most common diagnosis in the non-LGS group was Myoclonic atonic epilepsy 48% (MAE).

Conclusion:
A third of the children in this cohort were erroneously diagnosed with LGS early in their course. This has implications on their management and prognostic counselling. Reports from other centres support the challenges of differentiating between LGS and MAE especially. Identifying the indicators of early seizure onset especially epileptic spasms, structural brain pathology, moderate or severe intellectual/cognitive impairment and pharmacoresistant seizures are useful early markers which support a diagnosis of LGS and are viable for use in our setting.

Title: **DIFFERENTIAL COUNTS AS PREDICTORS OF MORTALITY IN CHILDREN WITH *KLEBSIELLA PNEUMONIAE* BLOODSTREAM INFECTION, AT RED CROSS WAR MEMORIAL CHILDREN'S HOSPITAL**

Authors: Johanna T Shapaka [1,2], Rudzani Muloiwa[1,3], Heloise Buys [1,2]

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

Objectives: Gram-negative bloodstream infection (BSI) caused by *Klebsiella pneumoniae* (*KP*), is among the leading causes of hospital-associated childhood mortality globally. Malnutrition and HIV co-infections are significant risk factors for acquiring *KP*BSI, however there is limited data on how *KPBSI* influence the various haematological cell lines in HIV-infected compared to HIV-uninfected children. This study aims to describe the profile of differential counts from full blood counts (FBC) taken at two time points in children younger than 13 years with *KP*BSI at the Red Cross War Memorial Children's Hospital (RCWMCH).

Methods: We conducted a retrospective study from the database of a previously published mother study that described KPBSI in children admitted to RCWMCH between January 2006 and December 2011 with KPBSI. FBC collected over two defined time-point: within 48 hours of blood culture and after 72 hours were reviewed. Differential counts were classified as abnormal if they were higher or lower than laboratory ranges for normal results. The risk of death was assessed for each category of abnormal differential counts. Risk ratios adjusted (aRR) for potential confounders were used to estimate the effect of abnormal cell counts on risk of death using multivariable analysis.

Results: Of the 299 children who were included, 82 were HIV positive and 152 (51%) were female. The median age was 5 months (IQR 1.6-15.6) while, 192 (64%) were moderately or severely underweight-for-age. A total of 95 (32%) of the children died. There were 39 (48%) of 82 HIV-positive children who died compared to 56/217 (26%) in the HIV negative group; *p-value <0.001*.

Table: Adjusted and unadjusted risk ratios for mortality with early and late differential counts

Period	Risk factor	Risk n/N (%)	RR (95% Confidence Interval) Crude	Adjusted*
Early	Absolute bands high	188/240 (78)	0.92 (0.63-1.33)	0.86 (0.57-1.27)
	Band % high	148/240 (62)	1.02(0.74-1.40)	0.87(0.62-1.24)
Late	Absolute bands high	81/128 (63)	1.80 (0.80-4.06)	1.82 (0.85-3.89)
	Band % high	48/127 (38)	2.25 (1.38-3.66)	2.06 (1.23-3.47)
Early	Neutrophilia	61/240 (25)	1.17(0.79-1.73)	1.34 (0.88-2.06)
	Neuropenia	55/240 (23)	1.51 (1.06-2.16)	1.53 (1.02-2.30)
Late	Neutrophilia	28/128 (22)	2.18 (1.26-3.77)	3.36 (1.78-6.35)
	Neutropenia	25/128 (20)	2.12 (1.19-3.80)	2.34 (1.26-4.36)
Early	Thrombocytosis	35/290 (12)	0.65 (.026-1.61)	0.92 (0.36-2.34)
	Thrombocytopenia	166/290 (57)	2.11 (1.37-3.24)	2.29 (1.42-3.67)
Late	Thrombocytosis	31/175 (18)	0.55 (0.16-1.88)	0.84 (0.24-2.93)
	Thrombocytopenia	89/175 (51)	2.40 (1.29-4.44)	2.75 (1.38-5.50)

Conclusion: Abnormal absolute neutrophil counts, high bands and thrombocytopenia are associated with significant mortality in children with *KP*BSI even after adjusting for potential confounders. In resource-limited countries where blood cultures cannot be done readily, these haematological markers could be used to predict *KP*BSI.

Title: **AN EXPLORATION OF DISCLOSURE AND NON-DISCLOSURE PATTERNS IN HIV-INFECTED CHILDREN IN CAPE TOWN, SOUTH AFRICA**

Authors: Robert Shea[1], Rudzani Muloiwa[2]

Affiliation: [1]MCH graduate; [2]Department of Paediatrics & Child Health, Groote Schuur Hospital, University of Cape Town, South Africa

Introduction:
Improved survival and health outcomes in HIV infected children has drawn attention to the psychosocial challenges related to growing up with a chronic, potentially life-threatening, stigmatised illness. As HIV infected children transition into adolescence, they must negotiate issues of disclosure and stigma. Improved access to antiretroviral medication and the associated positive health outcomes and survival makes HIV disclosure to children and adolescents an important aspect of HIV management.

Methods:
We conducted a mixed methods study to explore disclosure experiences of mothers and caregivers of HIV-infected children. The study involved a quantitative cross-sectional, descriptive design combined with open-ended (qualitative) interview questions.

Results:
The study enrolled 102 parents and caregivers at a tertiary hospital in Cape Town delivering care to 303 HIV-infected paediatric patients. The study sample included 102 caregivers, ranging in age from 16 years to 71 years. Caregivers included 73 mothers (72%), six fathers (6%), 11 foster-mothers (11%), and 12 caregivers or grandmothers (12%). The median age of the participants' children was 4 (IQR 2-8) years and ranged from five months to 16 years. Only 48 (47%) were old enough for disclosure to be possible. Only 16 (33%) of 48 participant caregivers actually disclosed the child's HIV status.

Disclosure or disclosure delay was associated with the child's age and ability to understand. Anxiety and guilt about being blamed for infecting the child, fear of exposing the child to stigma, discrimination and social exclusion related to the child 'accidentally' disclosing to others led to outright avoidance or delay in disclosure. On the other hand, the hope that the child would be adherent if they understood their illness and the way in which the medication could improve their health outcomes encouraged disclosure to the child.

Conclusions:
The results indicate that HIV-disclosure remains a challenging, emotionally-charged experience for mothers and caregivers. The findings of this research, and similar studies, point to the value of integrating disclosure support and planning into routine care for children and adolescents, as well as their parents and caregivers.

Title: **IDENTIFYING CHILDREN WITH CONSTITUTIONAL MISMATCH REPAIR DEFICIENCY (CMMR-D) SYNDROME IN THE EXPANDING LYNCH SYNDROME POPULATION IN CAPE TOWN**

Authors: Dr Sindy Jen-Yi Tu, Prof Komala Pillay (supervisor), Prof Raj Ramesar (co-supervisor) and Dr Annesu Wessels (co-supervisor)

Affiliation: Division of Anatomical Pathology. Department of Pathology. University of Cape Town. National Health Laboratories Services. Red Cross Children's Hospital and Groote Schuur Hospital

Introduction:
Constitutional Mismatch Repair Deficiency (CMMR-D) syndrome is a rare tumour predisposition and polyposis syndrome that presents in childhood. It is caused by mutations in mismatch repair (MMR) genes that result in a tumour spectrum including colorectal cancers, high-grade gliomas, non-Hodgkin T-cell lymphomas and leukaemias. It is characterized by biallelic germline mutation of one of four MMR genes resulting in loss of protein expression that can be identified by MMR immunohistochemistry (IHC). Use of MMR IHC is established in the setting of Lynch syndrome (LS); however, the pattern of loss of staining in the background, non-tumour tissue is unique to CMMR-D syndrome. CMMR-D syndrome occurs in LS families as a result of consanguinity or founder effect. The South African LS families are concentrated in the Western Cape and Northern Cape Provinces and the mixed ancestry population shows a unique *MLH1* c1528C>T mutation which may have implications on the incidence, penetrance and severity of CMMR-D syndrome seen in our population. The diagnosis of CMMR-D syndrome includes clinical findings outlined in the European Consortium's Care of CMMRD document and confirmation of the biallelic mutation in one of the MMR genes. MMR IHC can be used in the diagnosis of CMMR-D syndrome; however, MMR immunohistochemical staining patterns are not usually described in detail, the key feature of CMMR-D syndrome.

Methods:
We performed a retrospective analysis of archival formalin fixed paraffin embedded tissue of children attending Red Cross Children's Hospital with tumours that form part of the CMMR-D spectrum, outlined by the Care for CMMRD criteria. We used the criteria of high-grade gliomas (WHO Grade III or IV) occurring before 25 years of age, cutaneous lesions suggestive of CMMR-D syndrome and patients with a first or second degree relative diagnosed with LS. MMR IHC was applied, and the staining pattern was documented in terms of proportion of tumour staining and intensity of staining using a modified Allred Scoring system. Specific attention was given to the characterization of the staining pattern of the background normal tissue.

Results:
21 samples taken from 18 patients were evaluated. 16 samples represented high-grade gliomas. Three samples were excluded due to suboptimal staining despite positive external controls. 12 samples showed intact staining of all four MMR stains. Two samples showed staining of unknown significance. Four samples showed staining patterns compatible with MMR deficiency. This included two patients, each with a biopsy showing high-grade glioma and two samples of the same patient taken at a 1-year interval of a Burkitt lymphoma. Of these four samples, three samples showed loss of staining in background non-tumour tissue with positive external control, the unique staining pattern for CMMR-D syndrome. These cases will be referred for confirmatory testing by molecular genetic techniques.

Conclusion:
MMR IHC can be used in the evaluation of CMMR-D syndrome, but care is needed in evaluating adequacy of staining, the pattern and scoring of staining of both the tumour and the background non-tumour tissue. Endothelial cells, neurons and choroid plexus can be evaluated as background tissue in brain tumour samples. Selection bias resulted in underrepresentation of lymphomas and colorectal carcinomas. Use of MMR IHC in post-mortem samples is not recommended, even with a short post-mortem interval of 1 day. The diagnosis of CMMR-D syndrome depends on clinical application of Care for CMMRD criteria, MMR IHC in conjunction with molecular genetic testing. It is important to identify cases of CMMR-D syndrome and offer cancer screening to prevent development of other cancers in the index patient. It also provides an opportunity for genetic counselling and testing of the parents and at-risk siblings.

Title: **A RETROSPECTIVE INVESTIGATION OF SUDDEN UNEXPECTED DEATH IN CHILDREN INVESTIGATED AT SALT RIVER MORTUARY, CAPE TOWN**

Authors: Yuvika Vandayar[1], Laura Jane Heathfield

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Objective:
Sudden unexpected death in children (SUDC) is the tragic fatality of seemingly healthy individuals aged between one and 18 years. Little is known about the demographics and risk factors of these cases at Salt River Mortuary, Cape Town. The objective was to retrospectively investigate the burden and profile of SUDC cases admitted to Salt River Mortuary, between 1 January 2016 and 31 December 2018.

Methods:
A quantitative, retrospective and cross-sectional investigation of SUDC admitted to SRM for the stipulated period. Medico-legal cases folders were retrieved from the Salt River Mortuary archives and all SUDC cases were included. The variables collected from these documents included demographics, circumstances surrounding death, social and clinical history, post-mortem details and cause of death. Descriptive statistics and inferential statistics were performed using STATA and GraphPad Prism.

Results:
Of the total 11 588 cases admitted over this period, 117 were SUDC cases, wherein males comprised the majority (55.6 %). Individuals were a median age of 3 ± 5.7 years at death and there were no significant differences between age or sex when comparing position, location and activity at death. Risk factors included maternal level of education, annual household income, substance abuse, and co-morbidities with concomitant use of chronic medication. More than a quarter of individuals experienced vomiting (43.0 %) and breathlessness/chest pain (30.0 %) prior to death. Of cases with a confirmed natural cause of death, the main organ systems involved were pulmonary, gastrointestinal and central nervous system which parallels international trends. Akin to local studies, in analogous amounts, pneumonia and respiratory tract infections were the leading causes of death. Additionally, 24.8 % of cases were identified as candidates for genetic testing which may resolve undetermined cases or elucidate underlying predisposing factors to sudden death. Fortunately, 93.1 % of candidate cases have biological samples available for these retrospective analyses.

Conclusions:
Cases often had missing documentation which advocates for training to ensure compliance to standardised procedures. Nevertheless, this study shows that males aged 3 ± 5.7 years with pulmonary and gastro-intestinal symptoms or signs of illness are the most vulnerable for SUDC. Awareness interventions targeted at this population are thus needed in an attempt to reduce these tragic fatalities.

Ethics approval number: HREC 171/2020
This is new research (07/09/2020)